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Medication Reconciliation during Admission at University Hospital

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Abstract

Introduction: Medication reconciliation is the process of comparing the most accurate list of all medications that a patient is taking with the list of prescription drugs within the healthcare system while considering the patient's allergies and history of side effects.

Objectives: To reconcile medication upon the patients' admission to a university hospital in the municipality of Campo Grande, Mato Grosso do Sul, Brazil.

Method: A prospective, cross-sectional study was conducted between June 2018 and May 2019 at the medical clinic unit of an university hospital. Discrepancies observed between the prescription and the best possible medication history were classified as intentional discrepancy; undocumented intentional; and unintentional.

Results: A total of 1,134 discrepancies were found between home-based drugs and those prescribed upon admission to the MCU. Among the discrepancies, 815 (72%) were intentional, 89 (8%) were undocumented intentional, and 230 (20%) were unintentional. The number of consultation sources and the number of medicines in use at home showed significant correlation with the occurrence of unintentional discrepancies ($p = 0.039$ and $p = 0.008$, respectively). A total of 318 pharmaceutical interventions were performed, 230 related to unintended discrepancies. Of these, 138 (60%) interventions were not accepted.

Conclusion: The study verified the high frequency of drug omission, conferring treatment interruption and the need for pharmaceutical assistance of polymedicated patients.

Keywords: medication reconciliation, medication errors, patient safety, clinical pharmacy service

1. Introduction

Medication reconciliation is the process of comparing the most accurate list of all medications that a patient is taking with the list of prescription drugs within the healthcare system while considering the patient's allergies and history of side effects. The objective of this process is to provide the correct medications to the patient at all points within the healthcare system, resulting in a reduction in medication errors. (Penm, Vaillancourt, & Pouliot, 2019; The Joint Commission, 2017).

In 2017, the World Health Organization (WHO) launched its third global safety challenge, called "Medication Without Harm," aimed at reducing serious and preventable drug-related harm worldwide by 50%. Damage caused by medication errors accounts for at least one death every day and harms approximately 1.3 million people annually in the USA alone. Worldwide, the annual cost associated with medication errors has been estimated at $42 billion, or nearly 1% of the total global health expenditure (World Health Organization, 2017).

One of the strategies developed to reduce medication errors is the practice of medication reconciliation, which is designed to overcome challenges in the communication of medication information, reduce medication waste, and limit the number of hospital readmissions (Mekonnen, McLachlan, & Brien, 2016; Shekelle, et al., 2013; Wang,

Fogerty, & Horwitz, 2017).

In the USA, medication reconciliation is a routine process that has been undertaken since 2003, when The Joint Commission accredited the practice to improve patient safety. Since 2006, the process has been implemented, organized, and standardized, becoming a mandatory requirement in health facilities that are accredited by the organization (The Joint Commission, 2019).

Establishing a patient's best possible medication history (BPMH) at the time of hospital admission is an important step in the search for the safety of hospitalized patients, as it contributes to the design of the drug regimen prescribed during hospitalization. Although there are national studies describing the medication reconciliation process at the hospital admission stage, publications of this clinical practice in university hospitals are incipient (Mazhar, Akram, Al-Osaimi, & Haider, 2017; Lindenmeyer, Goulart, & Hegele, 2013; Lombardi et al., 2016; Spalla & Castilho, 2016). Therefore, investigations on medications added, altered, or interrupted in the transition between healthcare levels are necessary to improve patient safety strategies and prevent a repeat of the medication errors occurring in the Brazil scenario discussed below. Considering this, the objective of this study was to reconcile medication upon the patients' admission to a university hospital in the municipality of Campo Grande, Mato Grosso do Sul, Brazil.

2. Materials and Methods

2.1 Outline and Duration of the Study

A prospective, cross-sectional study was conducted between June 2018 and May 2019 in accordance with STROBE (Strengthening the Reporting of Observational Studies in Epidemiology) guidelines.

Institutional review board approval from the Federal University of Mato Grosso do Sul was obtained on April 4, 2018 (opinion nº 2.580.775) prior to initiation of the study.

2.2 Place of Study

This study was conducted at the medical clinic unit (MCU) of the Maria Aparecida Pedrossian University Hospital (HUMAP), in Campo Grande, Mato Grosso do Sul, Brazil, which was inaugurated and became a federal institution within the states of Mato Grosso and Mato Grosso do Sul in 1971.

The hospital area consists of specialist outpatient clinics, a surgical center, an obstetric center, adult and pediatric, neonatal, a coronary unit, emergency medical care, diagnostic imaging, radiology services, breast milk bank, hemodialysis (with medical residency in 22 specialties), residency in dentistry, and multiprofessional residency in critically ill patients.

HUMAP has 232 beds and is a reference in the state of Mato Grosso do Sul for infectious diseases and complex procedures, such as cardiovascular surgery, hemodialysis, and neurology, in addition to high-risk pregnancy, tomography, and lithotripsy.

The ward in the hospital's MCU provides full care of individuals over 12 years of age (male and female) who are hemodynamically stable and who has not undergone surgical treatment. In this unit, all prescriptions are electronic, and specialties include nephrology, neurology, cardiology, endocrinology, gastroenterology, pneumology, rheumatology, hematology, and vascular. It focuses on cases of medium complexity and has 30 beds. Patients undergo clinical treatment with varying lengths of hospitalization, depending on the cause.

2.3 Inclusion and Exclusion Criteria

Patients were invited to participate in this study of adults (18 years of age and older) who were transferring from the emergency medical care to the HUMAP MCU and were approached within 24 h of admission. All study procedures were conducted only after the patient had signed the informed consent form.

Patients who were transferred to another hospital unit without approached within 24 h of admission to the MCU were excluded from the study, as well as unaccompanied patients with lowered levels of consciousness and patients who were not using medication at home.

2.4 Interview and Registration of Data

To prepare the BPMH of the patient, two instruments were used. The first was the Guide to Developing the Best Possible History of Medicines, adapted from the Canadian Patient Safety Institute (Gleason et al., 2004). The second was the Admission Drug Reconciliation Form (ADRF), (Giménez Manzorro et al., 2011; Contreras Rey, Arco Prados, & Sánchez Gómez, 2016; Rose, Fischer, & Paasche-Orlow, 2017).

The BPMH assisted in the conduct of research, avoiding process deviations. The guide was used in the

interviews with patients and caregivers, and the questions it contained were related to home-based drugs. For the composition of the BPMH, a review was carried out on the patients' medical records and the medicines and prescriptions that the patients brought with them from home.

All data collected during the research were recorded in the ADRF, which was constructed for this study and was based on medication reconciliation surveys conducted in other countries.

The collected data of the medications were trade and generic name, dosage, route of administration, treatment time, and allergies. Medicinal plants and dietary supplements used as treatments were analyzed and noted by the attending physician during the pharmaceutical interventions. Regarding the origin of home-based drugs, they were categorized as prescription drugs and non-prescription drugs (self-medication). The class of drugs was categorized according to the Anatomical Therapeutic Chemical (ATC) classification system recommended by the WHO (World Health Organization, 2019).

2.5 The Medication Reconciliation

After obtaining all available information from various available sources (interview with patient, interview with companion, packaging of medicines brought from home, prescriptions, and medical records) regarding patient's home-based drug, the BPMH was compared with the patient's medication prescription upon admission to the MCU.

Discrepancies observed between the prescription and BPMH were classified as follows: (1) intentional discrepancy (wherein the difference was documented); (2) undocumented intentional (when there was a difference, but there was nothing in writing to justify it); and (3) unintentional (when there was a difference, there was no documentation, and the doctor confirmed that he/she was unaware of the discrepancy), (Vira, Colquhoun, & Etchells, 2006).

According to Almanasreh, Moles, & Chen (2020) the phases of the medication reconciliation process are as follows: (1) rearrangement of the medication lists into the same order; (2) identification of the reference list or the best possible medication list; (3) matching/reconciliation of the two medication lists (our assumption is that one of the lists should be the best possible medication list (reference list), and the other is a list of newly prescribed medications); (4) marking of any identical medications to simplify the process of identifying medication discrepancies; (5) classification of any mismatched medications (solo drug in any list) based on the first part of the taxonomy (drug mismatched); and (6) analysis of any partially matched (matched but not identical) medications for the presence of medication discrepancies based on a logical order, starting from the name and ending with the time of administration, and classification of any identified medication discrepancies using the second part of the taxonomy (drug partially matched). After classification, the need for pharmaceutical intervention was evaluated. Discrepancies confirmed by doctors as unintentional were considered medication errors.

Medication errors (unintentional discrepancies) were classified according to the medication discrepancy taxonomy (MedTax), (Almanasreh et al., 2020) as follows:

1. Drug mismatched

1.1. Drug omission

1.2. Drug commission (or addition)

1.3. Drug duplication

1.4. Therapeutic class substitution (medication change within a medication class)

1.5. Allergy or intolerance

1.6. Other

2. Drug partially matched

2.1. Discrepancy in the name of drug

2.1.1. Unclear or wrong name (brand name or generic name)

2.1.2. Omission of brand name

2.1.3. Omission of generic name

2.1.4. Different brand name but same generic name

2.2. Discrepancy in the strength and/or frequency and/or number of units of dosage form and/or total daily dose

2.2.1. Unclear or wrong strength

2.2.2. Omission of strength

2.2.3. Different strength and different total daily dose

2.2.4. Different strength but same total daily dose

2.2.5. Omission of unit of strength

2.2.6. Different or wrong unit of strength

2.2.7. Same strength but unclear/or wrong frequency

2.2.8. Same strength but omission of frequency

2.2.9. Same strength but different frequency and omission of the number of units

2.2.10. Same strength and same frequency but omission of the number of units

2.2.11. Same strength and same number of units but different frequency and different total daily dose

2.2.12. Same strength but different frequency and different number of units and different total daily dose

2.2.13. Same strength but different frequency and different number of units but same total daily dose

2.2.14. Same strength and same frequency but different number of units and different total daily dose

2.3. Discrepancy in the dosage form/route of administration

2.3.1. Unclear or wrong dosage form

2.3.2. Unclear or wrong route of administration

2.3.3. Omission of dosage form

2.3.4. Omission of route of administration

2.3.5. Different dosage form but same route of administration

2.3.6. Different dosage form and different route of administration

2.3.7. Same dosage form but different route of administration

2.4. Discrepancy in the time of drug administration

2.4.1. Omission of the time of administration

2.4.2. Different time of administration through the day

2.4.3. Discrepancy in the drug administration with respect to food/meal

2.5. Discrepancy in the duration or length of therapy

2.6. Other

During the interview with the patient and/or his/her companion, demographic data were investigated, and data regarding hospitalization (date of admission, comorbidities, diagnosis resulting from admission, medical specialty, date of departure, and mode of departure) were collected from the patient's medical records.

2.6 Pharmaceutical Interventions

In cases where unintentional discrepancies occurred, interventions were proposed to the prescriber. The pharmaceutical interventions were discussed verbally with the prescribing physicians (residents or tutors), and when the physicians were not present physically, they were contacted by telephone. Both interventions and outcomes (acceptance or nonacceptance) were classified according to the Pharmaceutical Care Network Europe (PCNE) 2019.

PLANNING OF INTERVENTIONS

1. At the prescribing level

   Prescribed only

   Prescriber asked for information

   Proposed intervention to prescriber

   Intervention discussed with prescriber

2. At the patient level

Drug-related advice

Information provided in writing (only)

Patient referred to prescriber

Dialogue with family member / caregiver / caregiver

3. At the drug level

Medicine changed to ....

Posology changed to….

Formulation changed to… ..

Instructions for use changed to… ..

Medication discontinued

New medicine started

4. Other intervention or activity

Other intervention (please specify)

Side effect reported to authorities

ACCEPTANCE OF THE PROPOSED INTERVENTIONS

1. Intervention accepted (by doctor or patient)

Intervention accepted and fully implemented

Intervention accepted, partially implemented

Intervention accepted but not implemented

Intervention accepted, implementation unknown

2. Intervention not accepted (by doctor or patient)

Intervention not accepted: not feasible

Intervention not accepted: no agreement

Intervention not accepted: other reason (please specify)

Intervention not accepted: unknown reason

3. Other (no acceptance information)

Proposed intervention, acceptance unknown

Intervention not proposed

A discrepancy could generate more than one intervention, according to the classification proposed by the PCNE.

Confirmation of the acceptance or nonacceptance of the proposed intervention(s) was verified in the prescription after the interventions. The justifications received at the time of the intervention(s) were immediately recorded without the need for further confirmation.

2.7 Data Analysis

The comparison between medical specialties in relation to the number of drugs used before and during hospitalization, and the amount of drugs kept during hospitalization was performed using the one-way ANOVA test, followed by the Tukey post-test.

To assess the association between the medical specialty and the occurrence of unintentional discrepancy, chi-square test was used, with Bonferroni correction when necessary. The same test was used in the univariate assessment of the association between unintentional discrepancy and the variables gender, alcoholism and smoking. The comparison between patients with and without unintentional discrepancy regarding the variables age, education, number of comorbidities, consultation sources, amount of medication before hospitalization and quantity of medication at admission was performed using the t-student test.

Multivariate analysis between the occurrence of unintentional discrepancy and the variables gender, smoking, consultation sources and medication before hospitalization (considering only the variables with $p < 0.100$ in the univariate analysis) was performed using the bivariate logistic regression test using the "Enter" method.

All the analyses were conducted using the statistical program SPSS, version 24.0, based on a significance level of 5%.

3. Results

During the 12 months of the study, of the 350 patients admitted to the MCU ward, 304 were included in the study, and 46 did not participate. The number of males (n = 143; 47%) and females (n = 161; 53%) admitted to the study unit was very similar. Regarding age, 170 patients (55.9%) were 61 years of age or older, 44 (14.5%) of these were between 80 and 90 years of age, and 8 (2.6%) were over 90 years old. The average age of the participants was 61.6 ± 18.64 years.

Regarding education, participants reported having attended incomplete elementary school (n = 103; 33.9%). A total of 92 patients (30.2%) were ex-smokers. Table 1 presents the sociodemographic, clinical, and lifestyle characteristics of the research participants.

The most frequent comorbidities observed in medical records were systemic arterial hypertension (n = 185; 25.5%) and diabetes mellitus (n = 117; 16.1%). A total of 83 patients (27.0%) had at least two comorbidities, and the average number of comorbidities was 2.4 ± 1.41. The most frequent admission diagnoses were related to the cardiac system (n = 72; 23.7%) and neurological disorders (n = 49; 16.1%).

The average length of stay in the MCU during the study period was 7.5 ± 8.21 days. Several sources were consulted for the completion of the BPMH. The interview with the patient was always checked first because it only happened after the patient consented to participate in the research. Following, or in parallel, the caregiver was consulted, and both were asked about the prescriptions brought from home and the packaging of the medicines in use. The medical records of all patients were accessed. The average number of sources consulted per patient was 2.9 ± 0.78 (Table 2).

A total of 1,684 drugs were identified for the preparation of the BPMH as being used before hospitalization, and self-medicated drugs and herbal medicines were also considered. The average number of medications taken by patients before hospitalization was 5.5 ± 3.55, and upon hospital admission, the average number of medication per patient was 12.1 ± 3.85, with a total of 3,704 prescription drugs.

Of the 1,684 medications used before admission, 724 were maintained on hospital prescription, an average of 2.4 ± 3.37 medications per patient (or 43% of the total medications used at home). Among the self-medicated drugs (n = 40; 2.4%), 35.0% were vitamins and minerals (n = 14), 25.0% were herbal medicines (n = 10), 22.5% were analgesics and/or myorelaxants (n = 9), 7.5% were antifungal ointments or antibiotic-containing ointments (n = 3), and 7.5% were omega 3 (n = 3).

From June 2018 to May 2019, 1,134 discrepancies were found between home-based drugs and those prescribed upon admission to the MCU, which gives an average of 3.7 ± 3.65 discrepancies per patient. Among the discrepancies, 815 (72%) were intentional, 89 (8%) were undocumented intentional, and 230 (20%) were unintentional, and they were therefore classified as medication errors. The performance indicators of the medication reconciliation process and the classification of medication errors are presented in Table 2.

Of the 230 unintentional discrepancies, 31% occurred in patients admitted by the general practitioner, 18% by nephrology, and 13% by cardiology, with drug omission featuring in all specialties.

In addition to one case of thalidomide omission, other situations of omission included treatment for depression (fluoxetine, duloxetine, amitriptyline, and alprazolam), glaucoma (travoprost, tenophthalm, and brimonidine), benign prostatic hyperplasia (doxazosin), chronic venous insufficiency (diosmin and hesperidin), and Alzheimer's disease (memantine, rivastine, and ketipine. All eye drops used by patients were omitted.

The medication reconciliation process seeks to improve patient safety in relation to the use of medicines, and this proved to be essential during the research. Medication errors by medical specialty are presented in Table 3.

Table 1. Characteristics of the patient population

	Medical specialty (n) %										
	Total	GC	Card	Neu	Nephr	Tire	Reu	Gast	End	Hemat	Others
Gender											
Female	(161) 53	(45) 28	(35) 22	(29) 18	(18) 11	(10) 6	(10) 6	(7) 5	(2) 1	(3) 2	(2) 1
Male	(143) 47	(31) 22	(38) 27	(19) 13	(13) 9	(10) 7	(10) 7	(3) 2	(5) 3	(7) 5	(7) 5
Age (years)											
61 or more	(170) 56	(50) 29	(46) 27	(30) 18	(19) 11	(12) 7	(3) 2	(3) 2	-	(3) 2	(4) 2
46–60	(76) 25	(16) 21	(23) 30	(11) 14	(9) 12	(3) 4	(5) 7	(6) 8	-	(3) 4	-
31–45	(31) 10	(5) 16	(4) 13	(5) 16	(3) 10	(2) 6	(6) 19	-	-	(3) 10	(3) 10
18–30	(27) 9	(5) 19	-	(2) 7	-	(3) 11	(6) 22	(1) 4	(7) 26	(1) 4	(2) 7
Schooling											
Illiterate	(46) 15	(19) 41	(8) 17	(9) 20	(3) 7	(5) 11	-	-	-	(1) 2	(1) 2
Incomplete elementary school	(103) 34	(30) 29	(28) 27	(13) 12	(14) 14	(7) 7	(7) 7	(1) 1	-	(1) 1	(2) 2
Complete elementary school	(73) 24	(13) 18	(26) 35	(15) 20	(4) 5	(4) 5	(2) 3	(5) 7	(1) 1	(1) 1	(2) 3
High school	(68) 22	(12) 18	(9) 13	(8) 11	(10) 15	(4) 6	(6) 9	(4) 6	(5) 7	(6) 9	(4) 6
University education	(14) 5	(2) 14	(2) 14	(3) 21	-	-	(5) 36	-	(1) 7	(1) 7	-
Comorbidities											
None	(13) 4	(5) 39	(3) 23	(2) 15	-	-	-	-	-	-	(3) 23
One	(81) 26	(16) 20	(11) 13	(16) 20	(6) 7	(8) 10	(8) 10	(2) 3	(6) 7	(5) 6	(3) 4
Two	(83) 27	(20) 24	(28) 34	(13) 16	(9) 11	(4) 5	(2) 2	(3) 4	-	(2) 2	(2) 2
Three	(63) 21	(17) 27	(17) 27	(9) 14	(3) 5	(5) 8	(5) 8	(4) 5	(1) 2	(1) 2	(1) 2
Four	(40) 13	(11) 28	(6) 15	(6) 15	(8) 20	(3) 7	(3) 7	(2) 5	-	(1) 3	-
Five	(17) 6	(6) 35	(7) 41	(1) 6	(1) 6	-	(1) 6	-	-	(1) 6	-
More than five	(7) 2	(1) 14	(1) 14	(1) 14	(2) 29	-	(2) 29	-	-	-	-

Lifestyle											
Tobacco user	(33) 11	(5) 15	(7) 21	(8) 25	(2) 6	(5) 15	-	(2) 6	(1) 3	(1) 3	(2) 6
Tobacco use history	(92) 30	(15) 16	(24) 27	(18) 20	(12) 13	(12) 13	(2) 2	(5) 5	-	-	(4) 4
Alcohol use	(21) 7	(6) 29	(5) 24	(4) 19	(1) 5	(3) 14	(2) 9	-	-	-	-
History of alcohol use	(33) 11	(4) 12	(6) 18	(7) 21	(4) 12	(6) 18	(1) 3	(4) 12	-	-	(1) 3

GC = General Practice, Card = Cardiology, Neu = Neurology, Nephr = Nephrology, Tire = Pulmonology, Reu = Rheumatology, Gast = Gastroenterology, End = Endocrinology, Hemat = Hematology.

Table 2. Performance indicators of the medication reconciliation process

		Medical specialty (n) %										
		Total	GC	Card	Neu	Nephr	Tire	Reu	Gast	End	Hemat	Others
Admitted patients		(304) 100	(76) 25	(73) 24	(48) 16	(31) 10	(20) 7	(20) 7	(10) 3	(7) 2	(10) 3	(9) 3
Medicines used before admission		(1684)	(360) 21	(462) 27	(241) 14	(219) 13	(105) 6	(156) 9	(47) 3	(13) 1	(32) 2	(13) 2
Medicines prescribed on admission		(3704)	(926) 25	(1001) 27	(516) 14	(386) 10	(274) 7	(238) 6	(118) 3	(61) 2	(103) 3	(38) 1
Medicines maintained during admission		(724)	(133) 18	(215) 30	(86) 12	(98) 13	(38) 5	(82) 11	(25) 3	(9) 1	(26) 4	(12) 2
Medication discrepancies	ID	(815) 72	(179) 22	(218) 27	(126) 16	(89) 11	(55) 7	(68) 8	(29) 3	(8) 1	(20) 2	(23) 3
	UND	(89) 8	(24) 27	(38) 43	(10) 11	(8) 9	(6) 7	(0)	(3) 3	(0)	(0)	(0)
	UN	(230) 20	(72) 31	(29) 13	(28) 12	(42) 18	(18) 8	(28) 12	(4) 1	(4) 2	(2) 1	(3) 2
Pharmaceutical interventions	Done	(188)	(57) 30	(25) 13	(19) 10	(41) 22	(13) 7	(23) 12	(3) 1,6	(4) 2	(0)	(3) 1,6
	Accepted	(92)	(34) 37	(8) 8,7	(14) 15	(9) 5	(9) 5	(13) 14	(1) 1	(4) 4	(0)	(0)
	Justified	(56)	(15) 27	(7) 12,5	(5) 2,6	(18) 9,6	(0)	(8) 4	(0)	(0)	(0)	(3) 5
Patient's medication sources consulted	Medical records	(304) 100	(76) 25	(73) 24	(48) 16	(31) 10	(20) 7	(20) 7	(10) 3	(7) 2	(10) 3	(9) 3
	Patient interview	(223) 73	(40) 18	(61) 26	(30) 13	(27) 12	(17) 8	(20) 9	(8) 4	(6) 3	(6) 3	(8) 4
	Medicine packaging	(91) 30	(27) 30	(23) 25	(10) 11	(8) 9	(4) 4	(11) 12	(3) 14	(0)	(4) 4	(1) 1
	Caregiver Interview	(194) 64	(60) 31	(44) 23	(40) 21	(19) 10	(9) 5	(8) 4	(2) 1	(3) 1	(4) 2	(5) 3
	Prescription	(70) 23	(13) 19	(21) 30	(12) 17	(6) 9	(4) 6	(5) 7	(3) 4	(1) 1	(2) 3	(3) 4

I = Intentional, UND = Undocumented Intentional, UN = Unintentional.

Table 3. Unintentional discrepancies identified by drug reconciliation according to the Medical Specialty

	Unintentional discrepancies by medical specialty (n) %										
	Total	GC	Card	Neu	Nephr	Tire	Reu	Gast	End	Hemat	Others
	(230) 100	(72) 31	(29) 13	(28) 12	(42) 18	(18) 8	(28) 12	(4) 1	(4) 2	(2) 1	(3) 2
1 Incompatible drugs											
1.1 Drug omission	(196) 85	(70) 36	(21) 11	(23) 12	(31) 16	(16) 8	(22) 11	(4) 2	(4) 2	(2) 1	(3) 2
1.4 Therapeutic Class Substitution	(1) 0,5	-	(1) 100		-	-	-	-	-	-	-
2 Drug partially matched											
2.2.3 Different strength and different total daily dose	(12) 5	(1) 8	(2) 17	(1) 8	(4) 33	(2) 17	(2) 17	-	-	-	-
2.2.4 Different strength but same total daily dose	(6) 3	-	(1) 17	(1) 17	(3) 49	-	(1) 17	-	-	-	-
2.2.7 Same strength but unclear/or wrong frequency	(2) 1	-	-	(1) 50	(1) 50	-	-	-	-	-	-
2.3.1 Unclear or wrong dosage form	(5) 2	(1) 20	(2) 40	-	-	-	(2) 40	-	-	-	-
2.3.2 Unclear or wrong route of administration	(3) 1	-	(1) 33	(1) 33	(1) 33	-	-	-	-	-	-
2.3.5 Different dosage form but same route of administration	(4) 2	-	(1) 25	(1) 25	(2) 50	-	-	-	-	-	-
2.3.6 Different dosage form and different route of administration	(1) 0,5	-	-	-	-	-	(1) 100	-	-	-	-

When analyzing the discrepancies between home-based drugs and those prescribed upon admission to the MCU, self-medicated drugs was not considered. The drugs most frequently listed in the unintentional discrepancies category were related to the cardiovascular system (28%), digestive system and metabolism (26%), and the nervous system (17%).

Drugs with five or more unintentional discrepancies in hospital prescriptions were related to the cardiovascular system (n = 10; 32%), vitamins and minerals (n = 9; 30%), hypoglycemic agents including insulin (n = 6.19%), eye drops (n = 4; 13%), and central nervous system (n = 2; 6%).

The risk factors, such as age, gender, educational level, alcoholism, smoking, number of comorbidities, consultation sources, number of medicines in use at home and number of medicines on admission were evaluated to determine their correlation with the occurrence of unintentional discrepancies. There was no statistically significant correlation in the following variables: age, gender, level of education, alcoholism, smoking, number of comorbidities, and number of medicines on admission (p value ranging from 0.052 to 0.903) when correlated with the number of unintentional discrepancies. Only the number of consultation sources and the number of medicines in use at home showed significant correlation with the occurrence of unintentional discrepancies ($p \leq 0.001$).

For multivariate analysis, variables with p value <0.100 in the univariate analysis were considered. The number of consultation sources and the amount of medicines on admission remained significantly related to the unintentional discrepancy ($p = 0.039$ and $p = 0.008$, respectively).

A total of 318 pharmaceutical interventions were performed, 230 related to unintended discrepancies. Of these, 138 (60%) interventions were not accepted.

During the study, certain barriers hindered the medication reconciliation process. The barriers included patients being unable to remember or pronounce correctly the names or dosage of medications and the caregiver's lack of knowledge about the patient's drug treatment. Regarding the prescribers, the barriers observed were the lack of autonomy to consider and disregard the proposed pharmaceutical interventions and the difficulty in finding the prescribers in the ward to perform the intervention.

Other research was being conducted concurrently at the MCU, and this proved to be a barrier to the medication reconciliation process, because sometimes, the patient included in the study exhibited stress and/or discomfort.

The healthcare professional performing the medication reconciliation process is required to have considerable time to access all available sources of information. At the MCU, the health professionals appeared to have not been able to continue the medication reconciliation process at the end of data collection by the researcher.

Throughout the research period, collaboration among the multidisciplinary team, especially the nurses, nursing technicians, physiotherapists, and occupational therapists, contributed positively to the research development. There was also an interest and appreciation of the study by patients and caregivers. Both of these factors made the medication reconciliation process easier.

4. Discussion

The homogeneous profile of the men and women observed in this research is due to the fact that the MCU is a mixed environment, which has female and male rooms, where patient admission to the sector occurs according to the availability of beds.

The average age of the patients was 61.6 years. Studies reveal that between 2000 and 2050, the proportion of people aged 60 and above will increase from 11% to 22% of the total population. The average life expectancy for women in Latin America and the Caribbean is expected to reach 74.7 years for men and 80.7 for women by 2030. This increase in life expectancy and the consequent increase in the proportion of economically dependent people pose a challenge to the healthcare system, which must meet the needs of the aging population (United Nations, 2019; Organização Pan-Americana da Saúde, 2015; World Health Organization, 2016).

Regarding education, the results reflect the reality of the Brazilian population seeking public health services. In Brazil, illiteracy is concentrated in the older population, despite attempts to improve this over time. In 2001, illiterate people aged 50 and above accounted for 27.5% of the Brazilian population, and this decreased to 18.3% in 2012 (Brasil, 2016).

Regarding lifestyle, 30% (n = 92) of the patients said they were former smokers. This result is above the national average (10.1%), as identified in the last National Health Survey (PNS) conducted by the Ministry of Health in 2017. Cardiovascular diseases are the leading cause of death worldwide, accounting for 44% of all deaths due to chronic noncommunicable diseases. Tobacco use is the leading cause of cardiovascular disease, including heart attacks and strokes. Approximately 11% of deaths due to cardiovascular disease in the Americas are associated

with tobacco use (Brasil, 2018).

Data published by the Ministry of Health (2018) reveals that in 2017, 19.1% of adults living in the 26 Brazilian state capitals and the Federal District reported abusive alcohol consumption (four or more units for women and five or more units for men –on a single occasion), and the Midwest region of Brazil had the highest rate (16.2%) of consumers (WHO, 2018).

Due to the number of comorbidities noted (mean 2.4 ± 1.41), there is a greater need for attention to these patients by health professionals. During the medication reconciliation process, polymedicated patients most often did not immediately remember the names of all the medications they were using or were unaware that non-pharmacological treatments, such as teas and dietary supplements, are relevant in pharmacotherapy.

In 65% (n = 193) of the medication reconciliation cases, three to four sources of information were used, of which five were established (interview with the patient, interview with the caregiver, packaging of medicines brought from home, prescriptions, and medical records). The elaboration of the BPMH in use before hospital admission ensured greater reliability and credibility of the findings and greater patient safety (The Joint Commission, 2006). Durán-Garcia, Fernandez-Llamazares & Calleja-Hernández (2012) state that the accuracy of the medication history used before hospitalization correlates with the number of available sources consulted.

Among the drugs used before hospital admission, only 2.4% (n = 40) were by self-medicated, despite the tendency of the Brazilian population to self-medicate (Galato, Madalena & Pereira, 2012; Naves, Castro, Carvalho & Merchán-Hamann, 2010). According to Arrais et al. (2016) the prevalence of self-medication in Brazil in 2016 was 16.1% (95% CI 15.0–17.5), mainly by women; inhabitants of the North, Northeast, and Midwest; and individuals who have had one, two, or more chronic diseases.

The average household medication collected by the BPMH was 5.5 (± 3.55 SD) medications per patient. Mongaret et al. (2018) conducted a study of patients using more than five home-based drugs and identified this as a predictive factor for discrepancies in hospital admission, as a result of the univariate regression analysis (OR 4.67; 95% CI 2.01–10.83; $p < 0.001$). Corroborating the previous study, De Antônio et al. (2019) also found that patients using five or more medications at home had discrepancies in 67.1% of cases, and the discrepancy rate was 33% for those using below five medicines.

The main classes of medicines used at home were those for the cardiovascular system (n = 665; 40%), digestive system and metabolism (n = 547; 32.5%), and nervous system (n = 220; 13%). During the medication reconciliation process in a Swiss hospital, Giannini et al. (2019) found that the drugs of these similar classes were the ones most involved in unintentional discrepancies (n = 32, 28.8% cardiovascular system; n = 25, 22.0% nervous system; and n = 15, 13.5% digestive tract and metabolism).

Drug standardization in hospitals is a common and recommended practice, as is the development of clinical therapeutic protocols. These, in addition to improving patient safety and saving the institution, also facilitate the preparation of prescriptions, proposing automatic therapeutic substitutions depending on the software used for electronic prescriptions (Wang et al., 2017).

However, such therapeutic substitution may, in some cases, lead to confusion when unmonitored and may increase the likelihood of unintentional discrepancies (Glaholt, Hayes & Wisniewski, 2014).

It was observed during the interview that some patients had been followed up for years in primary care without adequate monitoring of the evolution of their underlying diseases. Despite this follow-up, there was complication of the underlying disease, resulting in hospitalization and the use of new, more potent, more selective drugs to stabilize it.

In this study, 1,134 discrepancies between the home-based drugs and those prescribed at hospital admission were observed. Of these, 20% (n = 230) were unintentional, corroborating the unintentional discrepancy rate found in the study by Andreoli et al. (2014), (18.8%), the rate observed by Magalhães et al. (2014) in the cardiology unit of a teaching hospital in Bahia (17.7%), and the rate observed by Lindenmeyer et al. (2013) in an oncology unit in Paraná (17.7%).

However, other medication reconciliation studies conducted around the world have shown different results from unintentional discrepancies, highlighting the importance of this process in care transitions, regardless of the country or location to which it applies. Mazhar et al. (2017) performed the medication reconciliation process with elderly patients at the MCU at a university hospital in Saudi Arabia and found unintentional discrepancies at a rate of 37%. Tamiru, Edessa, Sisay, & Mengistu (2018) performed the medication reconciliation process on the internal transition from a university hospital in Ethiopia and identified a rate of 33.3%.

Unintentional discrepancies are considered medication errors and may affect the prescription, dispensing, consumption, and monitoring of medications, resulting in serious harm, disability, and even death (WHO, 2017). Also, of the total discrepancies between the drugs, 8% (n = 89/1134) were classified as undocumented intentional. Such discrepancies are not considered medication errors but have to the potential to be.

The three main classes of drugs involved in unintentional discrepancies are the same classes as those most commonly used at home, drugs for the cardiovascular system (65/230, 28.%), digestive system and metabolism (60/230, 26%), and nervous system (39/230, 17%), according to ATC level I classification. Similar results were observed by Giannini et al. (2019) (n = 32, 28.8% cardiovascular system; n = 25, 22% nervous system; and n = 15, 13.5% digestive system and metabolism) and Chung et al. (2019) (17/77, 22.1% nervous system; 15 / 77, 19.5% cardiovascular system; and 14/77, 18.2% digestive tract and metabolism). Therefore, reconciling the drugs belonging to these classes can contribute to the safety of the patients who use them.

In this study, the omission was the predominant unintentional discrepancy (196/230, 85%) in all MCU specialties, as well as in surveys conducted in Saudi Arabia (77%) (Abdulghani, Aseeri, Mahmoud, & Abulezz, 2018), Ireland (76.6%) (Holland, 2015), and Spain (65%) (Rodríguez Vargas, Delgado Silveira, Iglesias Peinado, & Bermejo Vicedo, 2016), demonstrating the importance of reconciling drugs and preventing treatment interruption (Mekonnen et al., 2016).

In institutions where the demand for pharmacists is scarce, it is recommended to direct the pharmaceutical reconciliation services to the specialties or hospital sectors with the largest number of unintentional discrepancies (Tamiru et al, 2018; Bilbao Gómez-Martino, Nieto Sánchez, Fernández Pérez, Borrego Hernando, & Martín-Sánchez, 2017; Patel, Pevnick & Kennelty, 2019).

The medication reconciliation process seeks to improve patient effectiveness and safety with regard to drug use, and this process proved essential during the research by identifying a case in which thalidomide was omitted in leprosy treatment, which could expose not only the patient himself/herself to the disease but also the other people he/she may have contact with. In addition, continuity of treatment is essential for its effectiveness in patients with depression, glaucoma, hyperplasia, chronic venous insufficiency, and Alzheimer's disease. In general, omitting a treatment may prolong hospital stays, thus increasing the cost of hospitalization, and reduce the turnover and availability of beds.

The pharmaceutical interventions performed in this study involved patients, caregivers, and prescribers, who contribute greatly to patient safety. Patients and caregivers received counseling on the use of self-medication, and those using eye drops were instructed on the correct application. Other counseling was given according to the needs expressed by the patients and caregivers during the interviews, emphasizing the importance of the clinical pharmacist in all hospital sectors.

All unintentional discrepancies found (n = 230, 85%) resulted in an intervention by the prescriber. A total of 318 interventions were performed in this study, most of them referring to incompatible drugs. The percentage of acceptance of interventions by prescribers was 71% (n = 226/318).

Medicines considered unnecessary included mainly vitamins, contraceptives, thyroid hormones, minerals, and omega 3. As in the study by Rodrigues et al (2019) vitamins were among the drugs most involved in pharmaceutical interventions, with vitamin B12 being the most commonly used drug associated with the "omitted drug reintroduction" intervention. Vitamin B12 deficiency, however, can trigger neuronal damage and neurological disorders, such as dementia and neuropathic pain (Moore et al., 2012).

Medication reconciliation is a process that depends on the collaboration of health professionals, patients, and caregivers to be well executed and to achieve good results (Karaoui et al., 2019). During this research, a noted barrier was the low educational level of patients, which implies a reduced knowledge about the names of prescribed drugs, indications for use, and general instructions, as identified in the study by Spalla & Castilho, 2016.

Pronouncing drug names correctly is not easy for anyone. Even health professionals sometimes stumble over words, which are long and similar to other medications. For polypharmacy patients, this difficulty becomes even greater, therefore requiring more time for the health professional to build the BPMH and to perform the medication reconciliation process.

An important factor for medication reconciliation, described by Cornish et al (2005), was the accuracy of the medication history at the time of interview with patients and family members. Accuracy is often compromised by factors, such as time available for the interview, language barriers, severity of the patient's disease, cognitive status, and familiarity of the patient and caregiver with their medication regimen.

The risk factors for the occurrence of unintentional discrepancies identified in this study were the number of consultation sources and the amount of medicines on admission, which were similar to the results obtained by Rodriguéz Vargas et al. (2016). Cornish et al. (2005) found no correlation between the number of medications used before hospitalization and the occurrence of discrepancies.

Other variables did not present statistically significant results when correlated with unintentional discrepancies. Two studies conducted in 2012 indicated age as a risk factor for drug errors, differing from the results presented in this study (Hellström, Bondesson, Höglund & Eriksson, 2012; Salanitro et al., 2012).

A study by Afonso (2015) in Portugal revealed that all hospitals that have implemented the medication reconciliation methodology, or even those that are still in pilot studies, face several barriers, which include the lack of the availability of a multidisciplinary team, the lack of an information system that enables the recording of all interventions performed, and the difficulties in integrating them efficiently. In this study, however, the multidisciplinary team contributed positively to the development of the medication reconciliation process and could be considered as a facilitator rather than a barrier.

5 Conclusions

This study reflects the observations from one hospital in Brazil where it was verified the high frequency of drug omission upon admission to the MCU and the need for greater pharmacotherapeutic follow-up of polymedicated patients. The medication reconciliation process proved to be effective in identifying medication errors, providing greater safety in drug treatment for all patients who were followed up.

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Competing Interests Statement

The authors declare that there are no competing or potential conflicts of interest.

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Exploring the Factors Associated with Infant Mortality in Rural Indonesia

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Abstract

Infant mortality is a sensitive indicator to measure the health condition of a population. Despite large declines in infant mortality rates in Indonesia, the people living in rural areas are the most affected. This study aims to analyze the causes of infant mortality in rural Indonesia and suggested strategies for its reduction. This study is an analytical cross-sectional design based on the 2017 Indonesian Demographic and Health Survey (IDHS) dataset for children. The information on infant deaths collected from those mothers who experienced infant deaths. Series of logistic regression models were used to select the significant factors affecting infant mortality in rural Indonesia. Infant mortality is associated with intermediate social determinants such as birth order, birth weight, and breastfeeding status. Socio-demographic factors such as the educational status of mothers, wealth quintile, the smoking habit of the mother, age of mother at first delivery, and sex of the baby are also related to infant mortality. The most crucial factors in rural Indonesia were the age of first-time mothers. As a strategy for addressing the issue of infant mortality in rural areas, the result of the study highlights the need for decreasing adolescent pregnancies among the youngest age groups. Pregnant mothers in the youngest age group should be supported by quality maternal health services to ensure their pregnancies in healthy condition. The focus of breastfeeding promotion programs should be encouraged, particularly on early initiation and duration of breastfeeding.

Keywords: infant death, infant health, rural children

1. Introduction

Globally, the well-being and health status of families and communities are estimated indirectly by infant mortality. Infant mortality becomes a general indicator used for public health measurements across areas and periods (Ely et al., 2017). Sustainable Development Goals (SDGs) have set to reduce newborns deaths to at least as low as 12 per 1000 live births and under-5 mortality to at least as low as 25 per 1000 live births (United Nations, 2017; WHO, 2018). Thus, infant mortality analysis is very crucial for development planning and evaluation programs. Indonesia had experienced a further reduction in infant mortality rate from 59 deaths per thousand live births in 1988-1992 (BPS et al., 1991) to 24 deaths per thousand live births in 2015-2017 (BKKBN et al., 2018). Although some improvements made in recent years, infant mortality has not been quantified, particularly in rural Indonesia.

Further analysis indicated that relationships between socioeconomic characteristics and infant mortality were strong in rural areas than in urban areas. Earlier studies revealed that rural infants were faced with higher probabilities to experience deaths compared to urban infants (Ajaero & Owoh, 2013; Mustafa, 2008). Higher infant mortality associated with proximate risk factors that were more common in nonmetropolitan areas, including birth order (Kynast-Wolf et al., 2019), birth weight (Chen et al., 2016), and breastfeeding status (Banerjee, 2018; Sari, 2016). Infant mortalities were more likely to be related to exogenous socio-environmental determinants, such as the educational background of the mother (Kiross et al., 2019; Santos et al., 2016); wealth quintile (Adewuyi et al., 2017; Kumar & Singh, 2014; Mohamoud et al., 2019); smoking habits of the mother (Ratnasiri et al., 2020), age of mother at first delivery (Weldearegawi et al., 2015), and the sex of the baby (Byberg et al., 2017; Boghossian et al., 2018).

Based on earlier research, the association between birth order and infant mortality revealed a u-curve, in which both first-and later-infants had a higher probability of dying compared with those in the middle curve (Mishra et al., 2018; Modin, 2002). Mothers to first-born infants tended to be inexperienced and have fewer material resources to access health care facilities that can cause higher probabilities of infant deaths. As the number of children within a

family increase, mothers to third or later-born infants had more likely to experience parental pressure (Ahrens et al., 2017). Those mothers who had third or later-born infants were also less likely to initiate prenatal care, consume prenatal vitamins, and breastfeed compared with their earlier-born infants (Ahrens et al., 2017). Moreover, based on the hypothesis of biological depletion, later-born infants were more likely than their elder siblings to be less healthy since those infants were born to elder mothers who had delivered to some infants before, thus, physiologically less able to have tougher infants (Riodan et al., 2011; Hotz & Pantano, 2015).

The low-birth-weight had a greater probability of infant mortality. Infants weighing less than 2500 grams are more likely to experience visual problems due to pulmonary dysplasia (Travers et al., 2018), retinopathy of prematurity (Natarajan et al., 2019), respiratory infections (Everard, 2016), and heart illness (Hughes et al., 2017). Low birth infants have a higher probability of hospitalizations, developmental failure, and growth disorders particularly in the initial year of life (Liang et al., 2018; Vilanova et al., 2019).

Breastfeeding status is also very much associated with infant mortality. World Health Organization (WHO) suggested exclusive breastfeeding for six months continued breastfeeding up to 2 years of age to prevent children from diarrhea's (Shahid et al., 2019) and pneumonia's illness (Oktaria et al., 2017). Christian et al. (2015) had emphasized that breastmilk's nutrition is crucial for brain development, physical growth, gut maturity, preventing infection and inflammation, and promoting mother-infant attachment.

In regards to the association between socioeconomic status and infant and child mortality, Kiross et al. (2019) emphasized the effect of the educational background of the mother on decreasing infant mortality. Furthermore, Motsa et al. (2016) reveal a notion that the mother's schooling would influence the mother's knowledge of general nutrition and health care practices that might encourage those mothers to perform better health behavior and by altering the traditional marital relationships. Mother's education can increase the chance of infant survival by postponing women to marry and enter motherhood later and have fewer children, employ prenatal care, and vaccinate their children (Akter et al., 2015, Muj & Bhradwaj, 2015).

Previous studies also showed that parents living in lower wealth index had a higher risk of infant deaths. Ladusingh et al. (2016) stated that lower households' wealth had fewer capacities to access health care, public infrastructure, clean water, nutritious food, and a safe environment than higher household's wealth. A study conducted by Roy and Haque (2018) in Bangladesh pointed out that the mothers of the wealthy family were more likely to have 45% lower probabilities of experiencing infant mortality (OR = 0.55, CI =0.42-0.720) compared to the mothers who were from the impoverished family.

The smoking habit of mothers during pregnancy is closely linked with increased risks of infant deaths. Ding et al. (2017) revealed that compared with non-smoking mothers, smoking mothers in the United States have a higher probability of infant mortality [light smoking: adjusted odds ratio (aOR) = 1.21, 95% confidence interval (CI), 1.03-1.43; heavy smoking: aOR = 1.30, 95% CI, 1.12-1.52], correspondingly. Prenatal smoking mothers in The United States might cause short-and long-term health issues, neurologic, developmental, and neurosensory illnesses (Dietz et al., 2010).

Maternal age at first delivery is known to raise the odds of infant mortality. Kramer and Lancaster (2010) showed that young mothers faced immature physical growth that stimulates neonatal outcomes. In contrast, elder mothers had higher odds in the incidence of hypertension (Kozuki et al., 2013), gestational diabetes (Shepherd et al., 2017), and congenital abnormalities (Carolan & Frankowska, 2011).

The sex of infants corresponded with infant mortality. A study of Humphrey et al. (2012) revealed that male fetuses are more likely to be born pre-term than female fetuses due to respiratory distress syndrome, Sudden Infant Death Syndrome (SIDS), and other infectious diseases.

Hence, this study aims to analyze the impact of socio-demographic and proximate determinants on the incidence of infant death at the age of 0-11 months in rural areas of Indonesia. This study emphasizes education level, wealth quintile, sex of the child, maternal smoking habits, and age at first birth to the incidence of infant mortality. This study also identifies the association between breastfeeding patterns, birth order, and birth weight as proximate determinants of the incidence of infant mortality, especially in rural Indonesia.

2. Method

2.1 Data

The data were obtained from 2017 Indonesian Demographic and Health Survey (IDHS). The 2017 IDHS sampling frame was prepared using the 2010 Population Census block (SP 2010) (BKKBN et al., 2018). The survey represents 1,970 census blocks in urban and rural areas with a sample of 49,250 households obtained by female

respondents aged 15–49 years about 59,100 respondents (BKKBN et al., 2018). The sampling technique was applied in two stratified stages, the probability proportional to size (PPS) systematically selecting the size of the number of households stratified into urban and rural areas and sorted based on the wealth index of the 2010 Population Census (BKKBN et al., 2018). Systematic random selection was carried out on 25 households selected in the census block. Free downloadable data can be accessed by registering through the Demographic and Health Survey (DHS) website. This study used a questionnaire for women aged 15–49 years to collect information from women of childbearing age regarding the number of children born alive to a certain age, socio-demographic factors, and the closest determinant of the incidence of infant mortality.

2.2 Inclusion and Exclusion Criteria

The inclusion criteria of this study were: (1) women of childbearing age 15–49 years who are married or live together; (2) children born alive to 11 months; (3) babies who die between the ages of 0–11 months or before reaching their first birthday; and (4) age of fertile women living in rural areas. The exclusion criteria were infants living in urban areas. This study selected 43,787 infants as the initial sample. After that, the study excluded 78 infants who reported missing information on selected variables. Therefore, the final sample used in this study was 43,709 babies from villages in 34 provinces in Indonesia.

2.3 Key Explanatory Variables

The infant mortality rate is calculated based on the mother's statement in this case, whether the mother has successfully given birth and the baby survives until the age of 11 month. The birth order is classified into the third child or more, second child, and first child. Birth weight is classified as greater than or equal to 2500 grams and less than 2500 grams. Breastfeeding status is identified by whether the mother has breastfed her baby up to 11 months of age. The education status of the mothers is classified into secondary education or above, primary education, and no education at all. The wealth quintile variable is divided into rich, middle, and poor groups. The smoking habits of mothers were grouped into non-smoking mothers, mothers who smoked daily, and mothers who smoked infrequently. The age of mother at first delivery was categorized into less than 20 years, 20 to 39 years, and 40 to 49 years. The sex of an infant's variable consists of female and male infants.

The initial stage of the analysis was carried out using a descriptive approach through univariate analysis by describing the frequency distribution of the respondent characteristics of each variable. A stage is an inferential approach through bivariate and multivariate analysis. The bivariate analysis aims to explain the relationship between each predictor variable on the response variable, testing the relationship between the two variables with the chi-square test (El-Habil, 2012). The multivariate analysis aims to determine the effect of the overall predictor variable on the response variable. This influence is seen both simultaneously and partially through multiple logistic regression with p-value ≤ 0.05 so that there is an influence of predictor variables in this case socio-demographic factors and the lowest determinant on infant mortality variables. Also, risk factors were measured for predictor variables for the incidence of infant mortality using odds ratios (ORs) with 95% confidence intervals (CIs) (Kleinbaum & Klein, 2010). Data analysis in this study was calculated using R-4.0.2 for Windows.

2.4 Ethical Consideration

This study does not contain private records or confidential information. All procedures and surveys for the 2017 IDHS have been reviewed and permitted by the ICF International Institutional Review Board (IRB). The survey procedures have been considered by the ICF IRB, the Indonesian Ministry of Health, and the Indonesia National Population and Family Planning Board for the protection of human subjects and in compliance with Indonesia's laws and norms.

3. Results

3.1 Characteristics of Respondents

Samples that met the requirements for data analysis were 43,709 infants in rural Indonesia in which 2,050 infants had been declared died before the age of 11 months and 41,659 infants who had survived until the age of 11 months. Table 1 revealed the frequency distribution of the respondent characteristics in this study. The results of the descriptive analysis showed that the proportion of first and second birth order was more than 40% compared to the third or more birth order (13.5%). Only less than 1.3% of infants were born with low birth weight (<2,500 grams). The majority of mothers did not breastfeed their babies (83.0%). About 50.1% of mothers had graduated from primary school education, 59.1% of mothers came from the poor level of wealth quintile, and more than 90.0% of mothers had a non-smoking habit. More than 50 percent of the mothers were delivered their first infants at the age of 20-39 years (53.0%). The proportion of sex of infants born was nearly equal between females and males infants.

Table 1. Characteristics of infant mortality (0-11 month), rural Indonesia, 2017 (N=43.709)

Variable		N	%
Infant mortality (0-11 month)	No	41,659	95.3
	Yes	2,050	4.7
Proximate determinant factors			
a. Birth order	Third or more	5,907	13.5
	Second	19,708	45.1
	First	18,094	41.4
b. Birth weight	≥ 2.500 gr	43,150	98.7
	< 2.500 gr	559	1.3
c. Breastfeeding status	Yes	7,431	17.0
	No	36,278	83.0
Socio-demographic factor			
a. Educational status of mother	Secondary and above	19,836	45.4
	Primary	21,915	50.1
	No education	1,958	4.5
b. Wealth quintile	Rich	9,469	21.7
	Middle	8,426	19.3
	Poor	25,814	59.1
c. Smoking habit of mother	Not smoking	42,439	97.1
	Daily	511	1.2
	Infrequently	759	1.7
d. Age of mother at first delivery	< 20 year	20,289	46.4
	20-39 year	23,396	53.5
	40-49 year	24	0.1
e. Sex of infant	Female	21,183	48.5
	Male	22,526	51.5

Note: Author's calculation.

3.2 The Result of Bivariate Analysis

Table 2 shows the results of the bivariate analysis to determine the relationship between the incidence of infant mortality and the predictor variables, namely socio-demography and the proximate determinant. The statistical results of the chi-square test showed a significant relationship (p-value ≤ 0.05) between the incidence of infant mortality and the proximate determinants, including birth order, and breastfeeding status of the infants. However, the infant's birth weight did not significantly relate (p-value > 0.05) to the incidence of infant mortality in rural Indonesia. Socio-demographic factors, namely the educational status of the mother, wealth quintile, smoking habit of the mother, age of mother at first delivery, and sex of the infant revealed a significant association (p-value ≤ 0.05) to the incidence of infant mortality in rural Indonesia.

Table 2. Bivariate analysis between infant mortality (0-11 month) and proximate and socio-demographic factors, rural Indonesia, 2017

Variable			Infant mortality				*Chi square*	*p-value*
			No		Yes			
			N	%	n	%		
Proximate determinant factor								
a.	Birth order	Third or more	5,564	13.4	342	16.7	42.5	0.00**
		Second	18,919	45.4	790	38,5		
		First	17,176	41.2	918	44.8		
b.	Birth weight	≥ 2.500 grams	41,133	98.7	2,018	98.4	1.36	0.24
		< 2.500 grams	526	1.3	32	1.6		
c.	Breastfeeding status	Yes	7,230	17.4	201	9.8	78.8	0.00**
		No	34,430	82.6	1,848	90.2		
Socio-demography factor								
a.	Educational status of mother	Secondary and above	19,158	46.0	678	33.1	204.3	0.00**
		Primary	20,732	49.8	1,183	57.7		
		No education	1,769	4.2	189	9.2		
b.	Wealth quintile	Rich	9,172	22.0	296	14.4	120.0	0.00**
		Middle	8,119	19.5	308	15.0		
		Poor	24.368	58.5	1,446	70.6		
c.	Smoking habit of mothers	Not smoking	40,474	97.1	1,965	95.8	16.7	0.00**
		Daily	485	1.2	26	1.3		
		Infrequently	700	1.7	59	2,9		
d.	Age of mother at first delivery	20-39 year	22,524	54.1	871	42.5	117.5	0.00**
		< 20 year	19,116	45.9	1,174	57.3		
		40-49 year	19	0.05	5	0.2		
e.	Sex of infant	Female	20,275	48.7	907	44.2	15.3	0.00**
		Male	21,384	51.3	1,143	55.8		

Note. Author's calculation, IDHS 2017 ; *(p-value ≤ 0.1); **(p-value ≤ 0.05).

3.3 The Result of Logistic Regression Analysis

Table 3 revealed the results of the final model of multiple logistic regression. The second (OR: 0.88; 95% CI: 0.78-1.01) or third (OR: 0.73; 95% CI) birth order: (0.66-0.81) were more likely to have an incidence of infant mortality than the first birth order. The odds of infant mortality with low birth weight (LBW: < 2,500 gram) was 1.59 times higher (95% CI: 1.10-2.29) than normal birth weight (≥ 2,500 gram). Infant mortality of a mother who did not breastfeed her child was 1.87 times (95% CI: 1.61-2.18) relatively higher than those mothers who breastfeed their infants. Mothers who come from the poor wealth index have the highest chance of infant mortality, compared to mothers who came from middle and rich wealth index (OR: 1.58; 95% CI: 1.38-1.80). Infant mortality among uneducated mothers had the highest risk compared to educated mothers (OR: 2.23; 95% CI: 1.87-2.67). The possibilities of mothers who smoked daily was 1.44 times more likely (95% CI: 1.09-1.88) to cause infant mortality compared to a non-smoker mother. Those mothers who delivered their infants at the age of 40-49 years were more likely to be 6.10 times (95% CI: 2.18-17.08) of the incidence of infant mortality compared to those mothers who delivered their infants at the age of 20-39 years. The mothers who gave birth to their infants at the age below 20 years were 1.37 times higher odds (95% CI: 1.24-1.50) of the incidence of infant mortality compared to those mothers who delivered their infants at the age of 20-39 years. Mothers who had male infants

were 1.19 times more likely to experience infant mortality than mothers who had female infants.

Table 3. Multiple logistic regression model for determinants of infant mortality (0-11 month) in rural Indonesia, 2017

Variable			*OR*	*95% CI*	*p-value*
Proximate determinant factor					
a.	Birth order	First	Ref		
		Second	0.88	0.78-1.01	0.06*
		Third or more	0.73	0.66-0.81	0.00**
b.	Birth weight	≥ 2.500 grams	1		
		< 2.500 grams	1.59	1.10-2.29	0.01**
c.	Breastfeeding status	Yes	1		
		No	1.87	1.61-2.18	0.00**
Socio-demographyc factor					
a.	Education of mother	Secondary and above	Ref		
		Primary	1.34	1.21-1.48	0.00**
		No education	2.23	1.87-2.67	0.00**
b.	Wealth quintile	Rich	Ref		
		Middle	1.08	0.92-1.27	0.35
		Poor	1.58	1.38-1.80	0.00**
c.	Smoking habit of mother	Not smoking	Ref		
		Daily	1.44	1.09-1.88	0.01**
		Infrequently	0.79	0.53-1.18	0.24
d.	Age of mother at delivery	20-39 year	Ref		
		< 20 year	1.37	1.24-1.50	0.00**
		40-49 year	6.10	2.18-17.08	0.00**
e.	Sex of baby	Female	Ref		
		Male	1.19	1.09-1.31	0.00**

Note. Author's calculation, IDHS 2017; *(p-value ≤ 0.1); **(p-value ≤ 0.05).

4. Discussion

This study investigated the impact of socio-demographic and the proximate determinant factors on the incidence of infant mortality in rural Indonesia using data from the 2017 Indonesia Demographic and Health Survey. This research showed that the contribution of factors that influence the incidence of infant mortality still varied in rural areas in Indonesia. The results showed that birth order had a significant effect on the incidence of infant mortality (0–11 months). The higher birth order had a higher probability of the incidence of infant mortality (0–11 months) (Ahrens et al., 2017; Mishra et al., 2018). The birth order of the first and last children is more likely to be at risk of infant mortality than middle birth order (Mishra et al., 2018; Mustafa, 2008). The first birth order had higher odds of infant mortality since the mothers had no experience taking care of their first child. Thus, the first child had a higher chance of dying from preventable injuries (Thoma et al., 2019). However, the last birth order with a high number of births can reduce the chances of survival of the baby because maternal fatigue decreases the mother's ability to concentrate (Iwata et al., 2018), which can increase the incidence of postpartum fatigue (Thomas & Spieker, 2016), feeling tight Senol et al., 2019), and caused their babies to wean their breast milk earlier (Fata & Atan, 2018).

The logistic regression model shows that there is a significant influence between low birth weight (LBW: <2,500 grams) on the risk of infant mortality in rural areas in Indonesia. Infants who experience low birth weight have a

higher likelihood of infant mortality due to immaturity in humoral, multi-organ, and cellular immunity (Hughes et al., 2017). LBW is a determining factor that is closely related to the risk of infant mortality due to preterm birth or intrauterine growth retardation (Sovio et al., 2012). Other studies have shown that babies who are small at birth are more likely to experience infant mortality than babies with a standard size or larger (Dube et al., 2013; Khadka et al., 2015).

In rural areas in Indonesia, mothers who breastfeed their babies are more likely to reduce infant mortality than mothers who do not breastfeed. Previous research also showed that babies who have not been breastfed by their mothers have twice the risk compared to babies who are breastfed by their mothers (Sankar et al., 2015). The duration of breastfeeding in the first six months is one of the predictors of a significant reduction in infant mortality (Oktaria et al., 2017; Sankar et al., 2015). A study in South Africa showed that exclusive or partial breastfeeding reduces the risk of infant mortality (Motsa et al., 2016)

This study found that maternal education has a significant effect on infant mortality in rural Indonesia. Mothers with higher secondary education are more likely to experience infant survival than mothers with primary or uneducated education in rural Bangladesh (Akter et al., 2015). Increased maternal education leads to delays in age at first marriage, delays in the first delivery, and job opportunities for women (Kiross et al., 2019).

The wealth index, which is created by the resources owned by households, is very close to income (Ladusingh et al., 2016). Babies who have mothers with a low wealth index tend to have the highest risk of death compared to babies who have mothers from the middle to upper wealth index (Tall et al., 2018). Previous research has shown that the infant mortality rate is higher for mothers with poor and middle status compared to mothers with richer status (Khadka et al., 2015). Previous research from Ezeh et al. (2015) showed a significant effect of infant mortality in poor households, living in rural areas, and having uneducated mothers in Nigeria. Community-based interventions for mothers living in rural areas with low economic status are needed to increase the survival rate of children in rural Nigeria (Ezeh et al., 2015). Babies born to families with a higher wealth index and mothers with higher education tend to receive better nutrition, health care, and education to reduce the risk of infant mortality (Hosseinpoor et al., 2006).

This study also reveals a significant relationship between maternal smoking habits and the risk of infant mortality in rural Indonesia. The more often the mother smokes, the higher the likelihood of infant mortality (Cerda et al., 2017; Ratnasiri et al., 2020). Mothers who quit smoking reduce the risk of infant mortality (Johansson et al., 2009). Previous research found that there was an association between smoking, premature infant mortality, and sudden infant death syndrome (Dietz et al., 2010). Patrick et al. (2016) emphasized that there is a relationship between an increase in tax and cigarette prices with a decrease in infant mortality so that stakeholders can implement policies and strategies for increasing cigarette taxes in the context of preventing infant mortality.

Maternal age at first delivery is closely related to the incidence of infant mortality. It is shown by the logistic regression model that mothers at a young age (15–19 years) and the end of the reproductive period (40–49 years) are more likely to be at risk of experiencing infant death than those at first age. - when the mother is 20–39 years old. These results are in line with previous studies, where babies born to mothers aged 20–35 years have a 0.31 times lower risk of neonatal death than babies born to mothers aged less than 20 years and more than 35 years (Sari, 2016). It is also clear that delaying the age at first birth in women in their 20s reduces infant mortality and improves infant health (Finlay et al., 2011). Mothers who have male babies are more likely to have a higher risk of infant mortality than female babies. It is in line with research in South Africa that revealed that female infants tend to have a lower risk of infant mortality than male babies (Motsa et al., 2016). Previous research has shown a higher relationship between infant mortality in males than in females (Sovio et al., 2012).

This study finding indicates the need to allocate more to girl's education and family planning. The increasing number of women studying in schools will encourage the increased age at marriage and subsequently increase the age at first delivery and reduce adolescent pregnancies. It would address the teenage pregnancy issue and reduce the risk of infant mortality.

This study is limited to the number of variables that show a statistically significant relationship with the incidence of infant mortality in rural areas in Indonesia. In general, cross-sectional studies find it arduous to identify causality because exposure, as well as the measured results, collected at the same time, thus, can create a memory bias.

5. Conclusion

In conclusion, infant mortality is a vital indicator of community health and general development of a nation, since it reveals the social, economic, and environmental circumstances in which infants and their communities live,

including their health systems. The study indicates evidence of disparities in the reasons for infant mortality among divergent socio-demographic subclasses. Yet, in the face of dwindling infant mortality in rural areas of Indonesia, there is a vital prerequisite to classify that only the most significant determinants that affect infant mortality. Decrease in infant mortality rate in the proximate determinant factor was associated with normal birth weight, breastfeeding, number, and spacing of controlled and planned births. In this regard, the socio-demographic factors that can reduce infant mortality are associated with factors such as higher education, better economic status, the ideal age at first birth (not too young or too old), smoking habits, especially during pregnancy. Another factor is maintaining the health of the baby during the prenatal and postnatal periods, especially male babies who are more prone to death than female babies.

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Authors' Contributions

DKI: Conceptualized the design and overall study. She analyzed, interpreted the data, and prepared the manuscript. IE: Supported in statistical analyses, interpretation of data, and reviewed the manuscript, and provided inputs. EP: Critically reviewed the manuscript and provided inputs. All authors read and approved the final manuscript.

Ethics Approval

This study involves the analysis of anonymous publicly available secondary data and therefore no ethical approval was required.

Data Availability Statement

Data are available in a public, open access repository.

Competing Interests Statement

The authors declare that there are no competing or potential conflicts of interest.

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Hegemony in Effective Communication on the Modern Health Services During Pregnancy, Give Birth, and Postpartum in Baduy Communities

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Abstract

Kanekes Village, where Baduy people live, is the biggest contributor to maternal deaths in the District of Lebak. Baduy awareness to check pregnancy at midwives has begun to increase, but for childbirth and childbirth examination has not been carried out. That is because there is a culture in the Baduy community regarding childbirth itself, as well as their adherence to the rules that have been issued by traditional leaders. The research uses a qualitative approach with the Participatory Action Research (PAR) approach. This study aims to examine the constraints and analyze the process of the formation of relationships between health workers, cadres, and heads of RT with the Baduy community in effective communication to improve modern health services during pregnancy, give birth, and postpartum in the Baduy community. The results showed that modern health services can be applied to the behavior of pregnancy, childbirth, and the puerperal of the Baduy community if the agents of change (organic intellectual) can change the idea of the modern health service into an ideology, then popular belief is obtained, then hegemony is formed from the agents of change. The final stage is that the country must be able to accommodate this effort. The efforts of agents of change (organic intellectuals) from the idea of modern health services to the created hegemony are sought by effective communication. Implementation of effective communication is pursued by provding explanations that are easily understood by the public through simulations.

Keywords: hegemony, modern health services, pregnancy, childbirth, postpartum

1. Introduction

The culture of childbirth that occurs in the Baduy community is the culture of childbirth performed by pregnant women themselves before labor or without birth attendants. Not infrequently in the process of labor, the mother experienced bleeding or complications of labor that ended in death because the mother was late getting medical help. This condition can occur, because pregnant women in Baduy are not accustomed to carrying out routine pregnancy examinations in health workers and delivery in health facilities. They still entrust the paraji shaman t check their pregnancy. The paraji helps the mother and baby after the delivery proces.

Cases of maternal deaths in Lebak Regency in 2018 there were 47 deaths or 195/100,000 live births, while infant deaths reached 450 cases or 19.7/1000 live births. That number has increased from 2017, which is as many as 40 cases of maternal death or as much as 166/100,000 and as many as 431 infant deaths or as much as 18.1/1000. Lebak Regency ranks third in terms of high maternal mortality rates. Kanekes Village, where Baduy people live, is the biggest contributor to the number of deaths in Lebak Regency. Childbirth itself contributes to the cause of maternal death.

To support the program to accelerate the reduction of Maternal Mortality Rate (MMR) and Infant Mortality Rate (IMR) in the Baduy community, in 2019 an activity was carried out to help open mindsets and provide understanding related to the health of pregnancy and birth. The implementation of these activities is by building effective communication in an integrated manner with traditional rituals or ceremonies hat are usually carried out during the process of pregnancy and birth in the Baduy community. This approach will facilitate the transfer of

knowledge related to understanding pregnancy and birth health through modern health services. It is hoped that the provision of effective communication interventions will also enhance the insights of the Baduy community so that they can think critically about modern health services. Hafaz, said that there is a relationship between competence (in this case increasing insight) with critical thinking so that someone who has good insight will be easier to apply his mindset. Therefore, by providing effective communication, it is expected that the three target groups can continue the transfer of knowledge to the Baduy community, especially pregnant and childbirth women. So, they will routine examine pregnancy from the beginning of pregnancy until delivery. Delivery by midwife is also expected to increase.

In previous years research indicated that there were three targets for establishing effective communication in the Baduy community. The three targets are midwives, cadres and RT heads. In 2019 the research team seeks to implement interventions towards these three targets and empower various components in the community to improve modern health services. There is a relationship stage that developed when the modern health service program was developed in the Baduy community. These stages can be used as learning if a policy is applied to people with specific cultures.

Gramsci's hegemony approach is used to analyze the implementation of effective communication in the implementation of modern health services during pregnancy, childbirth, and postpartum. Gramsci (1987) has written many things in Prison Notebooks. A collection of writings containing various things that can be used in social life. Faruk (1999) argues that there are at least six key concepts in Gramsci's thinking, namely culture, hegemony, ideology, popular belief, intellectuals, and the state. The hegemony of organic intellectuals is needed about to with concerning the ideology developed. The existence of an ideology about something at first might be immediately accepted without opposition. In reality, after the activity is running, there are some obstacles or disagreements about it. Such a situation requires the existence of hegemony from the disseminator of the ideology by considering the local culture so that other parties can be embraced to lead to a conducive situation that supports the smooth running of an idea. Ideology can be accepted by the community if it can be accepted by the common sense of the community, so it is considered not contrary to local culture. In the end, ideology is truly acceptable in people's lves and becomes something popular and trusted by them.

The process of creating hegemony requires what is called a 'historical bloc'. The historical bloc is an alliance of various social forces that are united politically in a set of hegemonic ideas. Hegemony itself is created through the practiceof submission and consent. The idea owner must be able to create a 'historical bloc' to fight for its ideas into a universal worldview. Therefore, 'ideas' play an important role. For a group to submit and win the approval of another group, it must 'import' ideas. Therefore, for Gramsci, an idea will only find its transformative momentum if it becomes an ideology. The ideology must have a material basis, be driven by an 'intellectual', and then become a universal view (Sugiono, 1999).

The concept of hegemony from Gramsci can be used for the application of new things which incidentally are not yet generally implemented in communities in certain areas. Initially, there were ideas in the form of modern health services during pregnancy, childbirth, and postpartum which would be applied to the Baduy community. The idea is difficult to apply because initial habits that exist in the Baduy community. For this reason, the idea must be encouraged by three target groups (midwives, cadres, and RT heads) who are termed as organic intellectual groups. The intellectual group must try to provide understanding so that modern health services can be understood, approved, and run by all levels of Baduy society. Therefore, modern health services must be the transformation from an idea into an ideology in the Baduy community. If this has happened, it can be said that the three target groups have gained "popular trust" from the community. If all community groups have accepted and implemented recommendations regarding modern health services in pregnancy, childbirth, and postpartum, then it can be said that the hegemony process has proceeded in that phase. For this reason, "the state" in this case is the center of public health and the Lebak District Health Office needs to accommodate the course of these activities.

The three target groups implementing effective communication are health workers (midwives), cadres, and RT heads. Effective communication is built by holding continuous meetings between the three targets with the Baduy community groups, conducting simulations to facilitate implementation in the field, and integrating traditional rituals or ceremonies that are usually carried out during the process of pregnancy and birth in the Baduy community.

1.1 Research Objectives

1. Assessing the obstacles of implementing modern health services during pregnancy, birth, and postpartum in the Baduy community. 2. Analyzing the relationship process between midwives, cadres, and heads of RT with the Baduy community in effective communication to improve modern health servces during pregnancy, birth, and

postpartum in the Baduy community.

2. Method

In this study, the respondents of the study were all the people of Outer Baduy who resided in the Village of Kanekes, Subdistrict of Cisimeut, District of Lebak, Province of Banten. The selection of informants and agents of change in this study was done by purposive sampling. The informants in this study are policymakers and managers of the Maternal and Child of Health Program at the district, sub-district and village level, village officials, health workers, and health cadres who were willing to be interviewed. To further explore the culture and rituals in the Baduy community, in-depth interviews were conducted with several community leaders, traditional leaders, and kokolot who knew more deeply about the culture and rituals of the Baduy community during the process of pregnancy to childbirth. Interviews were also conducted with pregnant and post-partum mothers as well as toddler mothers in the Outer Baduy village to complete information about Baduy behavior. The informants are expected to be able to provide the necessary information as well as provide recommendations among those who are willing to become agents of change as agents of community in helping to socialize the implementation of modern health services for pregnant and giving birth mothers.

Change agents to be selected are community leaders, traditional leaders, and religious leaders, health cadres. They are Outer Baduy people who have a spirit of volunteerism, care, willingness, and sincerity to encourage the community to do modern health services during pregnancy, childbirth, and postpartum. The change agent selection based on the results of discussions with traditional leaders, the village head, the center of public health team, and the Lebak District Health Office team. Change agents need to be aware of the variousleadership styles and the situations where they would be most effective (Fletcher, 1988).

This research uses Participatory Action Research (PAR) method because it is done by building participation from all parties involved in the research including the research team, the Lebak District Health Office team, the center of public health team, the village team chaired by the village head, community leader consisting of traditional leaders and other informants around the research location to link the research process to the process of social change.

3. Results

3.1 Assessing the Obstacles of Implementing Modern Health Services during Pregnancy, Birth, and Postpartum in the Baduy Community

In the Baduy community, there is a culture of childbirth itself. Until now, still many people who give birth on their own, only assisted by immediate family members. Some people ask for a shaman's help if the baby is born. Batubara's research (Batubara, 2012) stated that of the 12 informants, ten people answered giving birth alone and two others with the shaman. They usually give birth in a narrow room, there should be no light and holding on to cloth tied to the wood on the ceiling of the house. At the time of the birth lighted incense and one of family member bursts of panglay (plants whose tubers such as ginger) from the family for the smooth delivery process. The term of traditional ecological knowledge has interchangeably used with various terms, including local knowledge, indigenous technical knowledge, and folk knowledge (Ellen & Harris, n.d.). It can be defined as 'a cumulative body of knowledge, practice, and belief, evolving by adaptive processes and handed down through generations by cultural transmission, about the relationship of a living being (including humans) with one another and with their environment.

The independent birth process is usually carried out by mothers who give birth in Baduy. Previously, pregnant women also did not carry out antenatal care from the beginning of pregnancy to delivery, because they lived in a field. Many mothers give birth alone in the field without the help of midwives or shaman (paraji).

In the prenatal process, shaman usually helps to massage the stomach of a pregnant woman so that the fetus is in a good and correct position, or provide herbs for a smooth pregnancy during delivery. After childbirth, paraji helps the mother's healing during the postpartum, and if there are disturbances during breastfeeding, and helps care for the baby until the umbilical cord is removed. Paraji is also often regarded as shamans of all diseases, including diseases caused by spirits. They usually give information about plant information that can be used as a medicine, how to process, and use it. The treatment carried out by traditional healers is also accompanied by mantras or certain incantations. In the traditional hears of Baduy, there are paraji (shaman that help to give birth), panghulu (shamans who take care of deceased people), bengkong jalu (shaman for male circumcision), and bengkong bikang (shaman for female circumcision). Paraji not only takes care of the delivery but also helps from before to after delivery (Permana, 2009).

That habit creates its problems when the mother gives birth must be referred. Usually, for this purpose the process is complicated. Sometimes the family refuses to refer to the mother who is going to give birth. The reason the

family is because the mother can still be cured with spells. Midwives must talk first with the heads of RT or local leaders so that it is not difficult to refer them. The results of Nurhayati and Sugiharto's research stated that most of the informants chose a traditional birth attendant as the main birth attendant, because of local traditions (Nurhayati & Sugiharto, 2019). In the Baduy tradition, the role of traditional leaders is very large in giving approval to refer mothers who will give birth. They rely more on the shaman to handle cases that need to be referred.

Obstacles in the community in choosing the way of delivery and utilizing health services are very influenced by the formal education of the Baduy mothers. The average Baduy has not received formal education because of the rules that are still held by residents not to change everything that already exists. Formal education is needed to open up mothers' insights in utilizing health services. Kusuma's research (Kusuma, 2018) explains that good education opens up mothers' insights to think broadly about the utilization of health services. The level of education and sources of information received by pregnant women influence knowledge about pregnancy and childbirth so that pregnant women can decide delivery in health care facilities.

The midwives who work in Kanekes Village are mostly residents of Leuwidamar istrict. They all live outside the Kanekes Village because according to the prevailing custom, they cannot build buildings in the Baduy community area. If childbirth is not carried out in a health facility, in this case, the center of public health, then there is an assumption that their services in helping with childbirth cannot be paid. That assumption is wrong because Permenkes no. 97 of 2014 Article 14 paragraph (1) which says that labor must be performed in a health service facility does not mean that there is a prohibition on midwives to deliver labor outside the health facility (Kemenkes, 2014).

Other obstacles to the health of pregnant women and post-partum mothers also relate to certain dietary at that time. Pregnant women in sub-village of seven have restrictions on eating certain fruits because they worry will happen something to their babies. Postpartum mothers usually only eat cassava/tubers only. They are usually not allowed to eat eggs and meat, because they worry that the mother's uterus is swollen. Midwife in sub-village of four explained that the postpartum mother in that sub-village is not allowed to eat fish, spicy food, and foods with coconut milk.

2. Analyzing the relationship process between midwives, cadres, and heads of RT with the Baduy community in effective communication to improve modern health services during pregnancy, birth, and postpartum.

Various obstacles when the implementation of modern health services during pregnancy, childbirth, and postpartum in the Baduy community arise an idea about improving modern health services. Modern health services in this case are efforts to examine the mother during pregnancy, childbirth, and examine the mother and baby during postpartum to health workers. Deliveries at health facilities are also expected to increase. The development of these ideas in the Baduy community is not easy, because of the culture of childbirth itself that has been on them. Therefore, midwives as the spearhead of pregnancy and childbirth health services can be regarded as organic intellectuals. In this case, the midwife is one of the agents of change. Other agents of change are cadres and heads of RT.

Organic intellectual functions to change the idea of modern health services into an ideology or something that can be accepted by the Baduy community. If the ideology has been accepted by society, then it can be said that organic intellectuals (midwives, cadres, and heads of RT) have gained popular trust. Efforts to gain trust from the community are carried out by providing understanding to the community. Understanding will arise if the community has enough knowledge from people who are trusted. For this reason, effective communication is carried out with the Baduy community. Effective communication is a continuous effort from midwives, cadres, and heads of RT to increase knowledge and insight of the Baduy community so that modern health services can be understood and applied during pregnancy, birth, and postpartum.

The initial step is to equip the three target groups, namely midwives, cadres, and heads of RT with various matters relating to modern health services during pregnancy, childbirth, and postpartum. Midwives are given material about health and cultural aspects that they must understand. While for cadres and heads of RT, the material provided is balanced between the problems of modern health services and certain cultures that are obstacles in their implementation. These three groups were also carried out simulations to clarify the steps that they had to apply to the community. The essence of the simulation is so that pregnant women get attention from cadres, heads of RT, and local public figures (kokolot). The aim is to make it easier for pregnant women to get modern health services.

The next step is to hold meetings at various groups and levels in the Baduy community. Community groups that have been described regarding modern health services during pregnancy, childbirth and postpartum are groups of pregnant women, husbands or family members of pregnant women, a shaman that help labor (paraji), and village

officials. Baduy communities have traditional leaders who important role in decision making. Important decisions relating to the socio-cultural life of the community must be approved by traditional leaders. Meetings with various levels of Baduy traditional leaders were then held. The meeting began with the Kokolot, Kokolot Lembur, and Jaro Tujuh Tanggungan. The result of the meeting was the approval of modern health services for pregnant, childbirth, and postpartum. Community leaders also agreed to monitor and support examine mothers of pregnant and labor at midwives.

4. Discussion

The life of Baduy residents has a socio-cultural system that is based on local wisdom. Local wisdom can be interpreted as a way of life, knowledge, and life strategies that carried out by local communities in answering various problems, covering all elements of life; religion, science, and technology, social organization, language and communication, and art (Suparmini & Setyawati, 2013). Local wisdom about pregnancy, childbirth, and postpartum is in the form of traditional ceremonies to achieve good conditions for mothers and babies. The traditional ceremonies are as one of the media to carry out effective communication. Midwives can interact more with residents in the target area if present at these traditional ceremonies. The presence of midwives on that traditional ceremonies can be used to convey messages relating to the health of the pregnancy, childbirth, and postpartum. At the ceremony usually a paraji present. The presence of paraji can be used by midwives to establish partnerships. It seems, for this time, still no high interest from the midwives to attend the traditional ceremonies. Midwives felt that they were not invited to the event. Midwife Ros, as a midwife who has long interacted with the Baduy community, shared some of her experiences while attending a traditional ceremony. He said that he was not invited to traditional ceremonies related to pregnancy, childbirth, and postpartum. Mrs. Ros attended at the various ceremonies by directly. She came to the homes of residents and helping mothers who were cooking for ceremonial purposes. The presence of Midwife Ros on that ceremony is one of the effective ways to approach citizens. Therefore, the research team also tried to make midwives more often present at the traditional ceremonies.

In the process of ongoing effective communication at various community groups and levels of traditional leaders, as well as integration with traditional ceremonies, this is where hegemony with the cultural approach of midwives, cadres, and heads of RT begins. The three groups are also called organic intellectuals. Organic intellectuals carry out a continuous approach so that the community and traditional leaders want to examine pregnancy, childbirth, and postpartum on health workers. These efforts were successful in the community. Pregnant women in the Baduy community began to examine their pregnancy by midwives and to be referred to health facilities. The momentum indicated that the three groups that carried out hegemony efforts had gained popular trust from the public. The situation also illustrates that the hegemony of organic intellectuals (midwives, cadres, and heads of RT) has been realized in changing the Baduy community's perception of modern health services for pregnant, childbirth, and postpartum.

During the meeting of pregnant women at the center of public health, the coordinating midwife and village midwives explained important themes that should be known by pregnant women. The first theme is about nutritious food for mothers, the second theme is about pregnancy examinations by midwives, the third theme is information about babies with Low Birth Weight (LBW) and ways to prevent it. This theme is also explored, because of the high prevalence of underweight and stunting toddlers. The prevalence of underweight in Baduy toddlers is 26.4%. The prevalence of underweight for Baduy children is higher than the prevalence of underweight children in Indonesia as a result of the 2007 Basic Health Research (Badan Penelitian dan Pengembangan Kesehatan, 2007), which is 18.4%. The overall stunted prevalence is 60.6%. This prevalence is much higher than the prevalence of stunting of children under five years in Indonesia as a result of Riskesdas 2007 which is only around 36.8% (Anwar & Riyadi, 2009). The fourth theme is the signs of a problem pregnancy. The fifth theme concerning the integration of handling maternity mothers by midwife and paraji. Midwives provide help if bleeding occurs.

The coordinating midwife also explained the Mother and Child Health Book (KIA Book). The contents of the KIA Book were also elaborated so that the Baduy mothers better understand the pictures in that book. The first thing if there is a pregnant woman in the house, so the sticker posted on the door of the pregnant woman's house. Data on pregnant women who come to the posyandu are filled in the book. At the end of the meeting, Midwife Ros also appealed for pregnant women who began to feel heartburn to immediately notify the cadre, so that the cadre could immediately notify the midwife.

The support of community leaders from each village is different, some are ignorant, but also those who support. The community in sub-village of five explained that the traditional leaders were very supportive health workers. Health workers must permission from traditional leaders. A cadre in sub-village of seven tells us that community

leaders support, but not many people come to the midwife. In essence, mothers are allowed by community leaders (kokolot) to be examined at posyandu or in health workers. Example: Customary leaders in Kampung Cempaka, Subvillage of two, and Kampung Ciwaringin, sub-village of three are very supportive as long as they do not violate custom. Community leaders and religious leaders in sub-village of two, five, six, seven, eight, and nine also support efforts in the health sector. Even so, in the whole of the sub-village, there are still many people who come to paraji (shaman) at 1-9 months of pregnancy, because the paraji have spells and massage mothers. So the awareness of citizens to check with health workers is still lacking.

The head of RT (neighborhood association) supported the health sector. The support from them to encourage residents to examine her pregnancy. The head oh RT heads also explained that midwives would not harm the community, but would improve the public health.

Pak Ijom, one of the heads of RT in sub-village of five said:
"Our life patterns have changed. This is one factor. So we must also follow the changes. "
The heads of RT also admitted that there were heads of RT who were less concerned about health issues. Therefore, at each meeting stressed the importance of three-party interaction to effective communication. The active interaction of the three components (midwives, cadres, and heads of RT) is needed. If there is one less active component it will disrupt the objectives to be achieved.

All efforts that have been carried out by organic intellectuals need to be contained by the state. The state in this case is the center of public health than the Lebak District Health Office. The efforts of the center of public health and the district health office are aimed at the change in community perception that can be continued.

The district health office is aware that the Baduy community in Kanekes has specific something for helping labor. Their large area makes it difficult to refer to mothers who need further medical treatment. A mother who was referred to was certainly accompanied by other family members. The family members who accompany her certainly place to stay. The employee of the district health office then discussed with the employee of the hospital, so that the place could be provided. After that, there is a rule that allowed a mother who was referred could be accompanied by three people for three days. They can stay in the room that has been provided by the hospital and they also get food. The effort was carried out because so far the existing waiting houses have not been utilized by the community. Maybe family members have looked for a place that is closer to the family member who is being treated. The employee of the district health office will give information about the hospital to refer to. Therefore, mothers who are referred must be reported to the district health office. Currently, the district health office has provided various innovations related to improving maternal and child health. Efforts have continued to be increased in the last four years. One effort is to develop the application of Healthy Ambu. Healthy Ambu application is an application to monitor pregnant women to be healthy. The application is an effort to support the regulation of Banten Governor number 26 of 2016, because the head of Lebak District is indeed very responsive to the health of mothers and children. Besides that, *imah pangubaran* (waiting for a house) was also established. Another effort is cadre training. All midwives re also encouraged to approach the community.

Efforts from the center of public health to improve maternal and child health are the delivery of information to the community, encouraging the community to be examined and giving birth to midwives, referring high-risk pregnant women, and reminding that all center of public health staff is committed to encouraging pregnant women to examine and give birth at the center of public health. The center of public health has also tried to the relationship with the head of village and community leaders to reduce the number of deaths. The supports are the form of their interaction with community empowerment efforts. Effective communication carried out by the team aims to increase community empowerment.

5. Conclusion

There is an idea to increase the implementation of modern health services during pregnancy, childbirth, and postpartum in the Baduy community. An idea can be accepted by the community if the idea is considered not contrary to local culture and some organic intellectual actors have changed into an ideology. Midwives, cadres, and heads of RT are agents of change or organic intellectuals who have succeeded in changing the idea of modern health services into something that can be accepted by the Baduy community. The actions of the agents of change that have succeeded in changing the views of the Baduy community towards modern health services indicate that they have gained the trust of the community (popular trust). The agents of change or organic intellectuals have been able to apply their hegemony to lead the public in implementing modern health services. The final stage is the state's efforts to oversee the modern health service policy for the Baduy community to be sustainable.

The efforts of agents of change (organic intellectuals) from the idea of modern health services to the created

hegemony are developed by effective communication. Effective communication is an effort that is carried out continuously to communicate something that is the goal of the activity, in this case, is modern health services. In the Baduy community, there are several levels of traditional leaders. Effective communication is carried out in stages with these traditional leaders groups, so that, the modern health services get approval to be implemented in the Baduy community. The effort was carried out by considering the Baduy culture. Therefore, promotion about modern health services is also carried out through the presence of agents of change in traditional ceremonies relating to pregnancy, childbirth, and postpartum.

Implementation of effective communication is provided explanations that are easily understood by the public through simulations. The simulation of effective communication resulted in seven steps that must be considered by midwives, cadres, and head of RT in implementing modern health services. The seven steps are: 1. cadres go to pregnant women for data collection, 2. cadres come to the head of RT to report the results of the data collection, 3. head of RT comes to pregnant women to deliver messages regarding examine pregnancy and childbirth at the midwife and complete population administration, 4. cadres submit baseline data to midwives, 5. midwives accompanied by cadres visit pregnant women to carry out examinations and deliver health messages, 6. midwives with a head of RT visit to the kokolot. The kokolot is expected to support these activities, 7. midwives and cadres carry out promotive and preventive efforts include presence at traditional ceremonies related to pregnancy, childbirth, and postpartum.

6. Recommendation

1). Formulating policies for the implementation of effective communication based on various meetings that have been held with religious / community leaders and simulations that have been practiced between the community and cadres, religious/community leaders, and health workers.

2). Providing information about pregnancy and childbirth at traditional ceremonies.

3). Cisimeut Community Health Center and Lebak District Health Office monitor the implementation of a modern health service improvement system by means of effective communication.

4). Ensure the availability of a budget for cadres and budget for implementing maternal referral.

5). It is necessary to have additional health facilities in the form of auxiliary health centers or village health pos especially for bungur who are far from Cisimeut Community Health Center.

6). The need for improving the quality and retraining cadres of Kanekes Village.

7). There is a need for more intense support and coordination from the Health Office to the health workers at the Cisimeut Community Health Center.

8). The need to improve the overall quality of human resources in Cisimeut Community Health Center.

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The authors declare that there are no competing or potential conflicts of interest.

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Factors Contributing to Pregnancies Among Tertiary Students at the University of Namibia

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Abstract

The Government of Republic of Namibia through the services rendered by the Ministry of Health and Social Services (MoHSS) continues to provide various free health services including contraceptives to its citizens. Nevertheless, several challenges related to unplanned pregnancies among tertiary student's remains a challenge, which includes poor reproductive health status, socio-economic consequences rapid-population growth, rural-urban migration of youths accompanied by proliferation of informal settlements around cities, high youth unemployment and crime. This requires institutions of higher learning to establish which strategies are likely to address these problems of unplanned pregnancies among tertiary students. The aim of this study was to explore and describe the contributing factors to pregnancies amongst tertiary students at a selected satellite campus in order to make recommendations to the University of Namibia (UNAM).

An exploratory, descriptive and qualitative design was used. The study was contextual in nature. A convenient sampling was used. The data were collected through three focus-group discussions with 19 students from the three faculties namely: Education, Health Sciences and Management Sciences. Data were analyzed through qualitative content analysis. Strategies to ensure trustworthiness and ethical implementation of the study were implemented. It became evident from the study findings that factors which are contributing to pregnancies, as evidenced by the four emerged themes namely: Personal factors, institutional related factors and improvements measures. This study has implications for higher education institutions in terms of promoting sexual and reproductive health information and increasing access to a range of contraceptive methods of campus which are key in the prevention of pregnancies among tertiary students. Participants in this study recommended that peer educators and students counsellor within the campus should be used as a vehicle to provide support and guidance to students on reproductive health choices.

Keywords: challenges, contraception, factors, pregnancy, student

1. Introduction

Worldwide, every year, around 87 million women become pregnant unintentionally, and this is a significant number, (WHO, 2018). According to Bearak, Popinchalk, Alkema, and Sedgh, (2018), during the period between 2010 and 2014, an estimated 44% of pregnancies worldwide were unintended. This translates to a rate of 62 unplanned pregnancies per 1,000 women aged 15 to 44 years old Bearak et al. (2018). There was also a significant difference between overall unintended pregnancy rates in developing and developed regions. In the same period, there were 65 unintended pregnancies per 1,000 women aged 15 to 44 in developing regions, compared with 45 per 1,000 women in developed regions. The high rate of unintended pregnancy in developing regions is said to be related to the great unmet need for contraception in those areas, Bearak et al. (2018).

Additionally, in low and middle-income countries, an estimated 16 million young women aged 15 to 19, and about a million girls under 15 years of age give birth every year (Dick & Ferguson, 2015). Moreover, Adolescent child bearing (intended or not) has adverse effects at the individual, community, and societal level. Compared with their peers who delay childbearing, young women who have babies are less likely to finish high school, more likely to be poor as adults, and more liable to have kids who have poorer behavioural, educational, and health outcomes over the course of their lives (Cook & Cameron, 2015).

Statistics for South Africa for 2017 reported that prevalence of pregnancy increased with age, rising from 0, 6% for females aged 14 years, to 10, 7% for females aged 19 years (General Household Survey, 2017). Most students at higher institutions are actively involved in searching and discovering, as well as sexual experimentation. For this reason, students very so often engage in unsafe sex, which put them at a higher risk of contracting STIs, (including HIV/AIDS,) as well as unwanted pregnancies. In addition, unwanted pregnancy is the main cause for female students dropping out from school and poses serious health, social, and economic problems for student. At the same time, it reported that adolescent pregnancy is a major cause of interrupted and discontinue education (Fekede, 2015).

WHO, (2018) of the estimated 211 million pregnancies that occur each year, about 46 million end in induced abortion. The rate of adolescent pregnancies in the Kavango region is 27% of all adolescent pregnancies in Namibia, and this is the highest rate nationwide. Moreover, Kavango region has the lowest average age at first birth in Namibia, which is 19.3 years old (NDHS, 2013). The government of Namibia has a great policy in place, of providing different types of contraception free of charge, so as to prevent unintended pregnancies, (Consolidated National Reproductive and Child Health Policy, 2008). However, according to UNICEF, in Namibia, 76% of sexually active adolescent girls (aged 15 to 19 years) do not use modern methods of contraception, (UNICEF, 2013). Statistics also reveal that 6.8% of adolescent girls aged 15 to 19 have their first sexual encounter by the age of 15, and an additional 3.9% of women, by age of 20 to 24 years old. This therefore means that at the time of enrolling into universities, students are at an age of about four years above the popular age of first sexual encounter in Namibia, suggesting that they are usually sexually active, (UNICEF, 2013).

Adolescence is widely known as a developmental phase in the human lifecycle between childhood and maturity and a lot of changes take place which affects individuals in different ways (Thongnopakuin, Pumpaibool, & Somrongthong, 2018). During this phase young people go through different changes in terms of their physical, cognitive, emotional, and sexual development. These changes turn out to be risk factors for premarital sexual behaviour, adolescent pregnancy, abortion, and sexually transmitted diseases (STDs), such as acquired immunodeficiency syndrome.

The practices of university students with regards to contraception are reported to be low in Namibia (Tatenda, Ashipala, Endjala, & Tomas, 2019). However, throughout the world, female students are at risk of unplanned pregnancies as a result of ineffective use and non-use of contraceptives, Coetzee and Ngunyulu, (2015). Consequently, pregnancy among tertiary students is one of the major cause of interrupted and discontinue education (Fekede, 2015). Pregnancy has a detrimental effect on the education and future of tertiary students, this is because young mothers are obliged to attend to their education irregularly and sometimes drop out of school. Cultural practices is identified as one the factor to pregnancies among students as it prohibit young women to talk about sex at home with their mothers nor with anybody else (Krugua, Mevissena, Münkela, & Ruitera, 2018). Absence of designed programs that teach students regarding sex education at the campus was reported as a major contributing factor to pregnancies among tertiary students (Fekede, 2015). Additionally, female students who used alcohol and drug abuse were more likely to experience teenage pregnancy compared to those who did not use (Mathewos & Mekuna, 2018).

2. Methods

2.1 Design and Setting

The study used a qualitative research design, in particular, an explorative, descriptive and contextual research design to explore the factors contributing to pregnancies among tertiary students as described by them individually (Babbie & Mouton, 2016; Creswell, 2013). The study was conducted at the University of Namibia, north-east region of Namibia. The satellite campus is part of the University of Namibia and offers undergraduates courses through three faculties namely: Education, Health Sciences and Economic and Management Sciences. Qualitative research is concerned with the everyday human experiences within a natural environment (Maree, 2016). The focus group discussions which were conducted enabled the researcher to search for similarities in the meaning of the core factors that are deemed to be the root contributing factors of pregnancies among participants. The study focus group discussion focused on exploring the contributing factors of pregnancies among students as they have had occurred (Creswell, 2013,). The use of the used focus group interview was facilitated through the use of open ended questions which oriented the participants to the study (De Vos, Strydom, Fouche, & Delport, 2011).

2.2 Population and Sampling Strategy

Grove, Burns, and Gray (2013) define a study population as a bigger pool from which sample elements are

drawn. The population in this study consisted of 804 students enrolled at a University of Namibia, in three faculties, namely: Health Sciences, Education and Economic and Management Sciences. A sample is a subset of the population elements (Polit & Beck, 2017). The sample in this study comprised of all students studying at University of Namibia in 2019 on a fulltime study mode. The researchers approached participants face-to-face in the classroom at the university campus and the purpose and objectives of the study were explained to them. A convenient sampling was used to drew a sample of nineteen (n = 19) readily available students from a total of 804 registered at the campus (Brink, van der Walt, & van Rensburg, 2018).

2.3 Data Collection Methods

Grove et al. (2013,) define data collection as the exact, systematic gathering of information related to the research purpose of the intended study. Data in this study were collected between 10 July 2018 and 28 October 2018, through focus-group discussions. The students that were willing to participate in the study were recruited by the researchers, while the time and venue for discussions were arranged with them accordingly. A total of three focus-group discussions were conducted, which consisted of each six, six and seven participants each. The discussions lasted about 50 to 60 minutes, and the number of discussions held was determined by data saturation (Polit & Beck, 2017). The researcher used a semi-structured focus-group discussion guide, with a prepared written topic guide prior to the discussions; however, probing questions were used to further explore participants' responses and to stimulate more detailed information (Polit & Beck, 2017). All focus-group discussions were audio recorded using a digital voice recorder. Pilot testing was conducted with a focus-group discussion of 6 students, which helps to refine the topic guide and other data-collection plans (Creswell, 2013).

2.4 Analysis

The aim of the data analysis process is to organise, impose structure on and elicit meaning from data which has been collected (Groove, 2013). In this study content analysis was used to analyse the data as this is deemed to be the most reliable method used in qualitative research as it is fairly systematic and it allows the researcher to organise the information into themes and sub-themes (Leedy & Ormrod, 2013). The transcribed interviews and narratives from the research notes were organised into codes, main themes and sub-themes. An independent coder then verified the accuracy of the analysed data and held a meeting with the researcher to discuss and agree on the themes which had been identified. Data were stored in a computer encrypted with a password and restrict access to this document was only allowing primary investigators access.

2.5 Data Trustworthiness

Furthermore, trustworthiness was ensured following the principles of Lincoln and Guba (1985), which consists of the criteria of credibility, dependability, conformability and transferability.Credibility was ensured through prolonged and varied engagement with the participants in the field while objectivity was maintained throughout the data collection process. Testing of the interview guide was conducted with three students who were not part of the study. However, no major changes were made to the focus group interview guide questions after the testing of the focus group interview guide. In order to ensure both confirmability and dependability an experienced independent coder analysed the data. The final themes and subthemes were identified after a consensus has been reached during a meeting between the researcher and the independent coder. A chain of evidence was kept through the detailed recording of both the research methodology and the data analysis process.

2.6 Ethical Considerations

Ethical approval to conduct the study was obtained from the School of Nursing Research Committee at the University Of Namibia Faculty of Health Sciences. The researcher obtained the participants' personal consent in relation to their participation in the study after the purpose and significance of the study has been explained to them. Ethical principles were adhered to throughout the study in order to protect the rights, dignity and safety of the participants (Grove et al., 2013). Participation in the study was voluntary and the participants were free to withdraw from the interviews at any time if they so wished (Creswell, 2013). Confidentiality was ensured as each participant was given a numerical code at the beginning of the structured interviews which was then used to refer to the participant during the interviews and which subsequently appeared on the transcript of the interview to ensure anonymity (Grove et al., 2013).

3. Findings

3.1 Description of Study Participants

The participants were all fulltime undergraduate students studying at the University of Namibia, Rundu campus

situated north-east of Namibia. All the participants were under the age of 40. The majority of the participants were unemployed. The characteristic of study participants is given in the Table 1 below.

Table 1. Characteristics of participants

Age	
18–30	15
31–40	4
41–50	0
Ethnic tribe	
Oshiwambo	8
Kwangali	5
Nyemba	3
Others	3
Gender	
Male	0
Female	19
Marital status	
Single	17
Married	2
Faculty	
Health Sciences	6
Economic and Management Sciences	6
Education	7
Level of study	
First year	3
Second year	4
Third year	6
Fourth year	7

The themes and subthemes from the data analysis are indicated in Table 2 below.

Table 2. Themes and Sub-themes which emerged from the data analysis.

Themes	**Sub-themes**
3.2 Personal factors	3.2.1 Socio – economic factors
	3.2.2 Lack of sexual and reproductive health information
	3.2.3 Cultural factors
	3.2.4 Peer influence
	3.2.5 Alcohol and drug abuse
	3.2.6 Gender power relation
3.3 Institutional factors	3.3.1 Lack of recreational facilities
	3.3.2 Lack of contraceptive on campus
3.4 Mechanism for improvement	3.4.1 Access to the NSFAF funding
	3.4.2 Sexual awareness programmes and campaigns
	3.4.3 Accessibility to contraceptives
	3.4.4 Peer educators/counsellors within the campus

3.2 Theme 1: Personal Factors

This theme reflects the factors that are perceived to be contributing to pregnancies among tertiary students at the University of Namibia. The sub themes expressed by participants include socio-economic status, lack of sexual and reproductive health information, cultural factors and peer influence.

3.2.1 Socio-Economic Status

Participants revealed that students are dating of older men in the society who are able to render financial support to them. This was confirmed by few extracts which are provided below:

"It's a personal decision whether to date a man with money so you can buy yourself an iphone and other fancy stuff)" (P2G1)

Some participants who indicated to come from poor families confirmed that being at the university require smart phones as the university prefer to communicate through students' portal and most of the academic activities require the use of smart phones. Their family cannot afford to buy them one while dating a man you love, who can afford can be alternative.

"Just make a wise decision that fit your circumstance, but of course the problem if he wants a family it will mean I may sacrifice to get pregnant as his reason is that he can afford to take care of the baby" (P1G3).

3.2.2 Lack of Sexual and Reproductive Health Information

The storylines provided below attest that participants were worried by the fact that there is no sexual and reproductive health information on campus.

"Imagine you are first year, fresh from secondary school, it is difficult to make the right options with regard to sexual and reproductive health" (P6G2).

"There is no facilities on campus and public facilities have long queues, one must miss classes the whole day to access sexual and reproductive health information" (P5G3).

One participant indicated her disappointment on the unavailability of Awareness Clubs on campus to educate and sensitise students on sexual and reproductive health.

"I have never got any sexual information on the campus, maybe now that the school of nursing is her, things will improve"(P7G1).

3.2.3. Cultural Factors

Most participants acknowledged that parents are reluctant to discuss sex related issues even with grown up children. Most participants indicated that some culture expect women to give birth or even get married early in life. The expressions from the participants regarding culture presented below clarified how they felt:

"My parent would never talk to me about sex" (P3G1).

On the other hand, one participant who confirmed talking to her mother about sex was informed that it was a taboo to discuss sex with children.

"As I tried to talk to my mother about sex, she immediately told me to shut up" (P7G2).

3.2.4 Peer Influence

It was evident in most participants' responses that friends influence each other's' decisions about sex. Most participants acknowledged that they had discussed sex with their friends and that sometimes had to indulge into unprotected sex because a friend promoted it them.

"I was moved by my friend' statement…Sex is a basic need and having a child while younger have more benefits" (P6G3).

"If you cannot give your man a child, while having sex with him, you are regarded as a prostitute" (P5G1).

3.2.5 Risky Sexual Behaviours

Some participants believed that most of the students abuse alcohol and drugs end up indulging in unprotected sex.

"…You know how it feels to be tipsy… you may be less worried of the consequences and your guy may take advantage" (P4G1).

Most participants confirmed the abuse of alcohol by indicating that they spent most of their free time at bars and shebeens drinking alcohol.

"One get excited when it is a Friday, we contribute for booze" (P4G2).

One participant confirmed that some students especially man take drugs to give them extra power in bed.

"While drug may give him power to satisfy you in bed, he may not be himself in making decisions on the usage of condom" (P1G3).

3.2.6 Lack of Contraceptive Use

Most of the participants indicated that some students are just ignorant on the use of contraceptives.

"Sex emotions are too strong to look for a condom" (P5G1).

Some participants indicated that women now use the safe period to indulge in sexual activities and they no longer depend on the use of contraceptives.

"I often have sex immediately after my periods are over" (P5G2).

3.2.7 Gender Power Relation

Most participants acknowledge having placed men a superior social status that allows them to make decisions on sexual matters.

"If a man decides on having sex, you cannot stop him" (P4G3).

Some participants expressed that it is socially acceptable and sometimes encouraged for men to be involved in premarital sexual activities while women must be passive and sexually innocent.

"If a man does not care, he likely not to use condom…as a women you have little control" (P5G1).

3.3 Theme Three: Institutional Related Factors

This theme reflects the responses given by participants when described how institutional challenges contributes to pregnancies among students on campus. The sub-themes emerges out of this theme includes, lack of recreational facilities and lack of contraceptives on campus.

3.3.1 Lack of Recreational Facilities/Boredom

Most participants expressed that there are no enough recreational facilities on campus and this may force many students to indulge in unproductive activities including sexual activities.

"You hardly have sport games on campus" (P3G3).

"The gym facilities on campus are not utilised…gymming would kill my boredom" (P4G1).

3.3.2 Lack of Contraceptives on Campus

Most of the participants indicated that condoms are not readily available in the toilets. Both men and women would at least take if condoms are placed in places of convenience.

"I would go to the nearest bar if I need condoms" (P1G3).

"There is no clinic to provide reproductive health services on campus" (P1G2).

Some participants who reside in the hostel however indicated that condoms are available at the office of the student counsellor but, only placed at one place, making it difficult for every to feel comfortable to go there when others are watching.

"I feel embarrass to enter that office and request condoms when others can see me" (P1G2).

"Condoms are not being placed at the places of convenience" (P6G3).

3.4 Theme Three: Mechanisms for Improvement

This theme emanated from participants responses when asked to express their opinion on what can be done to improve the current situation with regard to high rate of pregnancy on campus. The suggestions include access to Namibia Students' Financial Assistance Fund (NSFAF) funding, sexual awareness programmes and campaigns, accessibility of contraceptives and having peer educators on campus.

3.4.1 Access to NSFAF Funding

When asked about what can be done to reduce high rate of pregnancy among student on campus, most participants yearned for access to NSFAF funding to address students' economic hardship.

"If only NSFAF can settle student's accounts and pay out non tuition fees on regularly basis" (P6G3).

"NSFAF system is ineffective and frustrating…I did not get my refund for last year" (P7G2).

3.4.2 Sexual Awareness Programmes and Campaigns

Participants in this study revealed that Student Representative Council (SRC) under the office of Dean of students encourage the establishment of Awareness Clubs on campus to sensitize and conduct sexual awareness campaigns.

"Let the SRC of Gender Affairs and Community development take the issues of sexual and reproductive health seriously" (P2G1).

Some participants' suggested for peer educator programmes to be active on campus.

"We can learn a lot from each other, if peer educators programmes are promoted and supported on campus" (P5G3).

One participant requested for the school of Nursing to be visible and provide sexual awareness campaigns.

"Now that the School of Nursing is here, let them focus on providing sexual awareness on campus" (P7G2).

3.4.3 Accessibility to Contraceptives

The study participants suggested that the university provide a site clinic on the campus to cater for students' needs.

"We need to be treated like students at the satellite campus; The University of Namibia must build a clinic on campus for us" (P1G3).

Some participants felt it would be better if the condoms can be placed in all toilets as it is the most used contraceptive.

"Someone must be tasked to ensure that condoms are always available in all campus *toilets" (P1G2).*

3.4.4 Peer Educators/Counsellors Within the Campus

Participants suggested for peer educator to be promoted and supported to be able to conduct peer teaching on sexual and reproductive health.

"Nursing needs to be encouraged to participate in peer education on sexual matters" (P10).

4. Discussion of Findings

The purpose of the study was to explore and describe the factors contributing to pregnancies among tertiary students at the University of Namibia. This section, presents discussion of the study in accordance with themes as emerged out of the study namely: Personal factors, Institutional factors and Mechanism for improvement.

4.1 Personal Factors

It is reported in this study that some university students from poor background preferred to get romantically involved with men that are working men, as this can enable them to get the needed financial support. The study findings were in line with the Legal Assistance Centre, (2017) report on gender analysis which asserted that ladies were quoted as preferring dating older men who are well off, as a way to gain financial independence.

The study revealed that the unavailability of Awareness clubs on campus. Awareness clubs are key in the distribution and utilization of health related information on sexual and reproductive health. The findings from this study were similar to those of Donatus, Sama, Tsoka-Gwegweni and Cumber, (2018) who indicate that if communication about reproductive and sexual matters is limited it will force the affected persons to rely chiefly on information from peers and boyfriends which often mislead them into risky sexual behaviours. Tladi and Jali (2014) also pointed out to absence of guidance on issues of sex education as one of contributing factor to pregnancy. It was reported in this study that friends have potential positive or negative influences on the decision regarding sex. This best aligns with Tladi and Jali (2014) who found that most early engagement in sexual activities were due to the influence of peers and that peer influence remain on of leading method of learning more about sex. Tatenda et al., (2019) attested that about 46% of the university students have learned sex through their peers.

Participants in this study reported that parents are not open or are reluctant to discuss sex related issues with their children as it is regarded as taboo in many culture in Namibia. (Krugua, Mevissena, Münkela, & Ruitera, 2018) also identified cultural practices as one the factor that prohibit young women to talk about sex at home with their mothers nor with anybody else.

Participants in this study reported that most students spent their free time drinking alcohol or taking drugs. Students admitted that being ignorant, being under the influence of alcohol or drugs make them vulnerable to

poor decision making on the use contraception and led to many getting pregnant (Qolesa, 2017; Conradie, 2019). Fekende, (2015) indicated that about 36% of unplanned pregnancies comes as result of indulging into sexual activities will under the influence of alcohol. The study revealed that most students know where to get contraceptives but are ignorant to find and use them during sex. The findings of this study concur with the study by Conradie, (2019); Tshomo, Dorji, Wangchuk, and Tshering, (2018); Zungu and Manyisa, (2009) which reaffirmed that most of the pregnancies were as a result of not using or inconsistence use of contraception. Mutinta, Govender, George, and Gow, (2014) echoed that being sexually aroused is a strong biological factor that encourages young people to lose control and engage in sexual acts without using contraceptives and that the use of contraceptive namely condoms is unnatural and hinder skin to skin contact that bring about intimacy experience.

4.2 Institutional Related Factors

The study participants pointed out the lack of a campus based clinic as a barrier to sexual health services use among the students. Qolesa, (2017) stated that sexual and reproductive health services are pronounced as organisational factors that influence the number of unplanned pregnancies among students. On the other hand, the study participants pointed out that the lack recreational facility on campus was responsible for student's boredom. Additionally, Qolesa (2017), stressed that boredom may result in inappropriate activities including sex.

4.3 Mechanisms for Improvement

Participants in this study acknowledge that an on-site clinic would improve access to sexual reproductive health services. The Legal Assistance Centre, (2017), emphasised that access to contraception prevent unintentional pregnancy and or abortions. Participants dwelled much on the importance of peer educators on campus. The finding lend support to Tatenda et al., (2019) study on knowledge, attitudes and practice of contraception among tertiary students, which revealed that there is lack of peer educators at the University of Namibia, Rundu campus. Tladi & Jali, (2014) reiterated that awareness campaigns on sexual reproductive health help to reduce unintended pregnancies among students.

5. Limitations of the Study

The results obtained in this study were obtained from undergraduate students studying at the University of Namibia, Rundu campus. Therefore, it is not possible to generalize the study results to other satellite campuses of the University. To generalise findings, a survey of a larger target population including their male counterparts who became fathers, should be conducted to assess to which the same findings would be uncovered. Additionally, there were limited literatures on the factors contributing to pregnancies among tertiary students as much of available literature was done on teenage pregnancy.

6. Implications for the University

The focus group discussions revealed that the tertiary students were all experiencing challenges related to personal factors, sexual behaviour related factors and institutional factors. Finally, this study highlighted some improvement measures for higher education institution as a way to mitigate the challenges identified in this study.

7. Recommendations

Based on the findings of the study the following recommendations were made:

Contraceptives should be made available and accessible to the students on campus. Thus, condoms should be made available in the campus premises to increase accessibility to students. Increase access to the NSFAF funding as a way addressing economic hardships during studies. Peer educators/counsellors within the campus should be used as a vehicle to provide support and guidance to students on life choices. Additionally, implementation of sexual and reproduction health awareness programmes and campaigns within the campus.

8. Conclusion

Pregnancies among tertiary students has been recognized as one of the major social problems affecting the tertiary students and it was found that various factors that contributed to the problem were Personal factors, sexual behaviours, Institutional factors, and Improvement measures. This study has implications for higher education institutions in terms of promoting sexual and reproductive health information and increasing access to a range of contraceptive methods of campus which are key in the prevention of pregnancies among tertiary students.

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Authors' Contributions

Victoria Ben, Daniel Opotamutale Ashipala and Nestor Tomas were involved in the conceptualisation, literature review, data collection, analysis, writing of the manuscript in this study. Both authors wrote the original manuscript and approved the final manuscript for publication.

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Competing Interests Statement

The researchers declare that they had no financial or personal relationship(s) which may have influenced them inappropriately in the writing of this article.

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Contribution of Metabolic Syndrome in Controlling Diabetes Mellitus According to Gender in Indonesia (RISKESDAS 2018)

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Abstract

Background: Metabolic syndrome (MetS) is a multiple risk factor for the development of type 2 diabetes mellitus (DM). It is important to understand the contribution of MetS in developing DM in different population characteristics. This study aims to obtain the prevalence of MetS and the magnitude of the contribution of MetS risk factors as a basis for developing targeted DM intervention programs.

Methods: This study used data from the 2018 Riskesdas survey, an Indonesia national health survey, with a total sample of 24,545 individuals aged 15 years and over. This study selected only respondents who had never been diagnosed with diabetes mellitus before the survey was conducted and have complete MetS data according to the National Cholesterol Education Program or Adult Treatment Panel III (NCEP/ATP III) criteria. Data had been analyzed for the Population Attributable Fraction (PAF) statistical test.

Results: A total of 29.2 percents of the population with MetS and the prevalence in women (17.2%) was higher than in men (11.9%) Three components of MetS that contribute greatly to DM were fasting blood glucose levels, hypertension and high triglyceride levels. If the men population can maintain two risk factors (fasting blood sugar levels and blood pressure) under normal conditions, the prevalence of DM can be reduced by as much as 15 percent. In women, if three factors (fasting blood sugar levels, blood pressure, and triglyceride levels) can be maintained under normal conditions, the prevalence of DM can be reduced by 29.9 percent.

Conclusion: Prevention strategy of DM need to include monitoring and controlling of the metabolic syndrome and behavioral risk factors, that can be applied in primary health center as well as in community-based setting of health program.

Keywords: metabolic syndrome, population attributable fraction

1. Background

Metabolic syndrome (MetS) is a multiple risk factor arising from insulin resistance, accompanied by abnormal fat deposition and function. It is a combination of risk factors for type 2 diabetes mellitus, coronary heart disease, fatty liver, chronic kidney disorders, and several types of cancer (Kaur, 2014; S. Stanley, 2018). Metabolic syndrome has become a public health problem and is a clinical challenge throughout the world. Although MetS is not a disease, early detection will give a very meaningful to be overcome immediately (Magdalena, 2014). Metabolic syndrome is related to urbanization, excessive energy intake, increased incidence of obesity, and a sedentary lifestyle and is related to the effects it causes. It is estimated that in the next 5 to 10 years there will be a threefold increase in the risk of DM and two-fold cardiovascular disease. Respondents with metabolic syndrome have a risk of stroke two to four times and the risk of myocardial infarction three to four times.

The metabolic prevalence of the syndrome based on the Framingham Study cohort study in the 26–82 years age group was 29.4 percent in men and 23.1 percent in women (Khanna et al., 2013). Whereas in Europe 15 percent

(Elabbassi & Haddad, 2005), in South Korea 14.2 percent (Park et al., 2004). While in Indonesia as much as 23.34 percent of the total population (Suhaema & Masthalina, 2015).

There are 9 global targets for controlling non-communicable diseases (NCD) by 2025, among others, there is no increase in the prevalence of diabetes mellitus or obesity, a reduction in deaths from NCD (heart disease, cancer, diabetes, and chronic lung disease) until 2025, and a decrease in high blood pressure as much as 25 percent by 2025 (PAHO/WHO, 2015; WHO, 2013).

In Indonesia, the government has tried to control DM by focusing on control through (1) strengthening the management of DM according to standards in first-level health facilities (FKTP); (2) accelerated discovery of NCD risk factors through "NCD health post (Posbindu PTM)"; (3) accelerated early discovery of potentially DM cases; (4) increased monitoring of the success of DM treatment with HbA1c; (5) strengthening interventions for the magnitude of metabolic syndrome, modification of NCD risk behaviors through Posbindu PTM (Ministry of Health, 2015). While the study of the relationship between sex and the prevalence contribution of the MetS component has never been based on a national basis.

Based on the above problems, further analysis of the National Health Survey 2018 aimed to obtain the prevalence of metabolic syndrome and the magnitude of the contribution of MetS risk factors as a basis for developing targeted DM intervention programs in the development of health strategies to manage MetS according to gender in preventing the occurrence of DM.

2. Conceptual Framework

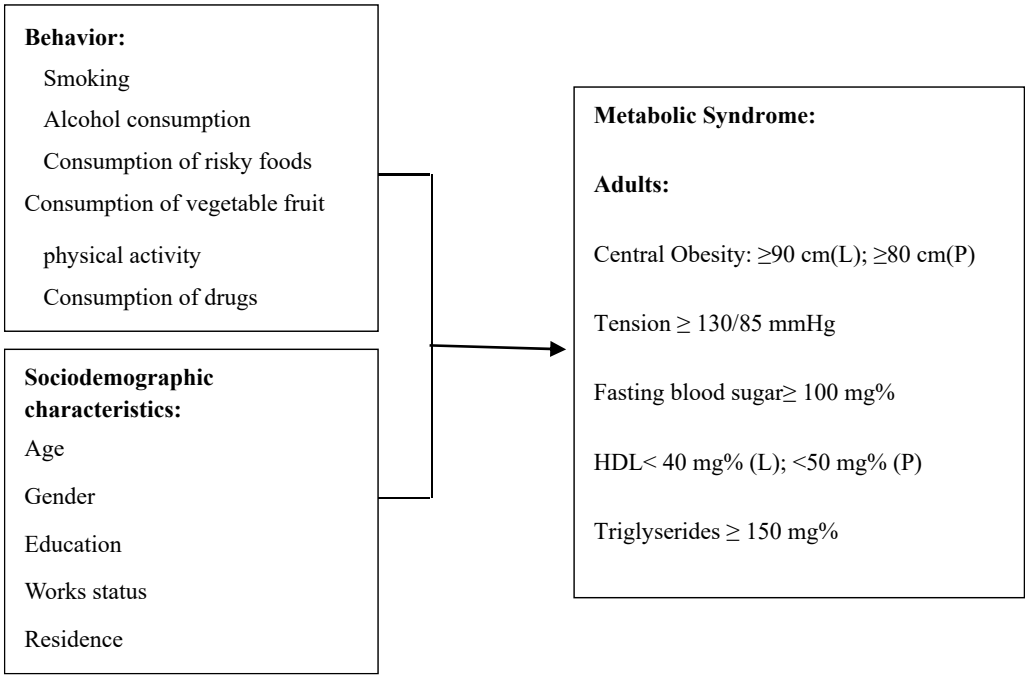

Figure 1. The conceptual framework of diabetes mellitus

3. Methods

This study uses the 2018 Riskesdas data, with a total population target of the age group of 15 years and over. The sample of the analysis were respondents who had never been diagnosed with diabetes mellitus before the survey was conducted. Respondents have complete SM data according to the National Cholesterol Education Program or Adult Treatment Panel III (NCEP / ATP III) (Cleeman, 2001). The criteria were modified in 2004 and adapted for Asians. According to the modified NCEP-ATP III criteria, the definition of MetS consists of clinical conditions of at least 3 or more than 5 risk factors, namely central obesity (abdominal circumference > 90 cm for men and > 80 cm for women), low cholesterol HDL (men < 40 mg% and women < 50 mg, or currently under treatment), high serum triglycerides (≥ 150 mg%, or currently under treatment), increased blood pressure (≥ 130/85 mmHg or currently under treatment), and fasting blood glucose (≥ 100 mg% or currently under treatment). Whereas in adolescents which include 5 indicators namely central obesity 90 percent of adult criteria

(abdominal circumference ≥ 81 cm in men or ≥ 72 cm in women); triglyceride levels ≥ 110 mg%; HDL levels > 40 mg% in men or > 40 mg% in women; systolic blood pressure ≥ 117 mmHg (90% of adult criteria) and diastolic blood pressure ≥ 77 mmHg (90% of adult criteria); and fasting blood sugar level ≥ 100 mg%. The definition of metabolic syndrome is based on the presence of 3 of the 5 indicators (Nolan et al., 2017). (Table 1)

The unit of analysis is the Individual aged ≥ 15 years, and taking into account the age groups of teenagers (15-24 years) and adults (≥ 25 years) in men and women. The types of analysis are descriptive, bivariate, multivariate, and Population Attributable Fraction (PAF) analysis (Gerstman, 2014).

Table 1. Criteria for metabolic syndrome for adult Asians according to NCEP's ATP III

Criteria	Adult	adolescents
Triglycerides mg%	≥150	≥110
HDL mg%		
Men	< 40 mg	≤ 40
Women	< 50 mg	≤ 40
Abdominal circumference		
Men	≥90 cm	≥ 81(90%)
Women	≥ 80 cm	≥ 72 (90%)
Fasting Blood Glucose mg%	≥ 100	≥ 100
Blood pressure mmHg	≥ 130/85	≥ 117/77 (90%)

Source: Cook, S et al. 2003. (Cook et al., 2003).

3.1 Data Analysis

The analysis will be differentiated based on groups of men and women. Data analysis was performed descriptively to obtain data on the characteristics of respondents who had never been diagnosed with diabetes mellitus before the survey. Bivariate analysis used cross-tabulation with 95% CI and p-value ($p < 0.05$) to obtain the prevalence of MetS and each component of risk factors in MetS. The analysis continued by focusing on respondents with diabetes mellitus (DM) based on the NCEP ATP III criteria. Multivariate analysis was performed to obtain risk factors from the MetS component that had a contribution to DM. As independent variables include demographic characteristics (age, education, occupation, residence, economic status) and behavior (physical activity, smoking based on the Brinkman index, consumption of vegetable fruits, mental-emotional disorders, and BMI).

After determining the determinant factors that have a relationship with DM in each group, the analysis continues with Population Attributable Fraction (PAF) calculation to get the contribution of each variable that can contribute to reducing the prevalence of DM.

3.2 Ethical Approval

Ethical approval for the study was obtained from the human ethics committee, National Institute of Health and Research Development of Indonesia, with number LB.02.01/3/KE.024/2018.

4. Results

Respondents in this analysis were 24,545 people, among them 50.5 percent of men (n = 12,392), slightly higher than 49.5 percent of women (n = 12,153).

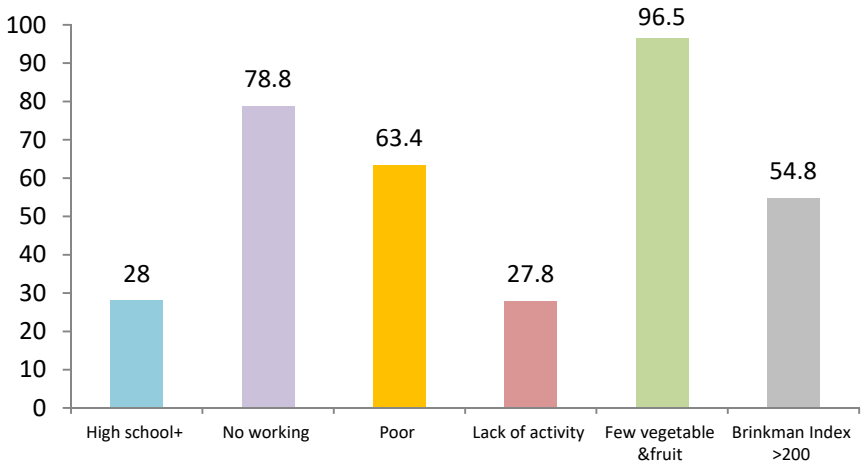

Figure 2. Graph of sociodemography and behavior of respondents who have never been diagnosed with diabetes by health workers, Riskesdas 2018

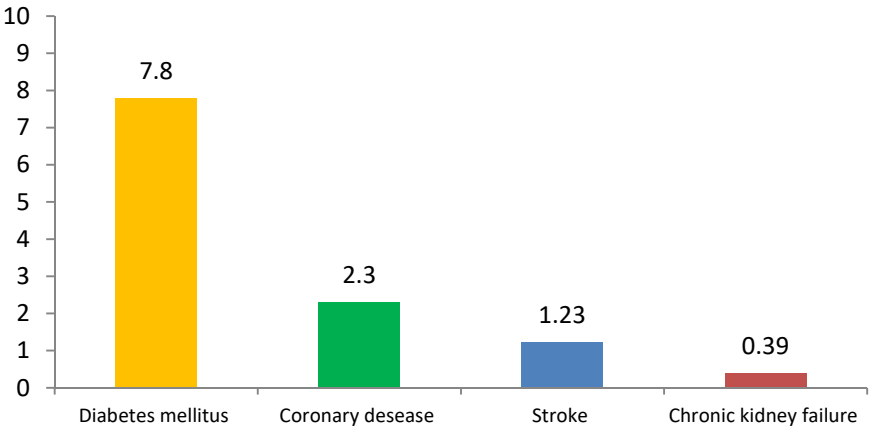

Figure 3. Graph of comorbid respondents who have never been diagnosed with diabetes by health workers, Riskesdas 2018

The mean age of respondents was 43.1 years, in men with slightly older age than women, more with high school education or more, less physical activity, more than one-half the smokers with a Brinkman index > 200 cigarettes (Figure 2), and more at risk of stroke than women. The mean body mass index, abdominal circumference, blood pressure both systolic and diastolic, lipid profile, and fasting blood sugar are still not at risk.

Women respondents with an average age of 42.3 years, most (90.1%) did not work, more suffer from DM and heart disease than men. The average body mass index is classified as overweight (24 kg/m^2), abdominal circumference (80.6 cm), and fasting blood sugar levels (100.1 mg%) are close to risky.

Table 2 shows the characteristic description of those who have never been diagnosed of having diabetes mellitus in population aged 15 years and above.

Table 2. Description of respondents who have never been diagnosed with diabetes by health workers, in the age group of 15 years and over, Riskesdas 2018

	All	**Men (49,2%)**	**Women (50,8%)**
	N=24.546	**n= 12.393**	**n= 12.153**
Average age (years)	43,1±15,7	43,9 ± 16,0	42,3 ± 15,2
High school+ %	28,0 (27,4-28,5)	30,1 (29,7-31,4)	25,9 (24,8 – 26,1)
No working %	78,8(78,5-80,0)	55,5 (53,8-57,3)	90,1(89,8-90,9)
Poor %	63,4(62,2-63,)	62,7 (61,2-63,1)	64,1 (62,9-64,5)
Lack of activity %	27,8(26,9-27,9)	31,2 (29,9-31,8)	24,2 (23,4 – 24,7)
Few vegetable &fruit %	96,5 (96,1-96,8)	96,4 (89,9-96,6)	96,5(96,1-96,7)
Brinkman Index >200 (%)	54,8(53,0-55,6)	54,9 (54,0 – 56,7)	22,7(19,6-29,9)
Diabetes mellitus %	7,8(7,3-9,6)	5,9 (5,4 – 6,5)	9,7(8,8-10,9)
Coronary desease %	2,3(2,1-2,5)	2,0 (1,8 – 2,3)	2,5(2,3-2,7)
Stroke %	1,23(1,1-1,4)	1,4 (1,2 – 1,6)	1,08 (0,93-1,25)
Chronic kidney failure %	0,39[0,32-0,47]	0,4 (0,3 – 0,6)	0,37 (0,29-0,47)
Average IMT (Kg/m^2)	23,7 ± 4,7	22,6 ± 4,1	24,0 ± 4,9
Average abdominal circumference (cm)	79,6 ± 11,9	78,7 ± 11,6	80,6 ± 12,2
Average systolic mmHg	130,9 ± 23,5	130,4 ± 21,3	131,4 ± 25,6
Average diastolic mmHg	84,0 ± 12,7	82,9 ± 12,2	85,2 ± 13,2
Average total cholesterol mg %	179,0 ± 39,2	173,7 ± 38,5	184,5 ± 39,2
Average HDL mg%	47,3 ± 11,1	43,9 ± 9,9	50,7 ± 11,3
Average triglyceride mg%	129,8 ± 90,9	142,3 ± 101,1	117,1 ± 76,9
Average fasting blood glucose mg%	99,3 ± 2,6	98,5 ± 19,8	100,1 ± 29,5

4.1 Metabolic Syndrome and its Components

In Indonesia, the prevalence of metabolic syndrome in the population aged 15 years and over, who has never been diagnosed with DM before the survey is 29.2 percent (95% CI, 28.6-29.8). (See table 3) The prevalence among men is 11.9 percent (95% CI, 11.5-12.4) and in women is 17.2 percent (95% CI, 16.8-17.7). In urban areas is 15.2 percent (95% CI, 14.7-15.7) is higher than in rural areas 13.9 percent (95% CI, 13.5-14.4). Population with lower economic status and low education (≤ junior high school education) have a higher prevalence of metabolic syndrome than higher economic and education status. Metabolic syndrome is higher among those who have sufficient physical activity, which is 21.6 percent (95% CI, 21.0-22.2) than those with less physical activity 7.6 percent (7.2-7.9) (P = 0.0002).

Table 3. The prevalence of metabolic syndrome and its components according to characteristics and DM

		Central obesity	High fasting Blood glucose	Hypertension	High Trigliserida	Low HDL	Metabolic Syndrom
Ages	45 + yrs	16.6(16.4-17.4)	19.8(19.2-20.5)	29.9(29.3-30.6)	14.7(14.2-15.2)	17.1(16.6-17.6)	16.4 (15.9-16.9)
	15-44 yrs	17.3(16.8-17.8)	11.9(11.4-12.5)	20.9(20.3-21.4)	12.5(12.0-12.9)	24.2(23.6-24.8)	12.8 (12.4-13.3)
Gender	Men	8.5 (8.1-8.9)	14.4 (13.8-15.0)	24.3 (23.8-25.1)	16.4 (15.8-16.9)	17.3(16.7-17.9)	11.9 (11.5-12.4)
	Women	25.7(25.1-26.3)	17.3(16.8-17.9)	26.4(25.8-26.9)	10.8(10.4-11.2)	23.9(23.4-24.5)	17.2(16.8-17.7)
Education	≤ junior high school	23.4(22.9-24.0)	24.4(23.7-25.2)	38.4(37.7-39.0)	19.4(18.9-19.9)	29.7(29.1-30.1)	21.5(21.0-22.1)
	≥ high school	10.8(10.3-11.2)	7.3(6.8-7.7)	12.5(12.0-12.9)	7.7(7.4-8.1)	11.5(11.1-11.9)	7.7(7.3-8.1)
Jobs	Not work	33.4(32.4-34.3)	23.8(22.8-24.8)	38.9(38.0-39.9)	17.1(16.3-17.8)	35.9(34.9-36.9)	23.3 (22.5-24.2)
	Work	7.3(6.8-7.9)	5.2(4.7-5.9)	9.6(8.9-10.3)	6.9(6.4-7.5)	8.3(7.8-8.9)	6.1 (5.6-6.6)
Areas	Urban	21.6(20.9-22.1)	15.6(14.9-16.2)	27.4(26.8-28.1)	15.3(14.8-15.9)	22.2(21.6-22.8)	15.2(14.7-15.7)
	Rural	12.7(12.2-13.1)	16.2(15.6-16.8)	23.4(22.8-23.9)	11.8(11.4-12.3)	19.1(18.6-19.6)	13.9(13.5-14.4)
Welfare	Poor	18.2(17.7-18.8)	20.4(19.7-21.1)	32.2(31.6-32.9)	16.5(15.9-17.1)	25.7(25.0-26.3)	17.8(17.2-18.3)
	Enough	14.8(14.3-15.3)	11.8(11.2-12.4)	18.8(18.2-19.4)	11.5(11.0-12.0)	14.8(14.3-15.4)	11.4(10.9-11.9)
Brinkman Index	≤ 200 sticks	6.8(6.1-7.5)	12.5(11.2-13.8)	18.6(17.5-19.8)	13.9(12.9-14.9)	17.5(16.4-18.6)	9.5(8.7-10.3)
	>200 sticks	9.2(8.4-10.1)	20.4(18.9-21.9)	27.3(26.1-28.6)	20.5(19.4-21.7)	20.8(19.7-22.0)	14.0(13.1-15.0)
Physical activity	Less	8.8(8.4-9.2)	8.4(7.9-8.9)	13.8(13.3-14.3)	7.8(7.4-8.2)	11.6(11.1-12.0)	7.6(7.2-7.9)
	Enough	25.4(24.8-26.0)	23.3(22.6-24.0)	37.0(36.4-37.7)	19.4(18.8-19.9)	29.7(29.1-30.3)	21.6(21.0-22.2)
Vegetable fruit portions	Less	32.8(32.1-33.4)	30.3(29.5-31.1)	49.0(48.3-49.7)	26.1(25.4-26.7)	39.7(39.0-40.4)	27.9(27.4-28.6)
	Enough	1.4(1.3-1.6)	1.4(1.2-1.6)	1.8(1.6-1.9)	1.1(0.1-1.3)	39.7(39.0-40.4)	1.2(1.1-1.4)
Diabetes mellitus	Yes	3.8(3.6-4.1)	8.7(8.3-9.2)	5.3(5.0-5.6)	2.8(2.6-3.1)	3.7(3.4-3.9)	5.6 (5.3-5.9)
	No	30.4(29.7-31.0)	22.9(22.3-23.7)	45.5(44.8-46.2)	24.3(23.7-24.9)	37.6(36.9-38.2)	23.6(23.0-24.2)
Total		34.2(33.5-34.9)	31.7(30.9-32.5)	52.0(51.4-52.6)	27.2(26.6-27.8)	41.3(40.6-41.9)	29.2(28.6-29.8)

4.2 Determinants Factors of Metabolic Syndrome in Diabetes Mellitus According to Gender

Table 4 shows multivariate analysis result of the relationship between MetS and DM after controlled by other factors, such as socio-demographic, health risk behaviors, nutrition status, blood lipid profile, and glucose. According to the magnitude of MetS risk factors, there appear to be differences between men and women the incidence of DM. In men, the risk factors that have a relationship with DM are fasting blood glucose levels > 100 mg% and hypertension, while the other 3 factors do not show a significant relationship. Whereas in women, the five MetS risk factors have a relationship with DM. Based on the order of strong relationships are fasting blood glucose levels >100mg%, hypertriglyceridemia, hypertension, central obesity, and low HDL levels. Overall the 3 main factors of metabolic syndrome which play a major role in DM are high fasting blood sugar, hypertension, and hypertriglyceridemia. (Tabel 4)

Table 4. The Relationship of Metabolic Syndrome Risk Factors and Diabetes mellitus in the age group 15 years and over, according to gender

	Men				Women				All			
	ajOR	Lower	Upper	p	ajOR	Lower	Upper	p	ajOR	Lower	Upper	p
Ages group	2,5	2,0	3,2	0,00	1,6	1,4	1,9	0,00	1,9	1,7	2,1	0,00
Hypertension	1,4	1,1	1,7	0,00	1,5	1,3	1,7	0,00	1,4	1,3	1,6	0,00
Central obesity	1,2	0,9	1,5	0,17	1,2	1,1	1,4	0,01	1,4	1,2	1,5	0,00
Low HDL	1,2	1,0	1,5	0,12	1,2	1,0	1,3	0,04	1,2	1,1	1,4	0,00
Triglyserides >150 mg%	1,2	0,9	1,5	0,18	1,8	1,5	2,0	0,00	1,4	1,2	1,5	0,00
FBG >100 mg%	6,3	5,1	7,8	0,00	5,9	5,1	6,8	0,00	5,9	5,3	6,7	0,00

Note. ajOR = adjusted Odd Ratio.

4.3 Contribution of Metabolic Syndrome Components to Diabetes Mellitus

In general, three of the five components of metabolic syndrome have a major contribution, including high fasting blood glucose levels, high triglyceride levels, and hypertension. (Table 5)

If the three components can be maintained in normal conditions, the prevalence of DM can decrease from 7.8 percent to 6.0 percent, this indicates a decrease in DM prevalence of 23 percent. This shows as many as 3,392,152 people will be free of DM from 14,748,486 people who were suffering.

In men aged 15 years and over, the risk factors for MetS that contribute to DM are high fasting blood glucose contributing about 0.71 percent and hypertension about 0.06 percent. If all men respondents with DM can reduce FBG to ≤ 100 mg%, then the prevalence of DM will decrease from 5.9 percent to 5.2 percent. Among males, those who had DM and maintained the blood pressure level to ≤ 130/85 mmHg then the prevalence of DM can be reduced to 5.8 percent. If these two factors (fasting blood sugar levels and blood pressure) can be maintained normally, the prevalence of DM can be reduced from 5.9 percent to 5.0 percent. This shows the prevalence of DM in men can be reduced by 15 percent, so as many as 856,327 men can free from DM.

For women aged 15 years and over, the risk factors for MetS that contribute to DM are high fasting blood glucose contributing 1.5 percent, hypertriglyceridemia levels 0.5 percent, and hypertension 0.2 percent. If all women respondents with DM could decrease FBG ≤ 100 mg%, then the prevalence of DM could change from 9.7 percent to 8.2 percent. If women DM respondents can maintain triglycerides < 150 mg% then the prevalence of women DM can be reduced to 9.2 percent, while women DM respondents can maintain blood pressure ≤ 130/85 mmHg then the prevalence of DM can decrease from 9,7 percent to 9,5 percent. If these three factors (fasting blood sugar, blood pressure, and triglyceride levels) can be maintained at a normal level, the prevalence of DM can decrease by 29.9 percent. It means the prevalence of DM can decrease from 9.7 percent to 6.8 percent, which is as many as 2,714,289 women can avoid DM.

Table 5. The contribution of MetS risk factors to DM by gender

Risk factors	Prev. DM men 5,9 %			Prev. DM Women 9,7 %			Prev. DM all 7,8 %		
	PAF	Contribution	DM proporsion tobe	PAF	Contribution	DM proporsion tobe	PAF	Contribution	DM proportion tobe
FBG≥100 mg%	0,12	0,708	5,2	0,153	1,484	8,2	0,138	1,076	6,7
Central obesity	-	-	-	0,013	0,126	9,6	0,019	0,148	7,7
Low HDL	-	-	-	0,01	0,097	9,6	0,012	0,094	7,7
Triglyceride ≥150 mg%	-	-	-	0,049	0,475	9,2	0,024	0,187	7,6

Hypertension	0,011	0,065	5,8	0,018	0,175	9,5	0,015	0,117	7,7
FBG+Hyperten	0,145	0,855	5,0	0,191	1,853	7,8	0,171	1,334	6,5
FBG+ Triglyser	-	-	-	0,251	2,435	7,3	0,188	1,466	6,3
Hypert+Triglyser ide	-	-	-	0,073	0,708	9,0	0,039	0,304	7,5
FBG+ Triglyser + Hypertensi	-	-	-	0,298	2,8906	6,8	0,225	1,755	6,0

5. Discussion

This study found that the prevalence of MetS was 29.2 percent (estimated 25,431,537 people) among the population aged 15 years or older who has never been diagnosed with DM by a healthcare provider. This prevalence increased compared to the results in 2013 (23.3%) (Suhaema & Masthalina, 2015), even though in 2013 it was reported in all age groups of 15 years or better who had been diagnosed or who had never been diagnosed with diabetes by health workers. Nearly one in 3 population, with an estimated 55,212,283 population aged 15 years and over were having MetS. The International Diabetes Federation (IDF) estimates that about 25 percent of the world's population suffers from MetS, in that estimation, there are variations in age, ethnicity, and gender of the population. (Nolan et al., 2017) Cohort data in Isfahan, Iran after 7 years of follow-up indicate that incidents of MetS were 27 percent with an incidence rate of 39.2 per 1000 person-years in men and 46.6 per 1000 person-years in women ($p = 0.04$) (Franklin & Wong, 2013). Compared to the results in Iran, the incidence of BC in Bogor is still low, this is related to different eating patterns between respondents in Iran and Bogor. Some research results in Asia show that the prevalence of metabolic syndrome is between 35.8 percent to 45.3 percent in India, 30.5 percent to 31.5 percent in China, and 16.5 percent in Malaysia (Harikrishnan et al., 2018).

The relationship between sex and the prevalence of MetS and its components among Indonesian adults shows that gender appears to be an independent predictor of the prevalence of most MetS components. The high prevalence of MetS and its components occurs mainly in women, in urban areas, respondents with low income (poor), and low education (≤ junior high school), except that the hypertriglyceridemia variable is found to be higher in men. Differences in the prevalence of MetS components may be related to gender characteristics (eg, biological traits and functional features) and gender-related determinants (eg, psychological and cultural habits) (PERKENI, 2015). Changes in hormone levels during and after menopause can contribute to gender differences in the prevalence of the MetS component in older populations (Sarah, 2004). There is an increase in metabolic syndrome in the younger age group due to lifestyle changes. Nevertheless, it is very important to obtain the prevalence of metabolic syndrome in the age group of 15 years or more because the presence of metabolic syndrome components can lead to an increased risk of developing diabetes mellitus and heart disease (Kaur, 2014).

This study shows the mean systolic blood pressure (SBP) and diastolic blood pressure (DBP) is relatively high, while. the average for women is higher than for men. The Framingham Heart Study shows that DBP is a better predictor for future chronic disease events than SBP in adults < 50 years; The truth has been proven after the age of 50 years that the underlying chronic disease is isolated diastolic hypertension (Franklin & Wong, 2013). There are observed differences between rural and urban respondents. This has been proven in several other studies relating to a more sedentary lifestyle in city dwellers (Harikrishnan et al., 2018). Gender disparities in blood pressure are believed to be due to differences in biological and behavioral factors including hormonal differences, higher prevalence of obesity, higher mean fasting blood sugar levels, and other determinants such as not working, residential areas. Similar risk factors have also been reported in other studies (Suhaema & Masthalina, 2015).

In Riskesdas 2018, the prevalence of diabetes mellitus in respondents who had never been diagnosed with diabetes by health workers was 7.8 percent (5.9% in men and 9.7% in women). Diabetes mellitus (DM) is a chronic disease due to impaired carbohydrate metabolism due to a progressive decline in pancreatic beta-cell function resulting in insulin resistance (PERKENI, 2015). The incidence of DM continues to increase both in developed and developing countries due to lifestyle changes. The number of people with DM in Indonesia ranks fourth in the world after India, China, and America. (Sarah, 2004) This is in line with the findings of the noncommunicable disease risk factors cohort study in Bogor City. This study found that the incidence of MetS in 2018 was 6.8 percent or 19.2 per 1,000 person-years. The cumulative incidence for 6 years in MetS was 151

people, with a hazard rate of 9 per mile (Ministry of Health Republic of Indonesia, 2018). It means that the increasing prevalence of DM in Indonesia is due to the increasing number of MetS occurring in the community. Diabetes mellitus as a cause of disability has increased in 27 years, from the ninth position in 1990 to the fourth position in 2017 (WHO, 2017).

Harikrishnan found that MetS respondents who suffer from DM amounted to 15.6 percent in India (Harikrishnan et al., 2018). Although the results in Indonesia were not as large as in India, vigilance against the risk of DM in MetS respondents needed special attention.

An impaired fasting glucose level is a state of prediabetes. In this study the mean fasting blood glucose levels in women were 100.1 mg% higher than MetS criteria of WHO criteria. The prevalence of fasting glucose disturbance (IFG) in men is 14.4 percent and in women is 17.3 percent. High fasting blood glucose levels are more common in women, urban dwellers, prevalence increases with age, higher in overweight and obese individuals, and individuals with low physical activity. These results are consistent with the results of the national health survey 2013, the more age increases the risk of hyperglycemia due to decreased work of the pancreas in producing insulin. This finding is an initial intervention to stop or inhibit the development of diabetes mellitus (World Health Organization, 2016).

Dyslipidemia is a risk factor for non-communicable diseases. This study shows that, hypertriglyceridemia was 27.2 percent and low HDL cholesterol level was 41.3 percent among those with dyslipidemia. Low HDL cholesterol levels in Indonesia were higher than Mohamud's study in Malaysia (34%) (Mohamud et al., 2011). But lower than Fernanda studies in Brazil showed a high prevalence of HDL cholesterol with low criteria (59.3%) (Vidigal et al., 2013). Likewise in the Indian Council of Medical Research - Indian Diabetes Study (ICMR-INDIAB) reported 13.9 percent had hypercholesterolemia, 29.5 percent had hypertriglyceridemia 72.3 percent with low HDL cholesterol and 11.8 percent had LDL high. Seventy-nine (79%) had abnormalities in one of the lipid parameters (Mohan et al., 2014).

These results are in line with previous studies which reported that dyslipidemia in people with type 2 diabetes can increase the risk of complications of other non-communicable diseases such as coronary heart disease (Nolan et al., 2017).

This study also shows, an increase in the prevalence of MetS with increasing age. Likewise, research in Malaysia shows that the prevalence of MetS tends to increase by 3 percent every year in respondent age (Mohamud et al., 2011).

In India, MetS respondents with a prevalence of central obesity were 58.6 percent (Harikrishnan et al., 2018). The Suhaema get results that the risk of central obesity in MetS respondents by 53 percent (Suhaema & Masthalina, 2015). This result is higher than central obesity. in Indonesia which is 34.2 percent.

This situation is closely related to diet, especially carbohydrate intake from each different country. As research in Poland found evidence that traditional carbohydrate diet patterns (high intake of wheat, potatoes, sugar, and sweet foods) gave high scores and correlated the occurrence of central obesity (p trend = 0.001), as well as increased triglyceride levels (p trend = 0.005) (Suliga et al., 2017).

According to a national health insurance and social security agency in Indonesia (BPJS) report, the amount of funding for DM is estimated to reach 20 trillion rupiahs in 2018. Meanwhile, results of 2013 Riskesdas, showed ten percent of the population suffering from DM visited to a health facility (Ministry of Health of the Republic Indonesia, 2013; Suliga et al., 2017). It can be estimated that a DM patient requires medical expenses of around 12,743,803 IDR (Indonesia Rupiah).

The contribution of normal blood sugar levels and blood pressure in preventing DM, implicates that around 856,327 men aged 15 years or older can be prevented from DM, consequently government can save health expenditure as much as 1.1 trillion in men and 3.5 trillion in women

8. Conclusion

This study shows that prevalence of MetS in populations aged 15 years and over in men and women in Indonesia remained high. Components of MetS that contribute greatly to reducing the prevalence of DM in men are high fasting blood sugar levels and hypertension. Whereas in women, MetS components that have a major contribution are fasting blood glucose levels, hypertriglyceridemia, and hypertension. Prevention efforts to reduce the prevalence of DM by considering the magnitude of the contribution of risk factors for metabolic syndrome. It can be planned to be implemented in primary health care facilities.

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Competing Interests Statement

The authors declare that there are no competing or potential conflicts of interest.

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Stroke Pentagon: Stroke Management Approach in Resource Poor Settings

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Abstract

Stroke is a neurological condition that is characterized by sudden onset focal neurological deficit due to spontaneous cerebral vascular occlusion or rupture. It is a neurological emergency and its prevalence is very high, especially in developing countries where it assumes an epidemic proportion. It is globally the second most common cause of death after ischaemic heart disease. The poor indices in developing countries are multifactorial and related to late case presentation, ignorance, poverty, and unavailability of comprehensive and well-coordinated stroke care. There is a need to identify the available and cheap stroke management steps in the developing countries and strengthen the system to maximize the benefits in reduction of the morbidity and mortality of stroke. It is against this background that we identified Stroke prevention, acute stroke management, Stroke rehabilitation, Stroke research, and Stroke support as five pillars (stroke pentagon) in stroke management in developing countries. There is a need to sensitize the stakeholders in stroke management as highlighted in the stroke pentagon to assume more responsibility. Moreover, there is the need to have a more coordinated and concerted stroke management approach which will involve all the identified five pillars to ensure improved stroke indices in the developing countries.

Keywords: approach, developing countries, management, pentagon, stroke

1. Introduction

Stroke is characterized as a neurological deficit attributed to an acute focal injury of the central nervous system (CNS) by a vascular cause, including cerebral infarction, intracerebral hemorrhage (ICH), and subarachnoid hemorrhage (SAH) (Sacco et al., 2013). It is a neurological emergency and its prevalence is high especially in developing countries where it assumes an epidemic proportion. It is globally the second most common cause of death after ischaemic heart disease according to the Global Burden of Disease Study 2015 (2017), and it is projected to remain so by 2030 (WHO, 2013). It has a global prevalence of 1300.6 per 100,000 in 2017 (Avan et al., 2019).

In Africa and other developing countries, the prevalence ranged from 963 to 1,460/100,000 (Khedr et al., 2014; Ezejimofor, 2017). In Abakaliki, Nigeria, a community-based survey revealed a stroke prevalence rate of 2,700 per 100,000 amongst adult population (Eze, Kalu, & Nnaji, 2020). It is a disease of the middle-aged and elderly population with male preponderance, though young people are not exempted (Nedeltchev et al., 2005; Varona, Guerra, Bermejo, Molina, & de la Camara, 2007; George, Tong, Kuklina, & Labarthe, 2011; Eze, Kalu, & Isiguzo, 2019). It constituted 14%–16% of admissions in the medical wards in Nigeria (Eze et al., 2013; Ezeala-Adikaibe et al., 2014).

Ischemic stroke occurs when a cerebral blood vessel is occluded by either a thrombus or an embolus leading to focal brain ischemia. The ischemic area has a central core where brain damage is irreversible and a peripheral penumbra where there is loss of function but not irreversibly damaged. The neurological function loss is that of the ischemic core and the penumbra. The acute management of stroke aims to restore the functions of the penumbra by ensuring adequate blood perfusion. Further recovery of neurological functions during subacute and chronic stages is achieved through brain plasticity (Kolb, 1995).

Conversely, hemorrhagic stroke occurs when a cerebral blood vessel ruptures due to severe hypertension or

defects in vascular wall integrity. This leads to the formation of hematoma within the brain parenchyma, subarachnoid space, or the ventricles. The clinical features are due to rise in intracranial pressure, meningeal irritation, and focal brain compression and ischemia. Reduction of intracranial pressure is pivotal in the management of hemorrhagic stroke.

The clinical presentation varies and depends on many factors which include the type of stroke, severity of stroke, part of the brain affected, and presence of co-morbidities. The common clinical features include hemiparesis, hemifacial paresis, speech impairment, headache, alteration in consciousness, and seizures.

The common risk factors are hypertension, diabetes mellitus, smoking, heart disease, dyslipidemia, obesity, alcoholism, and advanced age. The case fatality rate is still very high, especially in the developing countries (Walker et al., 2011; Eze, Okoro, Nwobodo, Nnaji, & Isiguzo, 2020). In Abakaliki, Nigeria, stroke constituted 19% of deaths in medical wards (Eze et al., 2020), 24% of deaths in medical emergency room (Eze & Kalu, 2019), and 31% in intensive care unit (Eze et al., 2020). The poor indices are multifactorial ranging from late case presentation, ignorance, poverty, and unavailability of coordinated and comprehensive stroke care. Hyperacute stroke interventional services like thrombolysis, thrombectomy, and embolectomy are not available in most stroke centres in Africa and other developing countries. There is a need to identify the available and cheap stroke management steps in these resource poor settings and strengthen the system to maximize the benefits in reduction of the morbidity, and mortality of stroke. It is against this background that we identified Stroke pentagon which includes Stroke prevention, acute stroke management, Stroke rehabilitation, Stroke research, and Stroke support as the pillars of stroke management approach in resource poor settings.

2. The Stroke Pentagon

Stroke pentagon is the five key pillars or steps in stroke management that are potentially available in the developing countries and in resource poor settings. They are cheap and available but may not be utilized fully if not highlighted. They can be strengthened and maximized to reduce the morbidity and mortality of stroke. The components of the pentagon include:

1). Stroke prevention.

2). Acute stroke management.

3). Stroke rehabilitation.

4). Stroke research.

5). Stroke support.

2.1 Stroke Prevention

Stroke prevention involves all the efforts put in place to ensure that people do not develop stroke. It includes health promotion and prevention, reduction, or elimination of cardiovascular risk factors. This is essential because “prevention is better than cure”. Stroke prevention is the most important pillar in stroke management because it is cheap, targets the populace, and all health professionals and community leaders are involved. The target is to reduce the burden of stroke. It includes primary and secondary prevention.

Primary prevention involves prevention of stroke in people that have not had stroke, while secondary prevention involves prevention of stroke recurrence in stroke survivors. The risk factors are sought for especially amongst middle-aged and elderly individuals and also in young people with family history of cardiovascular disease. The risk factors are classified into modifiable and non-modifiable risk factors. Modifiable risk factors include hypertension, diabetes, dyslipidemia, smoking, alcohol abuse, heart disease, obesity, sepsis, and inflammatory conditions (Romero, Morris, & Pikula, 2008), while non-modifiable risk factors include age, sex, race, and previous stroke. The emphasis is on the modifiable risk factors because they are potentially reversible. Hypertension is the most important stroke risk factor (Lackland et al., 2014).

Measures are put in place to reduce or eliminate the risk factors. The following interventional measures can be done to ensure reduction and elimination of the identified modifiable risk factors;

1). Regular physical exercise.

2). Consumption of fruits and green leafy vegetables (Owolabi et al, 2018).

3). Reduction in consumption of alcoholic beverages.

4). Cessation of cigarette smoking.

5). Reduction of consumption of refined food.

6). Regular medical checkup.

Adherent on medications for hypertension, diabetes, dyslipidemia, and heart disease.

2.2 Acute Stroke Management

Stroke is classified based on time from onset into hyperacute (24 hours), acute (1–7 days), subacute (8 days-6 months), and chronic (> 6 months).

Hyperacute stroke management services like thrombolysis, thrombectomy, and embolectomy are largely unavailable in most developing countries due to high cost and lack of expertise.

Acute stroke management involves measures put in place to ensure recovery of neurological functions, prevention of another event, prevention, and treatment of acute complications during the acute phase of stroke. This is commenced immediately the patient is brought to the emergency room. Delay in commencement of acute stroke treatment may be experienced at the home, on transit and at the hospital. Acute management may extend beyond the first seven days depending on the clinical situation. Conversely, it may last for less than 7 days in a mild stroke. The patients are triaged and managed in the general medical/stroke ward or intensive care unit (ICU) depending on the severity. The acute management should be strengthened to reduce the morbidity and mortality of stroke. The patients should be managed by a dedicated stroke team coordinated by a neurologist.

Indications for admission into the ICU include;

1). Severe hypertension/hypotension.

2). Status generalized seizure.

3). Oxygen desaturation.

4). Severe alteration in consciousness (GCS < 9).

Management protocols for ischaemic stroke include

1). Intravenous Isotonic fluid (normal saline, ringers lactate) 2000 ml daily (cautious fluid administration in hypertensive emergencies and in elderly patients).

2). Antiplatelets like Clopidogrel or Aspirin 75 mg daily.

3). Maintain permissive hypertension to ensure adequate blood flow to the penumbra (MABP-110-150 mmHg, SBP-160-220 mmHg, DBP- 90-120 mmHg).

4). Reduce the blood pressure towards normal if the patient has features of hypertensive emergency or chronic end-organ failure.

Management protocol for hemorrhagic stroke

1). Intravenous 20% mannitol 300ml over 10minutes, then 150ml over 5minutes 6hourly for 3 days.

2). Intravenous Furusemide 20 mg 12 hourly for 7 days.

3). Reduce the blood pressure (MABP-<120 mmHg, SBP-< 160 mmHg).

4). Analgesic for headache and neck pains.

5). Stool softener and indwelling urethral catheter to avoid straining.

6). Prophylactic antiseizure medications.

General management protocol

1). Gentle graded physiotherapy.

2). Use of water or air bed to minimize risk of pressure sores.

After the acute phase, the BP will be gradually reduced to normal values.

2.3 Stroke Rehabilitation

Stroke rehabilitation involves the pharmacological, and non-pharmacological measures aimed at encouraging recovery of functions following stroke or optimization of the functions. These include;

1). Physical rehabilitation/Physiotherapy.

2). Swallowing rehabilitation.

3). Speech rehabilitation.

4). Psychological rehabilitation.

5). Occupational rehabilitation.

These activities are carried out by the neurologist, physiotherapist, psychologist, speech therapist, occupational therapist, and the dietitian. Rehabilitation is usually commenced during the acute phase in the ward, though in a gentle and graded manner as vigorous physical therapy may precipitate a repeat stroke. During the Subacute and chronic stroke phases, physiotherapy is usually done on outpatient basis at the physiotherapy department or home visit.

a). Physical rehabilitation: There is strong evidence that exercise after stroke can improve cardiovascular fitness (Pang, Eng, Dawson, & Gylfadottir, 2006),walking ability (Veerbeek, Koolstra, Ket, van Wegen, & Kwakkel, 2011), and upper extremity muscle strength (Harris & Eng, 2010). Physical activity goals and exercise prescription for stroke survivors should be customized for the individual to maximize compliance and long-term adherence. It should emphasize low to moderate intensity aerobic activity, muscle-strengthening activity, and reduction of sedentary behavior. The interventions include proper positioning, movement on the bed, sitting, standing, and ambulation. The above activities are focused, graded, and customized. Physiotherapists carry out the above services and it is available in most tertiary health facilities in developing countries.

b). Swallowing rehabilitation: About 51-55% of patients develop swallowing impairment revealed by clinical testing after stroke (Mann, Hankey, & Cameron, 1999; Smithard et al., 1996). Swallowing tests are usually done before commencement of oral feeding following stroke. Nasogastric (NG) tube feeding is used for those that have swallowing impairment. Fluid diet is given through the NG tube initially at a low volume and gradually increased as tolerated. Gastric prokinetic agents and proton pump inhibitors are used to reduce the risk of aspiration. Percutaneous endoscopic gastrostomy (PEG) tube feeding may be considered if dysphagia persists beyond the early subacute period in order to avoid long term complications of NG tube feeding.

c). Speech rehabilitation: Post stroke speech disorders which include aphasia and dysarthria occur in about 82.37% on admission (Vidović, Sinanović, Sabaskić, Hatić, & Brkić, 2011). A significant number of them improve spontaneously with or without intervention. Treatment should be commenced early, as soon as the patient is able to participate. Speech-language pathologists play a significant role in the screening, formal assessment, management, and rehabilitation of stroke survivors who present with communication impairment. Speech-language therapy is grossly underdeveloped and even unavailable in most parts of the Sub-Saharan Africa (Wylie, McAllister, Davidson, & Marshall, 2016).

d). Psychological rehabilitation: Post-stroke depression (PSD) is common and may occur in about 35% of stroke survivors (Srivastava, Taly, Gupta, & Murali, 2010). The aetiology is multifactorial and includes the psychological effects of the disease, the effect of stroke on the brain, and the effects of some of the medications. Several studies suggested that large lesions in critical areas such as left frontal lobe and basal ganglia might interrupt the pathways of monoamines leading to depression (Chao, Min, & Xue-Yuan, 2014). Psychotherapy is essential in the management of PSD and it is provided by the family members, clinical psychologist and the neurologist. Antidepressants are given to some patients as they also provide anxiolytic effects.

e). Occupational rehabilitation: Due to the neurological deficits associated with stroke, most patients may not return to their previous job. There may be a need to reassign duty in their previous job or change their occupation entirely to suit their current reality. This may involve training and retraining of the residual abilities to acquire new skills. This is done by occupational therapists.

Rehabilitation continues until the patient is adequately reintegrated back to the community. This is done concurrently with stroke prevention measures.

2.4 Stroke Research

Stroke research is essential pillar of stroke management. It involves the synthesis of empirical evidence from stroke prevention, acute stroke management, and stroke rehabilitation and application of the same in reduction of stroke morbidity and mortality. The level and strength of scientific evidence is derived from the scientific method applied in its synthesis. The applicable methods include expert opinions, observational studies, case-control studies, randomized controlled trials (RCTs), and meta-analysis in order of increasing strength. Stroke research should be done by all the health professionals involved in stroke management to help strengthen each pillar. The study can be done in the wards, outpatient clinics, laboratory, and the community. Most of the studies are sponsored by the researcher though can also be sponsored by the government, non-governmental organizations, and pharmaceutical companies. It is important to encourage RCTs in developing countries as there is danger of blanket application of research findings from developed nations due to genetic and environmental

differences.

2.5 Stroke Support

This pillar plays a vital role in stroke management especially in the developing countries where health system is not well developed. Stroke occurs predominantly in low and middle income countries and its cost of management is very high (Owolabi et al., 2018; Kaur, Kwatra, Kaur, & Pandian, 2014). There is also an absence and acute shortage of hyperacute stroke management services and investigative modalities like computed axial tomography (CT) scan, magnetic resonance imaging (MRI), and functional imaging modalities in most developing countries. This makes comprehensive stroke management services unavailable, unaffordable, and inaccessible to the populace, especially in the absence of universal health insurance coverage. There is a need for government, non-governmental organizations (NGOs) and philanthropists to step in to bridge the gap. There should be legislation on stroke care as provision of above facilities will significantly reduce stroke morbidity and mortality. This should include total or part sponsorship of stroke care, provision of 24hour ambulance services to reduce the delays in patient hospital presentation, and also provision of all the investigative tools and treatment modalities in regional hubs of comprehensive stroke centres. Furthermore, NGOs and philanthropists could make contributions in reducing the infrastructural deficits, provision of psychosocial support to the stroke survivors, and support of stroke research.

3. Conclusion

The morbidity and mortality of stroke is very high especially in the developing countries due to poverty, ignorance, and unavailability of comprehensive stroke management services. There is a need to strengthen the available management steps as highlighted in the stroke pentagon and ensure that the stakeholders are responsive and responsible. This will help improve the availability, accessibility, affordability, and efficiency of stroke care and thereby reduce the burden of stroke.

Competing Interests Statement

The author declares that there are no competing or potential conflicts of interest.

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Cost-Effectiveness of Early Oral Feeding Following Total Gastrectomy

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Abstract

Background: Gastric cancer is a major health problem worldwide. Effectiveness of early oral feeding (EOF) following gastrectomy has been internationally evaluated, even though there is limited evidence available. In Japan, recently, a randomized controlled trial of EOF following total gastrectomy showed a decreased length of hospital stay, compared with conventional oral feeding (COF). To evaluate value for money of EOF following gastrectomy, cost-effective analysis was carried out based on this trial.

Methods: The analysis was carried out from a societal perspective as the base case. The subjects were randomly assigned to the EOF group (N=32) and the COF group (N=30). While the EOF group received a special diet (i.e., iEAT) from the postoperative day (POD) 1 to POD 3, the COF group received conventional diet (i.e., a liquid diet or rice gruel) on POD 4 and thereafter. The observation period was 3 weeks after total gastrectomy. As an effectiveness measure, quality-adjusted life days (QALDs) were estimated. Quality of life for health conditions was evaluated by using EuroQol-5Dimentions (EQ-5D)-3Levels among the subjects. Costs (e.g., nutritional support, hospitalization and treatment of adverse events) were estimated from trial data during observation. Qualitative and stochastic sensitivity analyses were performed to examine the robustness of the results.

Results: The mean QALDs per patient for the EOF and the COF groups were 14.93 and 14.19, respectively. Incremental effectiveness of the EOF group to the COF group was 0.74 QALDs (p=0.359, t-test). The mean total cost per patient in the EOF and the COF groups was $3,177.7 and $3,755.4, respectively. Incremental cost was -$577.7 (p=0.03, t-test, Welch). This means EOF is dominant (cost saving). The qualitative sensitivity analysis and the stochastic sensitivity analysis showed the relative robustness of these results.

Conclusions: Economic evaluation of EOF following total gastrectomy showed that EOF was cost-saving, with non-significant increase in effectives (i.e., QALD), compared with COF. This result can contribute to strengthen the evidence for wide use of EOF.

Keywords: early oral feeding; gastric cancer; gastrectomy; cost-effectiveness; quality-adjusted life days; EQ-5D

1. Background

Gastric cancer is a major health problem worldwide. It ranks third in all causes of death from cancer, with about 9.3 million deaths in 2018 (Bray et al., 2018; Rawla & Barsouk, 2019). In Japan, although its mortality ranked also third in 2018 and has decreased in recent years, it still has the highest incidence despite advances in prevention (The Editorial Board of the Cancer Statistics in Japan, 2018). As to treatment strategies, while complete resection is the only unimodal treatment with curative intent, surgery is a common treatment for all stages of gastric cancer (Coburn et al., 2018).

Recently, enhanced recovery after surgery (ERAS), or fast-track surgery, has been proposed and increasingly attracted attention (Gramlich et al., 2016; Paton et al., 2014). ERAS is a comprehensive and multidisciplinary framework for accelerating recovery during perioperative care and has been implemented mainly for colorectal surgery and spread to other areas including gastrectomy (Mortensen et al., 2014). An evidence synthesis of 17 systematic reviews and 12 randomized controlled trials (RCTs) showed that ERAS can reduce the length of hospital stay by 0.5–3.5 days without increasing readmission rate (Paton et al., 2014). In gastric cancer surgery,

also, similar results to those in ERAS were observed (Bermish, Chan, Blake, Karran & Lewis, 2015; Li, Wang, Li, Bai, & Zhao, 2017).

Although it has not been identified what component mainly contributes to the effectiveness of ERAS, early oral feeding (EOF) is considered as one of the most important elements of ERAS (Mortensen et al., 2014). While EOF usually initiates oral feeding of water or liquid diet on the post operative day (POD)1 before flatus and shifts to ordinary diets, conventional oral feeing (COF) usually initiate this oral feeding on POD3 or after flatus and gradually shifts to ordinary diets (Liu et al., 2014; Tweed et al., 2019). EOF for gastric cancer surgery has been widely diffused and implemented, and recently systematic reviews of EOF following gastrectomy, based on RCTs, were reported (Liu et al., 2014; Tweed et al., 2019). These reviews showed that EOF after gastrectomy shortened the length of hospital stay without increasing postoperative adverse events (AEs) or readmissions.

Recently, a RCT in Japan has been conducted to evaluate the efficacy and safety of EOF following total gastrectomy for gastric cancers, and showed that EOF shortened the length of hospital stay without increasing adverse events (Shimizu et al., 2018). Since there has not been any full economic evaluation of EOF following gastrectomy, based on a RCT, we conducted a study to evaluate the cost-effectiveness of this intervention.

2. Methods

2.1 Analytical Overview

Cost-effective analysis was conducted based on the RCT evaluating the effect of EOF following total gastrectomy among gastric cancer patients (Shimizu et al., 2018). The information on its methods and results has been presented in detail elsewhere (Shimizu et al., 2018).

Patients who underwent total gastrectomy were randomly assigned to either an intervention group (early oral feeding, EOF) (N=32) or a control group (conventional oral feeding, COF) (N=30). The EOF group was given iEAT® from lunch on POD 1 through dinner on POD 3. On POD 4 and thereafter, ordinary hospital diets were provided. iEAT® (EN Otsuka Pharmaceutical Co., Ltd., Japan) is a commercially available food, and its physical properties have been adjusted for shape-retention despite its softness. Although it retains an appearance similar to ordinary food, it can be disintegrated by the tongue. In a prior study that dissolved different foods in artificial digestive juices into small residues, iEAT was shown to disintegrate more quickly than ordinary foods (Higashiguchi, 2013).

In this study, iEAT offered as EOF consisted of one staple food (rice) and two side dishes. Its average calories and protein amount were approximately 450 kcal and 25g per meal, respectively.

As to an intervention, iEAT was used, instead of diets in conventional EOF, to enhance the effect of EOF. Its reasons are as follows. Firstly, it offers standardized intervention, since diets in conventional EOF vary from liquids to rice porridge. Secondly, the amount of nutrition intake of energy and protein for iEAT were significantly higher than those for conventional diets mentioned before (Higashiguchi, 2013). It is pointed out that patients after gastroenterological surgery require high energy and protein to prevent complications and accelerate recovery (Fukatsu, 2019).

On the other hand, the COF group received conventional nutritional management. The COF was usually started with a liquid diet or rice gruel on POD 3 or 4 and shifted to ordinary diets on POD 7 or 8, although it varied depending on the facility. Liquid diet or rice gruel in COF typically consisted of three dishes in both meals. Their average calories and protein amount were approximately 260 kcal and 8.3g per meal, and 430 kcal and 18 g per meal, respectively. For both groups, there were no limitations regarding infusions, eating between meals, and other means of perioperative management.

As is shown in Table 1, between the EOF group and the COF group, no statistical differences were observed in age, sex, height, clinical state, kind of surgery and operating time. As to clinical outcomes, a statistically significant difference was observed in feeding start day ($p<0.01$), and days reaching the specified oral energy intake ($p<0.05$). The length of hospital stay in the EOF was significant shorter than that in the COF ($p<0.05$), while there was no statistical difference in the proportion of adverse event between two groups. In this paper, all data were presented based on per-protocol instead of intention-to-treat, according to the research protocol predefined.

As a type of economic analysis (Drummond, Sculpher, Claxton, Stoddart, & Torrance, 2015), a cost-effective analysis was performed. Costs and effectiveness were evaluated and compared between the EOF and the COF groups. A societal perspective was adopted as a perspective of economic analysis to evaluate value for money of EOF compared to COF (Drummond et al., 2015). The effectiveness measure used was quality-adjusted life-days (QALDs) (Ioannidis & Graber, 2011). As to cost items, direct medical care costs (e.g., costs of nutrition,

hospitalization and treatment of adverse events) were examined. Indirect costs (i.e., time costs or production loss among patients) after discharge were examined for a base case analysis. However, they were excluded in the sensitivity analysis mentioned later. As a time horizon for evaluation, 3-week follow-up after gastrectomy was considered.

Table 1 Characteristics of subjects and interventional outcomes

Item	EOF (N=32)	COF (N=30)	p value
Sex (male)	78.1%	73.3%	0.566[a]
Age (years)	67.6 (7.3)	66.3 (9.8)	0.595[b]
Height (cm)	162.3 (9.5)	163.6 (8.1)	0.566[b]
Weight (kg)	61.3 (10.9)	58.5 (10.5)	0.308[b]
History of illness[†]	34.4%	50.0%	0.213[c]
Performance status (0)[‡]	96.9%	100.0%	1.000[a]
Clinical stage (less than II)	62.5%	63.3%	0.946[c]
Laparoscopic Surgery	56.3%	50.0%	0.622[c]
Operating time (mins)	294.8 (80.0)	301.0 (87.7)	0.772[b]
Outcomes (3-week follow up)			
Feeding start day	1.1 (0.3)	3.7 (1.3)	0.000[d]
Days reaching the specified oral energy intake#	6.1 (2.9)	9.4 (7.4)	0.028[d]
Length of stay (days)	10.4 (2.5)	12.8 (3.8)	0.005[d]
Adverse event[+]	9.4%	23.3%	0.176[a]

Notes. Numerical value: mean (SD), EOF: early oral feeding, COF: conventional oral feeding;

[†]experience of diseases prior to gastrectomy, [‡]normal activity by ECOG performance status;

[#] energy intake more than 700 kcal/day, [+]grade I or higher by Clavien-Dindo Classification;

[a] Fisher's exact test, [b] t-test, [c] chi-square test, [d] t-test (Welch).

2.2 Effectiveness

Quality of life among the subjects was measured using EuroQoL-5Dimentions-3Levels (EQ-5D-3L) (EuroQol Group, 1990). A questionnaire survey of EQ-5D-3L was carried out among all the patients on each day during a 3-week follow-up period. EQ-5D-3L responses were transformed to utility values according to the utility scoring algorithms from the general population survey (Tsuchiya et al., 2002). Utility value is preference based quality of life, which evaluates the value of health state in a single score (e.g., death =0, perfect health =1.0, as anchor points).

As a health outcome measure in this economic evaluation, quality-adjusted life day (QALD) was used. QALD combines two attributes (i.e., quality of life and length of life) into a composite measure of health. QALDs in each patient were estimated through weighting each day by its utility value. Namely, a number of QALDs = a number of days of life x utility value. In economic evaluation, quality-adjusted life year (QALY) is most widely used (Drummond et al., 2015). However, when the change is much less than one QALY, QALY is usually expressed in days (i.e., QALD) (Ioannidis & Graber, 2011). QALDs can be simply converted to QALYs by dividing them by 365.

2.3 Cost

Costs incurred for resources used during follow-up after gastrectomy were estimated from trial data. Resource utilization was derived from individual patient data. Items for direct costs such as nutrition, hospitalization and treatment of adverse events are examined. For these direct costs, the National Health Insurance reimbursement list and drug price were used (Jiho, 2010). The cost of hospitalization per day is $264.1 (hospitalization days 1-10), $195.2 (days 11-20), and $166.0 (days 21-33). There are two types of the costs of nutrition. While the commercial cost for iEAT was used from a societal perspective, insurance prices were used from a payer's perspective. The reason is that iEAT is not admitted yet for the national insurance plan. The costs per day for iEAT varied from

$10.3 to $12.1 depending on their contents during POD 1 and POD 3. In contrast, the cost per day for conventional oral feeding reimbursed by the National Health Insurance was $6.3.

On the other hand, as mentioned before, indirect costs (e.g., time costs or production loss among patients) were examined in a base case analysis. Indirect costs per patient were calculated by multiplying postoperative hospitalization days, and wages and employment rate for each day. Wages per day were estimated by the Basic Survey on Wage Structure in Japan (Ministry of Health, Labour and Welfare Japan, 2016), and employment rate was estimated by the Labor Force Survey in Japan (Ministry of Internal Affairs and Communications Japan, 2016). In addition, since there are several concerns about the inclusion of indirect costs (Drummond et al., 2015), indirect costs were excluded from the other social perspective in a sensitivity analysis.

Mean costs and their standard deviation per patient were calculated by summing up the costs listed above. All costs were converted from Japanese yen to US dollars based on Organization for Economic Co-operation and Development (OECD) purchasing power parity in 2016 ($1 = \101.6) (Organization for Economic Co-operation and Development, 2016). Discounting for the time value of money was applied to neither costs nor effectiveness, since intervention and follow-up were done within a short period (Drummond et al., 2015).

2.4 Sensitivity Analysis

The uncertainty of the results was explored by stochastic and qualitative sensitivity analyses of important factors (Drummond et al., 2015; Briggs, 2004; Glick, Briggs, & Polsky, 2001). Firstly, As to a base case, the impact of uncertainty on the estimated cost (e.g., hospitalization and nutrition) and effectiveness (QALDs) due to the stochastic nature of sampled data was analyzed by a stochastic sensitivity analysis, applying a bootstrap re-sampling technique (i.e., 3000 times) to both costs and effectiveness. Its results were shown as a contour curve, according to the distribution density of incremental cost-effectiveness between the EOF and COF groups (Briggs, 2004; Glick et al., 2001).

Secondly, as qualitative sensitivity analysis, three perspectives for economic evaluation were examined (i.e., a social perspective including indirect costs (a base case), a social perspective excluding indirect costs, and a payer's perspective). A base case analysis in this paper adopted a social perspective including indirect costs. Even though indirect costs should theoretically be included from a social perspective (Drummond et al., 2015), there has been debate about treating and estimating indirect costs (Drummond et al., 2015; Jönsson, 2009; Jacob & Fassbender, 1998). So, secondly, costs were estimated from a social perspective excluding indirect costs (i.e., a conservative point of view). Finally, from a payer's perspective, economic evaluation was conducted.

Therefore, as to costs, a social perspective (Drummond et al., 2015) including indirect costs included both direct and indirect costs. It should be noticed that it used commercial prices for iEAT as nutritional costs among the EOF group. On the other hand, a social perspective excluding indirect costs excluded indirect costs from the costs by a social perspective including indirect costs. The third payer's perspective (Drummond et al., 2015) included only direct costs. In this case, only reimbursement rates for nutritional care were used among both the EOF and COF groups.

The commercial prices for iEAT are higher than those reimbursement rates. From a payer's perspective, differences between these costs were not considered, and transferred to patients or in some cases healthcare providers.

2.5 Statistical Analysis

As to statistical analysis, quantitative data comparison between two groups was analyzed by using t-test, or t-test (Welch) when the variance of both groups is not the same. This analysis was based on the normal distribution according to the central limit theorem, since the sample sizes of both groups exceeded 30. However, simultaneously, data was analyzed by using Mann-Whitney U test, without any assumptions about the distribution of both groups. If there was a large discrepancy between these tests, additional information based on Mann-Whitney U test was given. In addition, 95% confidence intervals for incremental effectiveness and costs were shown. On the other hand, categorical data was analyzed by using chi-square test, or Fisher's exact test when the sample size of each cell in a table was less than 10. All statistical analyses were performed using SPSS 16.0J and TreeAge software.

3. Results

3.1 Effectiveness

The mean QALDs in each group are shown in Table 2. The mean QALDs for the EOF and the COF groups were 14.93 and 14.19, respectively. Incremental effectiveness of the EOF group compared with the COF group was 0.74

QALDs (p=0.359). EOF increased 0.74 QALDs (i.e., 2.03 x10^{-3} QALYs) per patient, compared with COF. This difference was not statistically significant.

Table 2. Incremental effectiveness and costs of EOF compared with COF per person

Item	EOF (N=32)	COF (N=30)	Incremental effectiveness and costs (95% confidence intervals)	p value
Effectiveness				
QALDs	14.93 (3.26)	14.19 (3.03)	0.74 (-0.86 ~ 2.34)	0.359[a]
Total costs ($)				
Societal perspective including indirect costs	3 177.7 (808.4)	3 755.4 (1 214.6)	-577.7 (-1 107.6 ~ -47.8)	0.033[b]
Societal perspective excluding indirect costs	2 707.7 (538.6)	3 151.8 (862.0)	-444.1 (-813.9 ~ -74.3)	0.020[b]
Payer's perspective	2 669.8 (538.0)	3 151.8 (862.0)	-482.0 (-851.7 ~ -112.3)	0.012[b]

Notes. Numerical value: mean (SD), EOF: early oral feeding, COF: conventional oral feeding, QALD: quality-adjusted life day, [a] t-test, [b] t-test (Welch).

3.2 Cost

The mean total costs per patient in each group are shown in Table 2. From a societal perspective including indirect costs, as a base case analysis, the mean total cost per patient in the EOF and the COF groups was $3,177.7 and $3,755.4, respectively (p<0.05). Incremental cost of the EOF group compared with the COF group was -577.7 (p=0.03). EOF saved $577.7 per patient, compared with COF.

The main cost component was costs of hospitalization (Table 3). That in the EOF group was statistically lower than that in the COF group (p<0.01). In contrast, the cost of nutrition (considering the price of iEAT) in the EOF group was higher than that in the COF group (not statistically significant). EOF increased $29.8 per patient, compared with COF. The cost for treatment of adverse events was not observed, since they were not so severe as to require specific treatments. As to indirect costs, that in the EOF group was lower than that in the COF group, but no statistical difference was observed.

In considering both incremental effectiveness and costs, EOF was cost-saving, with non-significant increase in effectiveness (i.e., QALDs). Therefore, from a societal perspective considering indirect costs, EOF was dominant, or at least weakly dominant (Drummond et al., 2015), compared with COF.

Table 3. Cost components of EOF and COF per person

Item	EOF (N=32)	COF (N=30)	p value
Direct costs ($)			
Hospitalization	2 475.0 (484.9)	2 948.9 (787.4)	0.007[b]
Nutrition	232.7(55.6)	202.9(78.9)	0.089[a]
Adverse event treatment	NA	NA	
Indirect costs ($)			
Return to work	470.0(401.0)	603.6(536.6)	0.269[a]

Notes. Numerical value: mean (SD), EOF: early oral feeding, COF: conventional oral feeding, a t-test, b t-test (Welch).

3.3 Sensitivity Analysis

The results of a stochastic sensitivity analysis are shown in Figure 1, which shows scatter plots of incremental cost and effectiveness between the EOF and COF groups. In this Figure, higher density of distribution for scatter plots

of cost and effectiveness, based on 3,000 samples, was shown as a darker area in a contour curve. More than 31% of the points resided in the southeast quadrant (i.e., cost saving and greater effectiveness). Also, if willingness to pay for additional QALY was set at \$5 x 10^4 (Grosse, 2008), more than 58% of the points resided below this threshold, which means that EOF is cost-effective or efficient.

The results of qualitative sensitivity analyses are shown in Table 2. As to the societal perspective excluding indirect costs, the mean total costs in the EOF group were significantly lower than those in the COF group ($p<0.05$). This is also true from a payer's perspective ($p<0.05$).

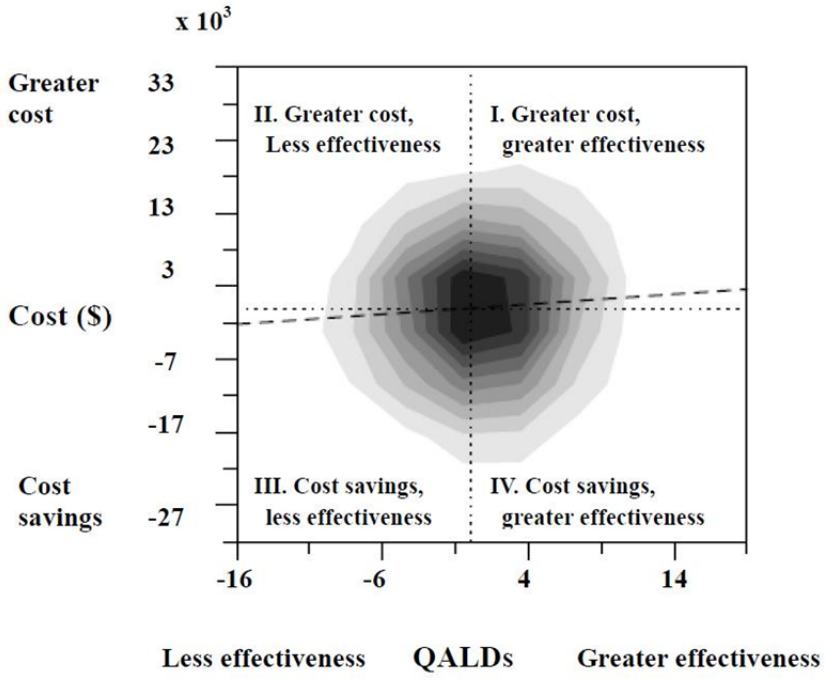

Figure 1. Stochastic sensitivity analysis

Incremental cost-effectiveness contour curve shows the relative concentration of points in the scatter plot for cost-effectiveness ratios, with a range of shades. An oblique line shows that cost-effectiveness ratio is \$5x10^4 per QALY.

4. Discussion

Evidence from systematic reviews (Liu et al., 2014; Tweed et al., 2019; Willcutts et al., 2016) indicates that EOF following gastrectomy for gastric cancer is effective for shortening the length of hospital stay without increasing averse events. However, the cost-effectiveness of EOF following gastrectomy has not been well explored. The only exception is a systematic review for ERAS, which indicated a reduction in hospital costs (Li et al., 2017). However, it has not fully examined both effectiveness and costs comprehensively, but only roughly mentioned costs.

Our study is the first attempt to evaluate the cost-effectiveness of EOF following total gastrectomy based on a RCT. The study adopted the societal perspective and showed that EOF after gastrectomy saved costs with small improvement of health outcomes (i.e., QALDs), compared with COF (Table 2). That is to say, EOF dominated COF. This dominance is not so strong, rather weak (Drummond et al., 2015), since increase in effectiveness is not statistically significant. According to qualitative sensitivity analysis on perspectives of economic evaluation, from both societal perspective, with or without including indirect costs, and payer's perspective, this result was confirmed. The most important cost component was the cost of hospitalization, of which the absolute value was around 10 times or 6 times higher than the costs of nutrition and indirect costs, respectively. This cost is clearly dependent on the length of hospital stay.

To estimate the uncertainty of this result due to sampling bias, stochastic sensitivity analyses (Drummond et al., 2015; Briggs, 2004; Glick et al., 2001) were performed (Figure 1). The cost-effectiveness contour curve showed

that more than 31% of cost-effectiveness plots located in the southeast quadrant (cost savings and greater effectiveness) on the cost-effectiveness plane. This result shows that the dominant cost-effectiveness of EOF is relatively robust.

This cost saving result could be ranked near the top of a league table of cost–effectiveness in health care, since less than 20% of published cost-effectiveness studies showed cost savings (Russell, 2009). Therefore EOF after total gastrectomy among gastric cancer patients is an efficient approach to postoperative management and can be considered as a cost-effective intervention to be accepted for wide use in Japan. Recently, in Japan, the application of cost-effectiveness of health technologies into health policy making has been tried. However, this is only applied for adjustment of the premium price based on the existing reference pricing system. Also, the subject drugs are restricted to new drugs with high price and high volume.

It is pointed out that this policy-making process is not evidence-based and is biased in many points (Hisashige, 2018). In addition, this analysis is primarily based on a payer's perspective for administrative approval. It would not fully capture the value of health technologies from a societal perspective. Moreover, although the administrative guidelines in Japan have been released (Study Team for "Establishing Evaluation Methods, Data Standardization, and Assessment Systems Toward the Application of Economic Evaluation of Healthcare Technologies to Governmental Policies", 2016), they mostly follow existing guidelines and issues unsolved among them have not been examined and still remain.

There are several points for discussions in the analysis that should be commented on, and the results should be treated with caution. First, the analysis was based on a small RCT (Shimizu et al., 2018). It would be vulnerable to uncertainty (Hackshaw, 2008). Systematic reviews of EOF after gastrectomy indicated that large RCTs with high quality are required to confirm current clinical evidence (Liu et al., 2014; Willcutts et al., 2016). It is pointed out that the main problem in each small study is that it produces a broad confidence interval (or imprecise estimate) of treatment effect, compared with a large study (Hackshaw, 2008). A funnel plot of studies shows that estimated effects among small studies scattered widely (i.e., a wide range of positive or negative results), even if there is no bias (Sedgwick & Marston, 2015). On the other hand, large studies often produce results far from definitive (Guyatt, Mills, & Elboume, 2008). Also, a recent study shows that a meta-analysis containing many small studies is better than a single large trial, even when there is some publication bias (Borm & Donders, 2009). Therefore, in the current paradigm, multiple small studies are conducted and subsequently combined in a meta-analysis with an examination of heterogeneity (IntHout, Ioannidis, Borm, & Goeman, 2015).

As to EOF, there is nothing wrong with conducting well-designed small studies a), accumulating the results of individual trials, regardless of small or large size, is best viewed as providing important information that contributes to the larger body of evidence (Guyatt, Mills, & Elboume, 2008).

Second, the time horizon for analysis is an important issue in sufficiently capturing relevant costs and health outcomes of EOF. In this study, the observation period of the trial (i.e., 3 weeks) was relatively limited, due to continuous diary survey for quality of life. As mentioned before, the length of hospital stay is a main cost factor. Since a small proportion of patients were still staying in a hospital, the time horizon in this study would underestimate the value of EOF in both hospital costs and indirect costs.

Third, the perspective of this analysis is that of a society. A societal perspective examines a broader range of costs compared with that of health care payers. A qualitative sensitivity analysis showed cost saving for EOF in both societal and payer's perspective. However, cost savings were much higher in the societal perspective including indirect costs. Also, there are some conflicts between theses perspectives. In Japan, fixed and bundling payments have been introduced to health care management in the national health insurance. Items such as nutrition support by iEAT are not listed in the national health insurance, so they are not reimbursed. Then, these costs are transferred to patients or healthcare providers. Therefore, changes in cost items due to a perspective of economic evaluation should be carefully examined.

Fourth, QALDs as a final outcome were used as economic outcome measures for the analysis. There were very few studies on quality of life for EOF or COF after gastrectomy. Hur et al. (Hur et al., 2011) used a disease specific instrument (i.e., EORTC) in evaluating oral feeding after gastric cancer surgery. However, it is not applicable in economic evaluation in healthcare. In our study, a general profile instrument (i.e., EQ-5D-3L) was used, and easily converted to utility (i.e., preference-based quality of life which evaluates the value of health states in a single score). Then, QALDs (or QALYs) can be used as a final outcome for economic evaluation.

Fifth, this study examined only EOF among total gastrectomy. A systematic review (Liu et al., 2014) showed that similar findings were found in both total gastrectomy and subtotal gastrectomy with regard to duration of hospital

stay and other items. However, in a recent RCT in Japan (Shimizu et al., 2018), EOF did not shorten the length of hospital stay in distal gastrectomy. So, it might still be needed to carefully assess cost-effectiveness of EOF for both total and partial gastrectomy, independently.

Sixth, this study showed the potential benefits of iEAT diet for EOF. In the past, as EOF, water, fluids or liquid diets have been widely used (Liu et al. 2014). Comparative effectiveness between iEAT and other diets for EOF has not been evaluated yet. Therefore, research exploring appropriate and optimal diet for EOF would be needed.

Also, it should be noticed that several components of ERAS have been introduced, more or less, into clinical settings in Japan (Kaibori, Miyata, Yoshii, & Fukushima, 2020). In our study, since components of ERAS except for EOF were randomized, they would not affect its results. However, the space for improvement by EOF alone seems to be limited.

Lastly, most of the studies on EOF following gastrectomy have been carried out in East Asian countries, such as Japan, Korea and China (Liu et al., 2014; Willcutts et al., 2016). It is clear that there is a paucity of studies in the Western countries. This seems to be due to the difference of incidence rates of gastric cancer. Also, health outcomes of EOF following gastrectomy would be influenced by racial, environmental, life-style or medical differences between the Western and Eastern countries. However, one RCT on EOF for total gastrectomy, conducted in the US showed a decreased length of stay (Selby, Rifkin, Yoon, Ariyan, & Strong, 2016). Therefore, the results of our study would be a helpful reference to the US or other Western countries. Since in general, economic evaluation can not be readily transferable to other countries (Drummond et al., 2009), economic evaluation of EOF should be carried out in each country.

5. Conclusion

In considering both incremental effectiveness and costs, economic evaluation of EOF following total gastrectomy showed that EOF was cost-saving, with non-significant increase in effectiveness (i.e., QALD). This cost saving result could be ranked quite highly in a league table of cost-effectiveness in health care. This result can contribute to strengthen the evidence for wide use of EOF.

Declarations

Ethics Approval and Consent to Participate

The study was based on a clinical trial approved by the institutional review board at each of the study sites and was performed in accordance with the principles of the Declaration of Helsinki. Informed consent was obtained from all the patients and/or guardians.

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Role of Each Author in the Work

AH: study concept and design, acquisition, analysis and interpretation of economic data, and preparation of manuscript

NS and YS: acquisition and analysis of subject and clinical data

Competing Interests Statement

The authors declare that there are no competing or potential conflicts of interest.

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Evaluating the Effectiveness of Peer Education Program on Health Knowledge, Attitudes and Practices

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Abstract

Kelab Doktor Muda (KDM) which translates as Young Doctors Club was established by the Ministry of Health (MOH) Malaysia to train a group of schoolchildren as educators in assisting their peers to adopt healthy practices. This research aims to assess the effectiveness of KDM as a peer education program to increase the health knowledge of school children, and instil healthy practices among schoolchildren by identifying the difference in the level of knowledge, attitude and health practice between school with KDM (SKDM) and school without KDM (NKDM). This is a nationwide comparative cross-sectional study between SKDM and NKDM. This study was carried out between March 2016 and March 2017. Data were obtained using a guided self-administered questionnaire through survey involving 2588 (1294 SKDM; 1294 NKDM) year 5 (11 years old) schoolchildren from 87 primary schools nationwide. The results revealed a significantly higher overall knowledge score of health practices, knowledge and practice score for No Smoking component, as well as hand hygiene knowledge in SKDM compared to NKDM. Schoolchildren in SKDM also had significantly lower BMI compared to NKDM, directly related to healthy eating, active lifestyle and ideal body weight, 3 of the 6 components in this program. As a conclusion, the program was found to be not only effective in increasing the overall knowledge of health practice among schoolchildren, but also results in a meaningful impact to the health of schoolchildren. Further improvements to the modules however should be undertaken to enable more comprehensive changes on the health practices of schoolchildren.

Keywords: peer education program, health education, healthy lifestyle

1. Introduction

Health problems among schoolchildren have been one of the highlights in many countries' national health program. The rising of health problems among the schoolchildren such as overweight and obesity are alarming that it becomes one of the top priorities in public health agendas. In 2016, more than 330 million children and adolescents worldwide were either overweight or obese (Abarca-Gómez et al., 2017). Children and adolescent periods are also crucial in providing future health opportunity through prevention and early intervention.

In Malaysia, obesity in children is a serious public health problem and the prevalence has been increasing dramatically over the last two decades (Dea, 2005). Past studies on obesity among schoolchildren showed a consistent prevalence of overweight and obesity between 25% to 30% (Institute for Health Behavioural Research, 2011; Institute for Public Health, 2012, 2015). This is likely due to reduced physical activity and changes in diet (Sabramani et al., 2015). Aside from obesity, there are many other health problems among children in Malaysia that needs attention. Prevalence of poor hand hygiene practices was also found to be quite high around 5% to 25% (Institute for Public Health, 2012), while dental hygiene was still at unsatisfactory level (Pau, 2012). It is imperative that these two practices be improved at an early stage. In the long run, inculcation of good personal hygiene will reduce the likelihood of developing risk factors to communicable diseases (Hammer, Brainard, & Hunter, 2018).

Health problems occur partly due to poor health knowledge that inevitably leads to poor health practices. Thus, instilling health knowledge and enforcing correct attitude are well known to be the key drivers towards good health practices as well as reducing diseases and disabilities (ul Haq et al., 2012). However, instilling healthy practices is often a challenge for many health educators and healthcare workers. This is even more challenging among children and adolescent as they are not aware and may not yet appreciate the long-term benefit of healthy life choices.

Recent studies have shown that intervention programs targeted on schoolchildren through peer-led teaching to be an effective method for improving knowledge, healthy lifestyle practices and attitudes towards health among children (Stock et al., 2007). The unique setting in school is able to help the children in developing positive insight and establishing healthy lifestyle. A study of a peer health education program conducted in a Ugandan Primary School suggested that children did not only learn important lessons about disease prevention, hygiene, sanitation, personal safety, avoiding bad peer relationships, puberty, and nutrition, but they were also changing their behaviour and behaviour of their peers (Falk, Pettet, & Mpagi, 2016).

In Malaysia, a similar peer-led teaching program has been implemented since 1989. *Kelab Doktor Muda (KDM),* which translates as Young Doctors Club involves a selection of schoolchildren who were trained as peer educators *(Doktor Muda)* (Suraiya, Pises, Faizal, Shahnaz, & Nor Asiah, 2017). This program aims to produce a group of schoolchildren as an agent for promoting good health to their peers, family members and community (Ali et al., 2018). The selected schoolchildren were trained using the KDM Training Module that emphasizes on six (6) health components; Healthy Eating, Hand Hygiene, No Smoking, Active Lifestyle, Dental Health, Ideal Body Weight with the aim to be a mentor or an agent of change towards instilling good knowledge, attitude and health practices among their peers. As of 2019, KDM has been implemented in 3286 number of schools nationwide.

A previous study evaluating the effectiveness of the KDM in primary schools was done in Kelantan, Terengganu and Pahang, focusing on three (3) fundamental areas of health, namely personal, environmental and dental hygiene. The results showed significant differences in knowledge, attitude and health practices between peers in schools implementing the KDM program and schools without KDM (Siti Haslinda M.D, 2005). As a decade passed since the last study, it is high time to re-evaluate the effectiveness of this program and provide the program managers with necessary inputs in improving this program. While the past study only covered three (3) states, this current study covers all the states in Malaysia with far more comprehensive evaluation.

1.1 Objective

This research was carried out to assess the effectiveness of KDM, as peer education program in affecting the health knowledge, attitude and practices of the peers. This was carried out by identifying the differences in the level of knowledge, attitude and health practices between schoolchildren in schools with KDM (SKDM) who were not enrolled in KDM (evaluation of the peers), and schoolchildren in schools without KDM (NKDM).

2. Materials and Methods

A nationwide comparative cross-sectional study between SKDM and NKDM was carried out between March 2016 and March 2017. A stratified two-stage cluster sampling was applied in this study; the first stage was the selection of school using proportionate sampling and the second stage, selection of the schoolchildren. The schools were selected to ensure equal representation of school from both urban and rural areas between each group. The schoolchildren were matched for gender between the two schools. The data was obtained using guided self-administered questionnaire. Year 5 schoolchildren were selected for this study to ensure participants had at least one year of exposure to peer educators. Members of KDM were excluded from the study as the aim of this study was to measure the effectiveness of KDM as a peer education program.

2.1 Sample Size

Based on previous literature, sample size was determined using two proportions sample size formula with 5% type 1 error and 80% power and equal ratio between the groups. Taking into account 20% non-response the final sample size needed for each group was 1282. (Kim, 2016)

2.2 Instrument and Pre-Test

The questionnaire was adapted from *The Youth Behavioural Risk Factor Surveillance* (YBRFS) (2011), *Global School-based Student Health* (GSHS) (2012) and covers the scopes in KDM Training Module.

Knowledge on Basic Health

The questions on knowledge consist of 22 items which include questions on healthy eating, hand hygiene, No Smoking, active lifestyle, dental health and ideal body weight. Knowledge questions were in the form of multiple choice. Score zero was given to the wrong answer and one for the right answer. The total score of this section

ranges from 0 to 22.

Attitude towards Health

The questions on attitude consist of 25 items which cover questions on healthy eating, hand hygiene, No Smoking, active lifestyle, dental health and ideal body weight components. The questions were designed as 5 points Likert Scale where the minimum score was 25 and the maximum score was 125.

Health Practices

The questions on practice consist of 24 items which include questions on healthy eating, hand hygiene, No Smoking, active lifestyle, dental health and ideal body weight. For the first 22 questions, a score zero was given to the non-compliance answer and score one was given to the compliance answer. The last question had 4 choices, whereby the respondents could choose multiple answers and each compliance answer was scored one. The total score of this section ranges from 0 to 26.

2.3 Data Collection and Management

The selected respondents were gathered in a classroom or school hall where their height and weight were measured by trained research officers to obtain the Body Mass Index (BMI). Briefing regarding this study was given to the respondents prior to answering the questions. The time allocated to answer the questionnaire was between 60 to 90 minutes. Completed questionnaires were reviewed at the field level and data entry was done centrally (Kuala Lumpur Office). The questionnaires were scanned using FormReaderTM software.

2.4 Data Analysis

Data were described using frequency, percentage and mean. Data were analysed using independent T-test to determine the mean difference between SKDM and NKDM, while Chi-Square Test was used to determine the association between the outcome variables. The data were analysed using Statistical Program for Social Science (SPSS) software version 23.0 at 0.05 significance level.

2.5 Ethical Issues

Ethical approval was obtained from the Medical Research and Ethics Committee, Ministry of Health Malaysia and Educational Planning and Research Division, Ministry of Education Malaysia. Approval from school administrators representing the parents/guardians was obtained as the samples were under the supervision of the school during the study and consent form to participate in the study by schoolchildren was obtained in writing form prior to the study. This study was registered under Malaysia National Medical Research Registry (NMRR) with the identification number NMRR-16-642-30447.

3. Results

A total of 87 schools (44 SKDM, 43 NKDM) and 2,588 schoolchildren (1,294 SKDM and 1,294 NKDM) participated in this study. Table 1 showed the demographic characteristics of the respondents, wherein the majority being of Malay ethnicity (84.0%) and living with both parents (88.2%). There was no significant difference in ethnicity (X^2 = 0.474, p = 0.491) and living arrangement (X^2 = 0.561, p 0.755) between schoolchildren in SKDM and NKDM.

Table 1. Demographic Characteristics of Selected Schoolchildren (n=2,588)

Demographic Characteristics		n	Frequency (%)		p value[¶]
			SKDM	NKDM	
Ethnicity	Malay	2161	1087 (84.0)	1074 (83.0)	0.491
	Others	427	207 (16.0)	220 (17.0)	
Living arrangement	Both Parents	2279	1141 (88.2)	1138 (87.9)	0.755
	Single Parents	210	101 (7.8)	109 (8.4)	
	Guardian	99	52 (4.0)	47 (3.6)	

[¶]Chi-Square Test.

Table 2. Comparison of Mean Scores for Knowledge, Attitude and Health Practices in SKDM and NKDM schools (n= 2,588)

		Score (Mean ± SD)		p value[†]
		SKDM	NKDM	
Knowledge	**Overall**	10.18 ± 3.06	9.91 ± 3.05	0.023*
	Healthy Eating	3.64 ± 1.45	3.54 ± 1.44	0.095
	Hand Hygiene	1.94 ± 0.79	1.87 ± 0.83	0.033*
	No Smoking	1.56 ± 0.94	1.49 ± 0.94	0.047*
	Active Lifestyle	1.34 ± 0.69	1.32 ± 0.71	0.500
	Dental Health	0.95 ± 0.80	0.99 ± 0.79	0.297
	Ideal Body Weight	0.74 ± 0.80	0.69 ± 0.80	0.108
Attitude	**Overall**	97.50 ± 9.09	98.11 ± 9.81	0.100
	Healthy Eating	24.41 ± 3.16	24.50 ± 3.28	0.494
	Hand Hygiene	12.94 ± 2.09	12.92 ± 2.13	0.823
	No Smoking	13.00 ± 2.13	12.94 ± 2.11	0.442
	Active Lifestyle	16.97 ± 2.86	17.34 ± 3.11	0.001**
	Dental Health	15.72 ± 2.45	15.88 ± 2.50	0.086
	Ideal Body Weight	17.79 ± 2.96	17.90 ± 2.97	0.375
Practice	**Overall**	16.18 ± 3.11	15.99 ± 1.28	0.111
	Healthy Eating	2.56 ± 1.28	2.55 ± 1.29	0.765
	Hand Hygiene	3.21 ± 1.09	3.19 ± 1.11	0.629
	No Smoking	4.46 ± 1.02	4.37 ± 1.00	0.034*
	Active Lifestyle	1.10 ± 0.78	1.07 ± 0.78	0.324
	Dental Health	1.65 ± 0.53	1.67 ± 0.54	0.487
	Ideal Body Weight	1.77 ± 0.95	1.65 ± 0.96	0.003**

[†]Independent T-test.

*p<0.05, **p<0.01.

Findings in Table 2 showed significant difference in overall knowledge of health practices between SKDM (10.18 ± 3.06) and NKDM (9.91 ± 3.05; t = 2.271, p = 0.023). Meanwhile, the overall score of attitude and practice of health practices showed no significant difference between both schools.

Detail analysis showed knowledge score for hand hygiene to be significantly different between SKDM (1.94 ± 0.79) and NKDM (1.87 ± 0.83; t = 2.137, p = 0.033). However, attitude and practice scores for the same component showed no significant difference.

Similarly, the results revealed that SKDM (1.56 ± 0.94) had significant higher score on knowledge for No Smoking compared to the NKDM (1.49 ± 0.94; t = 1.987, p = 0.047) but having no significant difference in their attitude scores. The No Smoking practice score also was significantly higher among SKDM compared to NKDM (p value= 0.034).

In addition, active lifestyle attitude score in SKDM (16.97 ± 2.86) showed to be significantly lower compared to NKDM (17.34 ± 3.11; t = -3.191, p = 0.001), however the practice scores for ideal body weight was significantly higher among SKDM schools (p value=0.003).

Table 3. Body Mass Index (BMI) of the selected schoolchildren in SKDM and NKDM schools (n=2,588)

		n	Frequency (Percentage)		p value¶
			SKDM	NKDM	
BMI	Underweight	226 (8.7)	125 (9.7)	101 (7.8)	0.004*
	Normal	1453 (56.1)	747 (57.7)	706 (54.6)	
	Overweight	452 (17.5)	227 (17.5)	225 (17.4)	
	Obese	457 (17.7)	195 (15.1)	262 (20.2)	

¶Chi Squared Test.

*p<0.01.

The BMI of the schoolchildren showed a significant association between the categories of BMI and the type of school, with p value of 0.004. A total of 20.2% of the students in NKDM were obese, with only 15.1% of students in SKDM being obese. Likewise, only 54.6% of school children in NKDM had normal BMI, compared to 57.7% of school children in SKDM. The result was incongruent with Ideal Body Weight practice score result (Table 2) where there was a significant difference in ideal body weight component and showed SKDM has a better score in ideal body weight compared to NKDM. However, we also found that 9.7% of school children in SKDM were underweight while only 7.8% of school children in NKDM being in this BMI category.

4. Discussion

This study found that the overall knowledge of health practice among schoolchildren in SKDM was significantly higher compared to schoolchildren in NKDM. This proves that this intervention has a positive impact in instilling health knowledge to the schoolchildren, fulfilling the main objective of this peer education program. Good knowledge is an essential component that leads to a positive attitude and subsequently translates into good health practices. (ul Haq et al., 2012). This study found that there was a significantly higher knowledge and practice score for No Smoking component in SKDM compared to NKDM. This finding showed that KDM activities at school and *Doktor Muda* (peer educator) have helped the peers to understand the downsides of smoking and make a decision to say no to smoking. Reports (Knut-lnge Klepp & Andrew Halper, 1986) have confirmed that the use of leaders in social groups as a model for school health curriculum has shown to be more effective than relying entirely on teachers in delaying smoking and marijuana use. KDM educates schoolchildren on health and raises awareness of the harmful effects of smoking. Early prevention of smoking among children is known to help prevent future smokers (Krainuwat, 2005). Thus, the intervention program through peer education is crucial in achieving that objective. A school-based smoking prevention program that uses peer leaders has shown to reduce smoking onset by 25–30%, and school plus community programs can reduce smoking onset by 35–40% by the end of high school (Flay, 2009).

In SKDM, there is an emphasis on practising proper hand hygiene. This was reflected on hand hygiene's knowledge score between both schools, where SKDM scored higher compared to NKDM. Proper handwashing practice is the most important basic hygiene in preventing infectious diseases (Issa, McHenry, Issa, & Blackwood, 2015). Congruent with a previous study (Young et al., 2017), peer-education was effective at changing knowledge around hygiene including hand hygiene, infection and antibiotic topics as well as a tool to educate young people on the importance of health and hygiene.

The study also revealed that schoolchildren in SKDM had significantly lower attitude score in active lifestyle compared to schoolchildren in NKDM. This, however did not translate into practice, where there was no significant difference between both groups. Thus, KDM needs to be improved to create a significant leap in attitude change towards active lifestyle. Past studies have shown that peer educators provide useful impact towards active lifestyle (Cui, Shah, Yan, Pan, & Gao, 2012). The vast majority of scientific evidence supports a beneficial role of exercise in achieving bodyweight stability and overall health (Chaput et al., 2011). Despite having lower attitude score in active lifestyle component, it is encouraging to know that SKDM had higher scores in practice of ideal body weight compared to NKDM.

The most convenient and simple to use tool in translating knowledge, attitude and practice scores to more objective measurements would be measuring the schoolchildren BMI. Measuring this would directly akin to healthy eating, active lifestyle and ideal body weight; three of the six components within the KDM program. This study has revealed that schoolchildren in SKDM had significantly different BMI compared to NKDM. There was a higher

percentage of schoolchildren in the normal BMI category and a lower percentage of schoolchildren in the obese category among schoolchildren in SKDM. This was the most encouraging and objective results of this program. Few other studies have also suggested peer education programs to be an effective means towards preventing obesity (Intan et al., 2016).

In making sure that the necessary health knowledge is properly delivered to the schoolchildren and being translated into attitude and practice, attention should be given on the dissemination of the health messages from the members of KDM to the peers to further improve the program. The discouraging results of knowledge, attitude and practice findings of SKDM in this study could be due to the low confidence in delivering the health messages by DM to the peers (Pises, Ha, Sm, S, & Suriya, 2012) and also the lack of interest by peers in learning on health, subsequently resulting to the poor feedback (Suraiya et al., 2017) (Muhamad et al., 2017). The magnitude of the difference was found to be small and could also be due to multiple factors such as the accessibility of health knowledge to the school children via multiple sources of health information (Al-darwish, 2015) and existing school programs besides the KDM (Christian et al., 2015).

The program manager can use the result of this study to improve the KDM training module and update the content based on public health needs. Modules that did not show an increase in knowledge and practice may need to be revised, and also made suitable according to the current times. Analysing the sub-components of the program, alerts us that there is a need to fine tune and improve the approach in the other components of this program. This study also lends supports that the program should be expanded further to more schools within Malaysia as school-based interventions have the potential to improve the health and well-being of students and their communities especially by focusing on both individual and environmental determinants of health (Mukamana & Johri, 2016).

4.1 Limitation

The strength of this study lies in the comprehensive enrolment from schools nationwide, at the same time providing a detailed analysis of the findings compared to the previous study. However, this study is not without limitation. By adopting a cross-sectional study, there is limited information available to measure the actual effectiveness of the program. The changes of health knowledge to practice for example could not be measured through a cross-sectional study. Moreover, this study only includes year 5 schoolchildren in primary school, in which the decision-making process is still quite limited. Majority of studies on peer education program measure the effectiveness from the perspective of adolescents. Hence, future study should give focus on different study type such as a cohort study.

There are more components in the knowledge module that are significant compared to attitude and practices. One of the things we must consider is the time of evaluation between the peer education program been introduced to the school children and the evaluation of its effectiveness. 1 to 2 years period of evaluation might be too early to result in inculcating changes in attitude and practice. An assessment after a longer period is thus necessary to detect the changes in attitude and practice and also determine the long term impact of this program.

5. Conclusion

As a conclusion, the *Doktor Muda* peer education program was found to be effective in increasing the overall knowledge of health practice among schoolchildren. The program also results in a meaningful impact to the health of schoolchildren, as schoolchildren in SKDM also had significantly lower BMI compared to NKDM, directly related to healthy eating, active lifestyle and ideal body weight, 3 of the 6 components in this program. Even though not all components of this program have significant results, there were still evidence of encouraging impacts shown by KDM towards schoolchildren's health behaviour. Further improvements to the modules however should be undertaken to enable more comprehensive changes on the health practices of schoolchildren, which is hoped that they will carry on to adulthood.

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Competing Interests Statement

The authors declare that there are no competing or potential conflicts of interest.

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Relationship between Vitamin D Deficiency and Insulin Resistance in Obese Children

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Abstract

Introduction: Obesity represents the major risk factor for development of insulin resistance during childhood and adolescents. In obesity, adipose tissue release free fatty acids, various hormones, and cytokines, resulting in insulin resistance. This study aimed to establish the correlation between vitamin D deficiency and the incidence of insulin resistance in obese children.

Design and Method: This analytical cross-sectional study was arranged from December 2019 - February 2020 included 96 students aged 11–17 years old from junior and senior high school who met the criteria for obesity in Makassar. The study subjects were parted into two groups, obese children with vitamin D deficiency (levels of 25-hydroxyvitamin D ≤ 20 ng/ml) and obese children without vitamin D deficiency group (levels of 25-hydroxyvitamin D > 20 ng/ml). Data were analyzed using univariate and bivariate analysis.

Results: The frequency of insulin resistance in obese children with vitamin D deficiency was 28 (54.9%), while obese children without vitamin D deficiency was 10 (22.2%). Based on statistical analysis, the frequency of the occurrence of insulin resistance in vitamin D deficiency obese children was higher than in obese children without vitamin D deficiency with OR = 4.261 (95% CI 1.744 – 10.411), p = 0.001.

Conclusion: The risk of insulin resistance in obese children with vitamin D deficiency is 4.261 times higher than obese children without vitamin D deficiency.

Keywords: vitamin D deficiency, insulin resistance, obese children

1. Introduction

Deficiency of vitamin D is an important issue in the world that involves all ages including children, and it is associated with levels of adiposity (Peterson, 2015). A previous study reported that 50% of obese adolescents in Poland have vitamin D deficiency (Garanty-Bogacka et al., 2011). A study of 125 obese children in Germany, found that 75% of subjects have vitamin D deficiency (<20 ng/ml) (Roth et al., 2011).

Vitamin D deficiency in obesity resulting from increased inflammation in muscle cells and increased infiltration of immune cells and pro-inflammatory activation of perimuscular and intramyocellular adipose tissue. With the secretion of pro-inflammatory molecules, immune cells induce inflammation of myocytes and developing insulin resistance through the paracrine effect (Wu & Ballantyne, 2017).

The link between vitamin D with obesity is not only a condition of vitamin D accumulation in adipose tissue but also higher leptin levels. Leptin through Fibroblast Growth Factor-23 (FGF-23), a phosphaturic factor that importance in the metabolism of vitamin D in the kidneys, suppresses the synthesis of 1,25-hydroxyvitamin D, which is the active form of vitamin D in the kidneys. Besides, leptin directly suppress circulating 25-hydroxyvitamin D binding with 1-hydroxylase (CYP27B1) and 1,25-hydroxyvitamin D 24-hydroxylase (CYP24) in kidney and adipose tissue. There is also a theory which states that with an increase in adipose tissue, fat-soluble vitamin D will be stored in adipose tissue, causing vitamin D deficiency (Peterson, 2015).

A study showed that deficiency of vitamin D has an important role as well as a risk factor for insulin resistance (Sung et al., 2012). The 1.25-dihydroxy vitamin D signal in Vitamin D Receptors (VDRs) induces insulin to uptake glucose in the liver, adipose tissue, and skeletal muscle. 1.25-dihydroxy vitamin D directly activates transcription and expression of insulin receptor genes and protein. It also increases the expression of GLUT-4 in muscle cells

and induces translocation in adiposity. In obese patients, vitamin D lowers the release of cytokines and chemokines by adipocytes and chemotaxis by monocytes, as well as its effect on systemic and tissue-specific inflammation involving a variety of factors including suppression of the NF-κβ pathway, inhibits the expression of toll-like receptor 4 (TLR-4), and decrease dendritic cell differentiation (Greco et al., 2019).

In obesity, there is an increase in FFA (Free Fatty Acid), various hormones, and also cytokines released by adipose tissue which results in insulin resistance. Besides, obesity causes vitamin D deficiency which also causes insulin resistance. Therefore, it is necessary to investigate the relationship between vitamin D deficiency and insulin resistance in obese children.

Insulin resistance is the basic pathophysiology of metabolic syndrome, which long-term complications are such as type 2 Diabetes Mellitus, stroke, and cardiovascular disease (Pulungan et al., 2013). Management of insulin resistance should be started at initial stage, when comorbidities such as obesity are still reversible so that the morbidity and mortality associated with metabolic syndrome decreases (Govers, 2015).

A previous study showed that 47% of insulin resistance cases could be explained by the interaction between a high BMI (Body Mass Index) and low levels of 25-hydroxy vitamin D (Kabadi et al., 2012). This statistical evidence supports the idea that the burden of insulin resistance in obese individuals could be reduced by increasing serum 25-hydroxy vitamin D levels. Considering the difficulty of managing obesity in certain individuals, recommendations to increase body vitamin D levels may be a cheaper and more practical way to reduce the burden of insulin resistance.

Vitamin D is essential in glucose homeostasis. Most studies show that vitamin D deficiency paly a role in disrupting glucose homeostasis in obese adults, however, this hypothesis is still controversial in children (Torun et al., 2013). This study was conducted to know the relationship between vitamin D deficiency and insulin resistance in obese children, because the data regarding deficiency of vitamin D in obesity and its relationship with insulin resistance are still debatable, with a lack of study in children. To the best of the writer's knowledge, this study has never been conducted in Indonesia.

Based on the explanation above, this study aimed to establish the relationship between vitamin D deficiency and the incidence of insulin resistance in obese children.

2. Design and Method

This analytical cross-sectional study was arranged from December 2019 - February 2020 in 96 students aged 11 - 17 years who met the criteria for obesity. This study has been approved by the Ethics committee of biomedical research on Human of Hasanuddin university and written informed consent has been obtained from the parents of all children.

Inclusion criteria are Junior High or Senior High school students aged 11–17 years with obesity. Children with a history of liver or kidney dysfunction, children with endocrinological disease, children in corticosteroid, antiepileptics, or anti tuberculin medication, and children who were not fasting before the blood sample was drawn were excluded. Data of age, sex, and anthropometric examination results to determine nutritional status, and laboratory examination results were recorded. Laboratory tests include: 25-hydroxy vitamin D levels, fasting blood sugar levels, and fasting insulin levels. Blood sample examinations were conducted at the Hasanuddin University Medical Research Center (HUMRC) Laboratory in the city of Makassar. The study subjects were parted into two groups, obese children with vitamin D deficiency ((levels of 25-hydroxyvitamin D $\leq$ 20 ng/ml) and obese children without vitamin D deficiency group ((levels of 25-hydroxyvitamin D > 20 ng/ml).

Vitamin D was measured using the 25-hydroxyvitamin D enzyme-linked immunosorbent assay (ELISA) kit, colorimetric method. Fasting blood glucose was measured using blood analyzer Cobas Integra 400 Plus with Chemiluminescence method.

2.1 Data Analysis

Data were analyzed using univariate and bivariate analysis. Univariate analysis was used to describe the frequency, mean, standard deviation, range, and median value. Bivariate analysis including the Mann-Whitney test and Chi-Square test was used to compare the variables to determine the significance between vitamin D and the incidence of insulin resistance. Odds ratio (OR) analysis with 95% confidence interval (CI) was used to establish the risk of insulin resistance. The $p \leq 0.05$ indicates statical significance.

3. Results

During the study period, there were 51 (53,1%) obese children with vitamin D deficiency and 45 (46.9%) obese children with normal vitamin D status.

In the groups of vitamin D deficiency, the number of boys was 32 (62.7%) and girls were 19 (37.3%). In the groups without vitamin D deficiency, the number of boys was 25 (55.6%) and girls were 20 (44.4%). Statistical analysis based on the chi-square test showed that there was no significant difference in gender distribution between the groups of vitamin D deficiency and without vitamin D deficiency in obese children, with a value of p = 0.474 (p> 0.05) (Table 1).

Table 1. Analysis of Gender Distribution in group of Vitamin D Deficiency and group without Vitamin D Deficiency in Obese Children

Gender	Vitamin D		Total	*p*-Value
	Deficiency	Without Deficiency		
Boys	32 (62.7%)	25 (55.6%)	57 (59.4%)	
Girls	19 (37.3%)	20 (44.4%)	39 (40.6%)	0.474*
Total	51 (100.0%)	45 (100.0%)	96 (100%)	

** Chi-square test.*

The average age in the groups of vitamin D deficiency was 13.82 years old, the median value was 14.00 years old with a minimum-a maximum value of 12.08-17.08 years old. Whereas in the groups without deficient vitamin D deficiency, the mean age was 14.34 years old, the median value was 13.75 years old with a minimum-maximum value of 11.83-17.92 years old. The Mann-Whitney test showed that there was no significant difference in the mean age values between the groups of vitamin D deficiency and without vitamin D deficiency in obese children with a value of p = 0.579 (p> 0.05) (Table 2).

Table 2. Average Age Value in group of Vitamin D Deficiency and group without Vitamin D Deficiency in Obese Children

Age(years old)	Vitamin D		*p*-Value
	Deficiency (n=51)	Without Deficiency (n=45)	
Mean	13.82	14.34	
Median	14.00	13.75	0.579**
Standard Deviation	1.16	1.75	
Minimum-Maximum	12.08 – 17.08	11.83 – 17.92	

*** Mann-Whitney test.*

The incidence of insulin resistance in obese boys was 25 (43.9%), while in the obese girls was 13 (34.2%). Statistical analysis based on the chi-square test showed that there was no significant difference in the frequency of insulin resistance based on gender in obese children, with a value of p = 0.300 (p> 0.05) (Table 3).

Table 3. Analysis of Frequency of Incidence of Insulin Resistance by Gender in Obese Children

Gender	Insulin Resistance		Total	*p*-Value
	Yes	No		
Boys	25 (43.9%)	32 (56.1%)	57 (100%)	
Girls	13 (33.3%)	26 (66.7%)	39 (100%)	0.300*
Total	38 (39.6%)	58 (60.4%)	96 (100%)	

** Chi-square test.*

The mean age in the groups of insulin resistance was 13.91 years old, the median value was 14.00 years old with a

minimum-maximum value of 12.08–17.25 years old. Meanwhile, in the groups of non-insulin resistance, the mean age value was 14.16 years old, the median value was 13.79 years old with a minimum-maximum value of 11.83 - 17.92 years old. The Mann-Whitney test showed that there was no significant difference in the mean age values in the groups of insulin resistance and non-insulin resistance in obese children, with a value of p = 0.783 (p> 0.05) (Table 4).

Table 4. Mean Age Value in group of Insulin Resistance and group without Insulin Resistance in Obese Children in Obese Children

Age(years old)	Insulin Resistance (n = 58)	Without Insulin Resistance (n = 38)	*p*-Value
Mean	13.91	14.16	0.733**
Median	14.00	13.79	
Standard Deviation	1.37	1.55	
Minimum-Maximum	12.08 – 17.25	11.83 – 17.92	

** *Mann-Whitney test.*

The incidence of insulin resistance in vitamin D deficiency obese children was 28 (54.9%), while children without vitamin D deficiency was 10 (22.2%). The results of statistical analysis showed that there was a significant difference in the frequency of insulin resistance between the groups of vitamin D deficiency and vitamin D deficiency in obese children, with a value of p = 0.001 (p <0.05). The odds ratio (OR) = 4.261 (95% CI 1.744 - 10.411), which means that the risk of insulin resistance in obese children with vitamin D deficiency is 4.261 times greater than obese children who are not deficient in vitamin D (Table 5).

Table 5. Analysis of Frequency of Incidence of Insulin Resistance in group of Vitamin D Deficiency and group without Vitamin D Deficiency in Obese Children

Vitamin D status	Insulin Resistance		Total	*p*-Value
	Yes	No		
Deficiency	28 (54.9%)	23 (45.1%)	51 (100%)	0.001*
Without Deficiency	10 (22.2%)	35 (77.8%)	45 (100%)	
Total	38 (39.6%)	58 (60.4%)	96 (100%)	

* *Chi-square test*; OR=4.261 (CI 95% 1.744-10.411).

4. Discussion

In this study, it was observed that there was no significant difference based on sex category of obese children between groups of vitamin D deficiency and without vitamin D deficiency. This result was similar to a study in Turkey which also stated there was no significant relationship based on sex between children with vitamin D deficiency and without vitamin D deficiency (Torun et al., 2013).

There was also no significant difference in the frequency of insulin resistance based on sex category. A similar result was found in a study in Jakarta (Pulungan et al., 2013). In contrast, A study by Kostovski in Macedonia showed that the percentage of female experienced insulin resistance was higher than the male with p = 0.009 (p <0.05) (Kostovski et al., 2018). The explanation to this finding was because 52.94% of the female were in adolescence while 68.89% the male was in the pre-adolescent age. This difference may be related to age and puberty status of the study subjects.

There was no significant difference in the mean age in the groups of vitamin D deficiency and without vitamin D deficiency. A study in Italy by Rusconi also found no significant relationship between the mean age in children with vitamin D deficiency and without vitamin D deficiency (Rusconi et al., 2015).

There was also no significant difference in the mean age of insulin resistance and non-insulin resistance children. which means that age is not associated with the incidence of insulin resistance. This is incoherent with a study on 60 obese children with a mean age of 8.56 $\pm$ 1.7 years in Spain (Mastrangelo et al., 2016). Meanwhile, a study on

220 obese children aged 5-14 years in Brazil found that the average age of children with insulin resistance was higher than in non-insulin resistance children (Romualdo et al., 2014).

Analysis of the incidence of insulin resistance in obese children with vitamin D deficiency and obese children without vitamin D deficiency showed a significant difference. So, it is recommended to examine the level of vitamin D and insulin resistance in obese children. The proposed biological mechanisms by which vitamin D influences insulin resistance in obesity include enhancing peripheral/hepatic uptake of glucose and reducing inflammation. The chronic inflammation that accompanied obesity develop to insulin resistance by the increased production of inflammatory cytokines from immune cell such as macrophages and adipocytes (Peterson et al., 2014). Similar to a study in China, it was stated that children with vitamin D deficiency had 4.15 times more at risk of developing insulin resistance than children without vitamin D deficiency (Fu et al., 2020). On the contrary, a study on 301 children aged 11–18 years in Turkey showed no significant relationship between insulin resistance and vitamin D status. The differences in the study population and gene polymorphism found in Turkey might make it different from our study. Besides, the study in Turkey divided vitamin D status into 3 categories, namely vitamin D deficiency (25-hydroxy vitamin D levels <10 ng/ml), vitamin D insufficiency (25-hydroxy vitamin D levels 10-20 ng/ml), and normal vitamin D (25-hydroxy vitamin D content > 20 ng/ml). It was indicating that other mechanisms cause insulin resistance other than vitamin D deficiency (Erdönmez et al., 2011).

In this study, there were 23 (45.1%) obese children with vitamin D deficiency who does not experience insulin resistance. This might be due to the lack of data on how long the subjects had been obese and how long they had vitamin D deficiency. Although, this group had a risk of developing insulin resistance in the future. Likewise, it was also found that 10 (22.2%) children without vitamin D deficiency had insulin resistance. The incidence of insulin resistance in obese children could happen as the result of other mechanisms, apart from the intermediary of vitamin D. Excessive energy in obesity can cause hyperplasia and hypertrophy of adipocytes resulting in oxidative stress. Oxidative stress from adipocytes triggers chronic inflammation in adipose tissue and produces free fatty acids and inflammatory mediators (van der Aa et al., 2015).

Children with vitamin D deficiency need vitamin D supplementation and adequate nutrition containing calcium and phosphate. Vitamin D supplementation is given orally as much as 1000 IU / day for babies less than 1-month-old, 1000-5000 IU / day for babies aged 1-12 months old, and 5000 IU / day for children over 12 months old, given for 2- 3 months. After 2-3 months, a control 25-hydroxy vitamin D level should be examined, then continued with vitamin D supplementation at a maintenance dose of 400 IU / day, or 800 IU / day for obese children. Monitoring of 25-hydroxy vitamin D levels shall be done in 6 months and 12 months afterward (Lee et al., 2013).

The limitation of this study is that the study was conducted in a cross-sectional manner, the data obtained were data at the time of sampling so that a causal analysis of obesity, vitamin D, and insulin resistance could not be provided. In this study, genetic factor analysis was not performed, however, its contribution could be minimized because the research samples were taken from the same population, namely from the same ethnicity.

The strength of this research is that the sample is randomly selected from schools with middle and upper economic status in Makassar so that it can describe the health condition of children with middle and upper economic status in Makassar. In addition, it is not necessary to analyze pubertal status because almost all study samples reflect puberty age.

The researchers concluded that the incidence of insulin resistance in the group of obese children with vitamin D deficiency was higher (54.9%) compared to the group of obese children without vitamin D deficiency (22.2%), in schools with middle and above socioeconomic levels. The risk of insulin resistance in obese children with vitamin D deficiency was 4,261 times greater than obese children without vitamin D deficiency. Researchers suggest the need for special attention to obese children, by conducting initial screening examinations for vitamin D tests and insulin resistance (fasting blood sugar and fasting insulin), as obese children have a risk of vitamin D deficiency and insulin resistance. The proactive intervention in obese children in managing obesity can prevent the risk of developing diabetes mellitus.

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Competing Interests Statement

The authors declare that there are no competing or potential conflicts of interest.

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Happiness, Subjective Well-Being, and Life Satisfaction: A Compared Study between Long-Lived Elderly People in Northeast and Southeast Brazil

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Abstract

This cross-sectional study aims to investigate and compare factors associated with happiness, subjective well-being, and life satisfaction in elderly people aged 80 and older in two different regions of Brazil. Face-to-face interviews were performed with 417 Brazilians aged 80 years and older, 179 from Northeast and 238 from the Southeast. The prevalence of feelings of happiness, subjective well-being, and overall life satisfaction were very similar for the older elderly in both regions. While in the Southeast, the predictive factors were literacy, higher income, and better economic situation, with many elderly people living alone; in the Northeast, the affective ties with more people seem to predominate, as well as having a more frequent and diverse support network, and practice leisure activities. Our findings support a view of social bonds and family support enables the older elderly people to feel more satisfied with life, performing activities that bring happiness and subjective well-being.

Keywords: Happiness, subjective well-being, aging, public health, developing countries

1. Introduction

Since the 1940s, the World Health Organization (WHO) has broadened its understanding of the concept of health by reviewing its indicators, postulating that health is a state of complete physical, mental and social well-being. Thus, the concept of subjective well-being gained space in scientific literature and became a health indicator with different instruments to measure it. Subjective well-being means the assessment of people about their lives, grouping cognitive and affective components such as happiness, life satisfaction, positive feelings and low negative feelings (Diener & Tay, 2015). WHO itself has created an instrument called WHO-5, known as the "Welfare Index", as a parameter for measuring and comparing data between different populations.

In addition to subjective well-being, research has used other similar or associated concepts such as happiness and life satisfaction. Happiness is understood to be a positive psychological state resulting from the degree to which a person enjoys life, and life satisfaction can be considered a synonym for this, encompassing an overall assessment of life that involves all the criteria that involve the human mind (Veenhoven, 2015). Other scales were also created to measure these parameters such as the "Subjective Happiness Scale" (Lyubomirsky & Lepper, 1997) and the "Global Life Satisfaction Scale" (Cantril, 1966).

Changes in health, in addition to improvements in living conditions, especially after the second half of the twentieth century, an increase in life expectancy, lower mortality and lower fertility were verified, defining a process of demographic transition that led to a continual increase in the proportion of elderly people in the world, which leads to longer lifespan (OPAS, 2017). As a developing country, Brazil has followed the demographic transition, and is one of the fastest-growing countries in terms of population age. It was estimated that in 1995 there were 4.7% people aged 60 years and over in the total population of the country (Miranda, da Cruz Gouveia Mendes, & da Silva, 2017), and, according to IBGE, in the last census conducted in 2010, this contingent increased to 7.4%,

with 1.54% of older elderly people (aged 80 and over).

Given the recognition of the population aging process in Brazil, several laws and policies were created seeking to ensure social rights and promote the social integration of the elderly, valuing their autonomy and participation. In fact, the development of public policies for the elderly has been featured on the agenda of international health organizations regarding the proposition of guidelines for nations that still need to implement social and assistance programs to meet the emerging needs of this population group (OPAS, 2017).

At the beginning of the 21st century, the Pan American Health Organization (PAHO), in partnership with Argentina, Cuba, Uruguay, Barbados, Mexico, Chile, and Brazil, developed research on the health of the elderly known as the SABE Study (Health, Aging, and Well-being) to respond to the need for specialized information, as well as indicators on the various spheres of life and health of the elderly. In Brazil, this study has become a cohort study with over 2,000 elderly people evaluated every five years (Lebrão & Laurenti, 2005). In recent years, this study has expanded its collaborative network to conduct studies on aging and longevity processes in high consanguineous communities of Northeastern Brazil. There was also interest in broadening the study of other populations with vulnerability characteristics and biological characteristics different from those previously studied. This multicenter survey allowed to collect systemic information about the living conditions and health of the elderly, and has been important to propose new goals and specific care policies for this population.

From this scenario in which a longer lifespan is observed and from the range of factors involved in the health of an individual, including the insertion of subjective indicators of health, it is worth questioning: Does subjective well-being, happiness and life satisfaction contribute to increase the life expectancy of individuals? Do long-lived populations differ from these indicators, such as those living in poor regions of the Northeastern backcountry compared to other urban populations that did not have so many restrictions?

A few studies have been conducted in Brazil seeking to associate living conditions of older elderly people and the degree of happiness, subjective well-being, and life satisfaction. Therefore, it is relevant to understand the factors that lead to healthy aging and greater longevity, since these factors play a very relevant role in the Brazilian context, given the rapid process of demographic and epidemiological transition that the country is going through.

In this paper, the objective is to investigate, understand and compare the factors associated with subjective well-being, life satisfaction, and happiness in two different older elderly populations: one in Northeast Brazil and one in Southeast Brazil, explaining the differences and specificities and suggesting associations between subjective factors and indicators.

2. Methods

This study is a cross-sectional, descriptive and analytical design. It was carried out in two locations: in a rural area in the Northeastern Brazilian backlands, in the state of Paraíba, in 2017, and in an urban region of southeastern Brazil, in the state of São Paulo, in the last cohort in 2015. The inclusion criteria was people aged 80 years or older residing in the area at the time of collection, and having answered all questions of self-assessment and the scales used in the dependent variables (happiness, subjective well-being and overall life satisfaction) on their own, without the help of an informant or substitute. Out of 179 respondents in the Northeast, 135 was included in the sample for the variable happiness, 134 elderly participants for the variable subjective welfare, and 140 elderly participants for the variable overall life satisfaction. In the Southeast region, out of 238 respondents, 208 was included in the analysis for the variable happiness, 202 elderly people for well-being, and 224 elderly participants for the variable global life satisfaction were totaled.

The Health, Aging, and Well-being - SABE questionnaire has been applied for twenty years in São Paulo (SABE-SP). In Paraíba, the questionnaire was adapted to local conditions with the removal of some items, but continues to encompass the eleven sections of the last version (A15), which covers various aspects of the elderly people's life and health, such as: personal data, cognitive assessment, health status, functional status, medications, use and access to services, family and social support network, work history and sources of entry, housing characteristics, anthropometry, flexibility and mobility.

The data was collected by interviewees, in both regions, at the homes of the participants after explaining the aims of the study. On agreeing, they signed the Informed Consent Form. Thus, the research is in accordance with the ethical aspects involving research with human beings, in accordance with Resolution number 466/2012 of the National Health Council of the Ministry of Health.

The dependent variables were happiness, subjective well-being, and overall life satisfaction. To analyze the self-perception of happiness, only the first question of the Happiness Scale was used. To investigate the level of subjective well-being, the entire WHO5 (Adapted) instrument (WHO) was used. To study overall life satisfaction,

we used the question on overall life satisfaction (questionnaires attached). Independent variables include gender, age, self-reported ethnicity, literacy, marital status, income adequacy, family economic status in childhood, starvation in childhood, co-residence, self-rated health, number of chronic noncommunicable diseases, medication use, depressive symptoms, physical activity, importance of religion, smoking, taking walks or leisure, having pets, importance and interference of animals in the mood, living with other people in daily life, home arrangements, family and social support network, and role of the elderly person in this network, offering and/or receiving support.

Data were tabulated in the Epidata 3.1 double data entry program. The statistical software R was used for descriptive analysis showing the frequency of the data, and in order to identify associations between the variables, the initial multiple logistic regression model was adjusted with all variables taking as an association measure the odds ratio (OR) and confidence intervals at 95% (IC95%). Adjustment variables with $p \leq 0.20$ in the initial model were included in the final multiple analyses. In the interpretation of the regression results, $p < 0.05$ was considered as indicating a statistically significant association for the dependent variable.

3. Results

Regarding sociodemographic characteristics, the two populations studied show a very different profile. In rural Northeastern Brazil, there is a predominance of older females (54.7%) compared to males (45.3%), and most of them had no access to formal education (62%) and live with up to one minimum wage (67%). The vast majority (86%) lives in the company of other people, especially spouses and children; only 14% lived alone. Regarding the older elderly in the southeastern urban center, a higher predominance of women (70.6%) was observed. Most of the elderly had self-reported white ethnicity (61.7%), with good literacy conditions (78.7%) and income (57.8%); and live mainly with their children. In the Southeast there is almost twice the proportion of the elderly people (27.3%) living alone than in the Northeast (Table 1).

Table 1. Profile of elderly people aged 80 years and older in the Northeast (PB) and Southeast (SP) regions regarding sociodemographic characteristics, health aspects and lifestyle. SABE-SP study, 2015 / SABE- PB, 2017

Brazilian Populations	**SABE Study**	**PB**			**SP**		
Variables	**Categories**	**N total**	**n**	**%**	**N total**	**n**	**%**
Dependent							
Happiness	Most happy	135	97	71.9	208	150	72.1
	Less happy		38	28.1		58	27.9
Subjective Well-being	Best well-being	134	103	76.9	202	159	78.7
	Worst well-being		31	23.1		43	21.3
Overall Life Satisfaction	High satisfaction	140	122	87.1	224	181	80.8
	Low satisfaction		18	12.9		43	19.2
Independent							
Gender	Feminine	179	98	54.7	238	168	70.6
	Masculine		81	45.3		70	29.4
Age	80-89 years	179	142	79.3	238	173	72.7
	90 or more years		37	20.7		65	27.3
Literacy	Literate	179	111	62.0	230	49	21.3
	Illiterate		68	38.0		181	78.7
Co-Residence	Lives Alone	179	25	14.0	238	65	27.3
	Lives with other people		154	86.0		173	72.7
Self-reported Ethnicity	White	168	91	54.2	227	140	61.7
	Non-white		77	45.8		87	38.3
Marital Status	With Partner	179	102	57.0	238	188	79.0
	Without Partner		77	43.0		50	21.0

Income	Up to 1 MW	176	118	67.0	204	86	42.2
	More than 1 MW		58	33.0		118	57.8
Income Sufficiency	Doesn't consider sufficient	177	69	39.0	225	90	40.0
	Considers sufficient		108	61.0		135	60.0
Religion	Has	178	177	0.6	223	215	3.6
	Doesn't Have		1	99.4		8	96.4
Economic Situation in childhood	Good	160	34	21.3	224	74	33.0
	Regular		52	32.5		100	44.6
	Bad		74	46.3		50	22.4
Starved in Childhood	Yes, I was hungry	162	67	41.4	223	33	14.8
	No, I wasn't hungry		95	58.6		190	85.2
Health self-assessment	Bad	131	14	10.7	214	28	13.1
	Regular		66	50.4		93	43.5
	Good		51	38.9		93	43.5
Number of chronic diseases (nDCNT)	Two or more	179	94	52.5	223	164	73.5
	One		64	35.8		42	18.8
	None		21	11.7		17	7.6
Depression Symptoms (GDS)	Suggestion of depression symptoms	90	38	42.2	238	118	49.6
	No depression symptoms		52	57.8		120	50.4
Number of drugs	Five or more (Polypharmacy)	179	94	52.5	219	139	63.5
	Between 1 and 4		80	44.7		80	36.5
	None		5	2.8		0	0.0
Physical Activity (last 3 months)	Didn't Practice	179	144	80.4	235	186	79.1
	Practiced		35	19.6		49	20.9
Importance of Religion	Little importance	168	13	7.7	209	24	11.5
	Important		155	92.3		185	88.5
Leisure Activity (Walking)	Doesn't do any	169	70	41.4	226	93	41.2
	Does		99	58.6		133	58.8
Smoking	Smokes/Has smoked	178	102	57.3	234	83	35.5
	Never smoked		76	42.7		151	64.5
Spends Most of the Time With	Alone	156	3	1.9	231	75	32.5
	Children and teenagers		7	4.5		12	5.2
	Adults		63	40.4		67	29.0
	Elderly People		83	53.2		77	33.3
Family Arrangements	Alone	179	25	14.0	233	62	26.6
	Only Spouse		37	20.7		29	12.4
	Only Children		45	25.1		64	27.5
	Children and Grandchildren		32	17.9		41	17.6
	Other Arrangements		40	22.3		37	15.9
Receives support	No	179	34	19.0	237	73	30.8
	Yes		145	81.0		164	69.2

Gives Support	No	179	41	22.9	237	95	40.1
	Yes		138	77.1		142	59.9
Support Network – has someone to count on	Never	137	10	7.3	205	6	2.9
	Sometimes		16	11.7		11	5.4
	Always		111	81.0		188	91.7
Domestic Animal (Pet)	Doesn't have	179	104	58.1	235	158	67.2
	Has		75	41.9		77	32.8
Interference of the animal in the mood	Doesn't interfere	71	18	25.4	76	15	19.7
	Interferes positively		53	74.6		61	80.3
Importance of the domestic animal (Pet)	Little importance	71	21	29.6	75	9	12.0
	Important		50	70.4		66	88.0

In the Northeast, the elderly lived in poverty and experienced periods of drought that restricted access to food. When the elderly was asked if they "starved" in childhood, 41.4% of the Northeast population answered affirmatively; this contrasts with 14.8% of the Southeast population in the same condition (Table 1). Therefore, regional economic asymmetries are associated with social inequalities between the two groups studied.

Despite differences in material and educational conditions, the indexes of happiness, subjective well-being, and overall life satisfaction are very similar in both populations studied, with 71.9% (rural Northeast) and 72% (urban Southeast) for happiness; 76.9% (rural) and 78.7% (urban) for better subjective well-being, and 87.1% (rural) and 80.8% (urban) for overall life satisfaction. There are practically no differences in the proportion of elderly people who experience happiness, subjective well-being, and overall life satisfaction between both groups (Table 1).

Regarding health conditions, the two populations show significant differences. More than half of the older elderly people in the Northeast (61.1%) and Southeast (56.6%) rate their health status as fair or poor; 73.5% of the elderly in urban areas have one or more chronic diseases and 63.5% of them use more than five drugs. In rural areas, 52.5% of the elderly have one or more chronic diseases and use polypharmacy. Regarding mental health, the results are similar: 42.2% of the older elderly people in the Northeast and 49.6% in the Southeast showed symptoms suggestive of depression.

Regarding whether they have religion, most of the older elderly people in this study have religion (99% in the NE and 96.4% in the SE). In relation to the practice of physical activity, most practice some leisure activity, such as walking (58.6% in the NE and 58.8% in the SE). In the urban region, there was a higher proportion of elderly people who reported having someone to turn to when they needed it (91.7%) than in the rural region (81%), receiving financial and material support, personal care and tasks, emotional support and companionship. In the Southeast, 30.8% of the elderly reported living alone and not having support from anyone compared, to 19% in the Northeast.

In the Northeast, the elderly lives more with other elderly (53.2%) and more adults (40.4%) in their daily lives than in the Southeast (33.3% and 29%, respectively). The configuration of family arrangements shows us that in the urban center of the Southeast 26.6% of the elderly live alone and 75.4% live with other people. Most of them live with only their children (27.5%), or with only a spouse (12.4%), with children and grandchildren (17.6%) or have other arrangements (15.9%). In the rural Northeast, only 14% of the elderly live alone. Of the 86% who live with other people, most live with their children (25.1%), their spouses (20.7%), children and grandchildren (17.9%) or have other arrangements (22.3 %). Regarding the presence of animals in the home and their influence on the mood of the elderly, the elderly in the Northeast have more domestic animals (pets)(41.9%) than those in the Southeast (32.8%), showing their positive influence on mood more (74.6%) in relation to the urban population (80.3%) (Table 1).

Table 2 shows the gross and adjusted values of factors associated with happiness among the elderly in the Northeast and among the elderly in the Southeast. In both populations, the absence of symptoms suggestive of depression was a predictor of happiness; In the Northeast, this group is 8.06 times more likely to feel happy than those with depressive symptoms, while in the Southeast those without these symptoms are 3.73 times more likely to feel happy.

In the Northeast, three more variables were associated with happiness, the most important of which was the

support network. More than 80% of the Northeast's older elderly people said they had someone to turn to when they needed to. Older people who receive support from their family or friends are 27.46 times more likely to feel happy than those who do not. Those who live with a partner feel happier than those without a partner. Elderly people who practice leisure activities, such as walking, are 5.28 more likely to feel happy than non-practitioners (Table 2).

In the Southeast, the results were quite different, as no other variable besides the absence of depressive symptoms was associated with happiness, as shown in Table 2.

The results for the association study with the dependent variable subjective well-being were shown in Table 3. In this case, for the Northeast population, the only variable that had a significant association was self-assessed health. Elderly people with good self-assessed health are 5.51 more likely to have better subjective well-being than those who report their own health as regular or bad. For most of the other variables it was not possible to obtain the value of odds ratio.

For the Southeast population, marital status, income sufficiency and absence of depressive symptoms were associated with the dependent variable. In this region, elderly people with no symptoms suggestive of depression are 9.43 more likely to have better subjective well-being than the group with symptoms. Those who live with their partners, being married or living together, are 5.77 more likely to have better subjective well-being than the single, widowed, separated, or divorced. Those with income sufficiency are 3.2 more likely to also have a better perception of well-being.

Table 4 presents the results found from the analytical point of view for the dependent variable overall life satisfaction, and it can be verified that no odds ratio results were obtained for some of the independent variables. For the Southeast region, again it was found that the elderly who do not have symptoms suggestive of depression are 6.29 more likely to be satisfied with their life. Elderly people with good support network are 9.3 times more likely to be more satisfied with life than those who reported never receiving support. In the Northeast region, the factor that showed a strong association with life satisfaction was the practice of leisure activity. Elderly people who perform walking or walking activities are 8.1 times more likely to be satisfied with life than those who do not (Table 4).

Table 2. Multiple logistic regression model for the association between happiness and sociodemographic, health, and lifestyle aspects of older elderly people living in the Northeast (SABE-PB) and Southeast (SABE-SP) of Brazil

	HAPPINESS - SABE-PB						**HAPPINESS- SABE-SP**					
	Less happy N(%)	**More happy N(%)**	**OR gross (IC 95%)**	**p**	**OR ajusted (IC 95%)**	**p**	**Less happy N(%)**	**More happy N(%)**	**OR gross (IC 95%)**	**p**	**OR Ajusted (IC 95%)**	**p**
Gender				0.147		0.154				0.130		0.128
Feminine	26 (37)	44 (63)	1		1		38 (26)	107 (74)	1		1	
Masculine	12 (18)	53 (82)	2.43 (0.86-6.84)		2.64 (0.7-10.03)		20 (32)	43 (68)	2.32 (1.06-5.09)		2.07 (0.81-5.26)	
Literacy				0.097		0.117						
Yes	14 (25)	43(75)	2.06 (0.71-6.01)		3.58 (0.73.17.7)		41(25)	126(75)				
No	24 (31)	54(69)	1		1		17(45)	21(55)				
Co-residence				**0.02**		**0.029**						
Lives alone	7(29)	17(71)	**1**		**1**		16(26)	45(74)				
Lives With Others	31(28)	80(72)	**0.69 (0.18-2.75)**		**0.03 (0-0.7)**		42(29)	105(71)				
Ethnicity				0.24		0.25						
White	15(22)	52(78)	1.85 (0.67-5.09)		2.23 (0.56-8.89)		35(27)	93(73)				
Non white	21(33)	43(67)	1		1		23(29)	56(71)				
Economic Situation in childhood				0.318		0.135				< 0.001		0.104
Good	10(33)	20 (67)	0.65 (0.18-2.31)		0.27 (0.05-1.51)		10 (14)	61 (86)	4.33 (1.48-12.66)		2.87 (0.81-10.24)	
Regular	13(33)	26 (67)	0.83 (0.26-2.68)		0.61 (0.13-2.88)		32 (36)	58 (64)	0.89 (0.39-2.01)		0.44 (0.15-1.3)	
Bad	15(23)	50 (77)	1		1		16 (35)	30 (65)	1		1	
Insufficiency of food up to 15 Years				**-**		-				0.613		0.611
Yes	17(31)	37(69)	-		-		10(36)	18(64)	1		1	
No	21(26)	59(74)	-		-		47(26)	132(74)	1.53 (0.6-3.86)		1.35 (0.42-4.34)	
Number of chronic diseases				0.117		0.062						

(nDCNT)									
Two or more	21(30)	48(70)	1	1	37(26)	107(74)			
One	13(25)	38(75)	1.11 (0.38-3.27)	0.19 (0.03-1.09)	11(28)	28(72)			
None	4(27)	11(73)	1.36 (0.31-5.9)	0.68 (0.09-5.21)	6(40)	9(60)			
Depression Symptoms			**0.011**	**0.006**			**0.001**		**< 0.001**
Yes	15(41)	22 (59)	**1**	**1**	38 (43)	51 (57)	**1**	**1**	
No	8(16)	42 (84)	**3.64 (1.28-10.35)**	**8.06 (1.6-40.48)**	20 (167)	99 (83)	**3.66 (1.8-7.44)**	**3.73 (1.68-8.26)**	
Importance of Religion			0.065	0.053					
Little importance	3(30)	7(70)	1	1	7(29)	17(71)			
Important	34(28)	89(72)	1.53 (0.26-9)	8.83 (0.97-79.96)	50(28)	126(72)			
Leisure Activity (Walking)			**0.024**	**0.03**					
Doesn't perform	20(43)	27(57)	**1**	**1**	22(29)	53(71)			
Performs	18(20)	70(80)	**3.43 (1.2-9.81)**	**5.28 (1.17-23.83)**	33(26)	96(74)			
Receives support			**0.02**	**0.027**					
Yes	28(26)	79(74)	**1.3 (0.4-4.26)**	**27.46 (1.44-521.92)**	40(28)	101(72)			
No	10(36)	18(64)	**1**	**1**	18(27)	49(73)			
Support Network			-	-					0.157
Never	0	0	-	-	3(50)	3(50)	1	1	
Sometimes	4(27)	11(73)	-	-	6(55)	5(45)			
Always	24(24)	75(76)	-	-	44(24)	141(76)	2.55 (0.65-9.97)	0.122	3.35 (0.72-15.52)

Table 3. Multiple logistic regression model for the association between subjective well-being and sociodemographic, health and lifestyle aspects of older elderly people in the Northeast (SABE-PB) and Southeast (SABE-SP) of Brazil

	SUBJECTIVE WELL-BEING (SWB) - SABE-PB						**SUBJECTIVE WELL-BEING (SWB) - SABE-SP**					
	Worse SWB N(%)	**Best SWB N(%)**	**OR gross (IC 95%)**	**P**	**OR ajusted (IC 95%)**	**p**	**Worse SWB N(%)**	**Best SWB N(%)**	**OR gross (IC 95%)**	**P**	**OR ajusted (IC 95%)**	**p**
Literacy				0.923		0.923						
Yes	13(23)	43(77)	0.92 (0.38-2.26)		1.05 (0.39-2.79)		32(20)	129(80)				
No	18(23)	60(77)	1		1		10(26)	28(74)				
Ethnicity				0.903		0.903						
White	16(23)	55(77)	1.06 (0.43-2.58)		1.06 (0.4-2.79)		22(18)	102(82)				
Non white	13(22)	46(78)	1		1		21(27)	56(73)				
Marital status				**-**		-				**0.023**		**0.031**
No partner	21(30)	49(70)	-		-		37(23)	121(77)	**1**		**1**	
With partner	10(16)	54(84)	-		-		6(14)	38(86)	**2 (0.73-5.53)**		**5.77 (1.18-28.33)**	
Income Sufficiency				0.434		0.44				**0.035**		**0.037**
Yes	20 (24)	64 (76)	0.89 (0.36-2.25)		0.67 (0.24-1.85)		18 (15)	106 (85)	**3.4 (1.63-7.11)**		**3.2 (1.07-9.52)**	
No	11 (22)	39 (78)	1		1		25 (33)	50 (67)	**1**		**1**	
Insufficient food up to 15 Years				**-**		-				0.201		0.199
Yes	18(32)	38(68)	-		-		8(30)	19(70)	1		1	
No	13(17)	62(83)	-		-		35(20)	140(80)	1.71 (0.65-4.49)		2.38 (0.63-8.95)	
Self-assessment of health				**0.062**		**0.037**				**< 0.001**		0.926
Bad	5 (45)	6 (55)	**1**		**1**		18 (67)	9 (33)	1		1	
Regular	16 (27)	43 (73)	**1.82 (0.45-7.36)**		**2.08 (0.49-8.84)**		16 (18)	73 (82)	0.12 (0.05-0.32)		0.11 (0.03-0.41)	
Good	6 (13)	41 (87)	**4.56 (1.02-20.99)**		**5.51 (1.1-27.5)**		8 (9)	77 (91)	2.69 (0.99-7.34)		0.94 (0.28-3.24)	
Depression Symptoms				-		**-**				**< 0.001**		**< 0.001**
Yes	12(34)	23(66)	-		-		35(43)	47(57)	**1**		**1**	

No	7(14)	43(86)	-	-	8(7)	112(93)	**8.69 (3.69-20.47)**		**9.43 (3.02-29.42)**	
Physical Activity (last 3 months)			-	-				0.253		0.27
Didn't do any	27(26)	78(74)	-	-	39(25)	114(75)	1		1	
Did	4(14)	25(86)	-	-	4(8)	45(92)	3.32 (1.11-9.94)		2.28 (0.53-9.88)	
Importance of Religion			-	-				0.756		0.755
Little importance	3(30)	7(70)	-	-	6(26)	17(74)	1		1	
Important	28(23)	94(77)	-	-	35(20)	136(80)	1.42 (0.52-3.9)		1.26 (0.29-5.52)	
Leisure Activity (Walking)			-	-				0.083		0.086
Doesn't perform	16(33)	32(67)	-	-	24(35)	44(65)	1		1	
Performs	14(16)	71(84)	-	-	16(12)	113(88)	3.52 (1.68-7.37)		2.56 (0.88-7.48)	
Domestic Animal (Pet)			-	-				0.102		0.104
Doesn't Have	16(21)	62(79)	-	-	22(17)	108(83)	1		1	
Has	15(27)	41(73)	-	-	21(30)	50(70)	0.5 (0.24-1.02)		0.42 (0.15-1.19)	

Table 4. Multiple logistic regression model for the association between overall life satisfaction and sociodemographic, health and lifestyle aspects of older elderly people living in Northeast (SABE-PB) and Southeast (SABE-SP) Brazil

	Overall Life Satisfaction (OLS) - SABE-PB						**Overall Life Satisfaction (OLS) - SABE-SP**					
	Low OLS N(%)	**High OLS N(%)**	**OR gross (IC 95%)**	**p**	**OR adjusted (IC 95%)**	**p**	**Low OLS N(%)**	**High OLS N(%)**	**OR gross (IC 95%)**	**p**	**OR ajusted (IC 95%)**	**p**
Gender				-		-				0.436		0.442
Feminine	11(15)	61(85)	-		-		33(21)	126(79)	1		1	
Masculine	7(10)	61(90)	-		-		10(15)	55(85)	1.42 (0.64-3.14)		1.44 (0.57-3.67)	
Literacy				-		-				0.438		0.433
Yes	8(14)	50(86)	-		-		31(18)	142(82)	1.64 (0.69-3.88)		1.52 (0.54-4.29)	
No	10(12)	72(88)	-		-		11(24)	34(76)	1		1	
Co-residence				0.053		0.053				0.371		0.369

Lives alone	5 (20)	20 (80)	1	1		11 (17)	52 (83)	1	1
Lives with others	13 (11)	102 (89)	3.81 (1.04-14.02)	4.71 (0.98-22.64)		32 (20)	129 (80)	0.82 (0.37-1.81)	0.46 (0.08-2.52)
Health self-assessment			-	-				0.215	0.180
Bad	3(21)	11(79)	-	-		12(43)	16(57)	1	1
Regular	7(11)	55(89)	-	-		20(22)	71(78)	0.43 (0.17-1.07)	0.74 (0.25-2.15)
Good	6(12)	44(88)	-	-		11(12)	81(88)	2.4 (1.02-5.68)	2.01 (0.72-5.56)
Depression Symptoms			0.567	0.567				**< 0.001**	**< 0.001**
Yes	7 (19)	30 (81)	1	1		34 (33)	70 (67)	**1**	**1**
No	5 (10)	46 (90)	2.15 (0.62-7.39)	1.54 (0.35-6.76)		9 (8)	111 (92)	**7.43 (3.28-16.85)**	**6.29 (2.54-15.59)**
Importance of Religion			0.151	0-133					
Little importance	3(27)	8(73)	1	1		6(25)	18(75)		
Important	15(12)	112(88)	0.35 (0.06-2.06)	0.19 (0.02-1.66)		36(20)	144(80)		
Leisure Activity (Walking)			**0.008**	**0.012**					
Doesn't perform	10(21)	38(79)	**1**	**1**		20(24)	64(76)		
Performs	8(9)	83(91)	**3.47 (1.02-12.16)**	**8.1 (1.6-41.13)**		21(16)	110(84)		
Smoking			0.081	0.102					
Smoked/Has smoked	14(18)	63(82)	1	1		18(23)	61(77)		
Never smoked	4(6)	59(94)	2.43 (0.61-9.68)	3.83 (0.77-19.21)		25(17)	118(83)		
Support network			-	-				**0.008**	**0.004**
Never	0	0	-	-		2(33)	4(67)	**1**	**1**
Sometimes	2(13)	13(87)	-	-		7(64)	4(36)	**3.5 (0.43-28.45)**	**2.99 (0.25-35.39)**
Always	14(14)	89(86)	-	-		31(17)	155(83)	**8.58 (2.36-31.14)**	**9.3 (2.07-41.79)**

4. Discussion

For the first time in Brazil, this study compared two populations of older elderly people with very different profiles in relation to sociodemographic, health and lifestyle aspects, in order to investigate how these differences could influence the perception of happiness, subjective well-being, and life satisfaction. In the Northeast, the older elderly people have lower incomes and had little access to formal education, and part of them suffered from childhood food restriction. These restrictions, however, do not seem to have negatively influenced the perceptions of the elderly people aged 80 or older to the point where they feel less happy, less well-being, or dissatisfied with their lives compared to elderly people in a large urban center. The prevalence of these feelings was not different between the two populations despite the evident socioeconomic differences.

These results corroborate other studies that did not associate happiness and income (Easterlin, 2003; Lawrence, Rogers, & Wadsworth, 2015). On the other hand, the findings of this paper differ from a study in Germany, where low socioeconomic status was a robust and independent risk factor for low subjective well-being in both genders, thus highlighting the detrimental effect of severe economic constraints on elderly people (Lukaschek, Vanajan, Johar, Weiland, & Ladwig, 2017). The southeastern population is more diverse in relation to literacy than the Northeastern, and for this reason, the results corroborate literature, verifying the association between literacy and subjective well-being (Blanchflower & Oswald, 2000).

In the studied population, there is a higher prevalence in the Northeast of Brazil of men aged 80 years or older than in the Southeast, as well as more elderly people living with their spouses and fewer older people living alone; the support network for the elderly was one of the factors most strongly associated with the perception of happiness. In the Southeast, the elderly were found to be lonelier; however, those who live with a partner have a better perception of subjective well-being. These results corroborate findings in literature showing an association between marital status and happiness, subjective well-being and life satisfaction (Haring-Hidore, Stock, Okun, & Witter, 1985; Lucas, Clark, Georgellis, & Diener, 2003; Veenhoven, 2005; Marks & Fleming, 1997). Regarding the support network, a longitudinal study conducted in England (Rafnsson, Shankar, & Steptoe, 2015) showed that the size of the social network and the frequency of network contact were positively and independently associated with life satisfaction and quality of life. That is, frequent contact with other people is important for the elderly to feel more satisfaction with life.

In the Northeast, there was a positive association between leisure activities, such as walking, and life satisfaction. These results corroborate other studies conducted in the United States (Chang, Wray, & Lin, 2014; Ragheb & Griffith, 1982). In addition, the elderly interviewed in this paper reported that domestic animals (pets) contribute positively to mood enhancement. Although no associations were found between the presence of domestic animals (pets) and feeling happier and more satisfied with life, frequency data show a tendency towards that. Some studies have already suggested the potential benefits of animals on physical and psychological health in humans (Cherniack, Paul Cherniack, & Cherniack, 2014); and others, specifically from a cohort of the elderly, demonstrated that owning animals was associated with improved cardiovascular disease survival in a hypertensive population (Chowdhury, Nelson, Jennings, Wing, & Reid, 2017).

The self-assessed health indicator is a widely used and recommended tool in studies with the elderly to understand the aspects that influence it and its relationship with well-being (Confortin, Giehl, Antes, Schneider, & d'Orsi, 2015). A Korean study revealed that better self-assessed health increases life satisfaction (Lee, Choi, & Lee, 2020). Elderly people in the Northeast reported having suffered food restrictions in childhood due to poverty. Overcoming these difficulties and being older may have contributed to better acceptance of current health conditions, awakening an overall sense of positive happiness and subjective well-being.

Another factor that contributes significantly to the improvement of these perceptions is the absence of symptoms suggestive of depression. In the elderly, the development of depression is common, mainly because, over the years, the number of successive losses of loved ones and the withdrawal from their daily activities lead the elderly to question about life and its meaning. These questions may or may not lead the elderly to the construction of new meanings in life, which may happen from the creation and execution of a job or practice of an act; experiencing something or finding someone to love; or by the attitude towards suffering that cannot be changed (Frankl, 2013). For this reason, family members and others who make up the elderly support network should be aware of signs of loss of interest in performing daily activities and the desire for isolation, as well as other signs of depression. A Korean study showed that emotional support from family and/or friends attenuated the negative influence of life satisfaction events. The results revealed that the life satisfaction trajectories of the elderly increased with maturity and good family relationships (Lee, Choi, & Lee, 2020).

The study has its limitations, such as the cross-sectional design itself that does not allow associations of cause and

effect. The analyses performed are not intended to define the origin of the results found, but to explore the factors associated with the variables in the two different regions studied, contributing to expose the importance of studying health indicators related to subjective health. It is noteworthy that the international studies brought to discuss the studied aspects present different cultural issues, which limits the comparison with our results. Another limitation concerns the population itself that has an advanced age and low cognition, and sometimes needs an auxiliary informant to answer some questions, which may cause some bias. In addition, it was not possible to perform statistical analysis for many of the Northeast population variables, which may be improved in the near future.

Regarding the sampling methods, because the surveys were financiered by two different funding agencies (FAPESP and CAPES/CNPq), data was collected in different years (2015 and 2017). In Brejo dos Santos, the totality of seniors aged 80 or older was included in the study while, in São Paulo, the sample was randomly chosen, being probabilistic and representative of the population. The SABE questionnaire has been used for many years, having been validated previously; and a few adaptations was performed for its application in Brejo dos Santos. This population was selected by convenience, because the health workers had already participated in a previous research (Lopes et al., 2017).

5. Conclusion

The prevalence of feelings of happiness, subjective well-being, and overall life satisfaction were very similar for the older elderly in the Northeast and southeast of Brazil. However, different factors were associated with these perceptions in each region. While in the Southeast, the predictive factors were literacy, higher income, and better economic situation, with many elderly people living alone, in the Northeast the affective ties with more people seem to predominate, as well as having a more frequent and diverse support network, and practice leisure activities.

Our findings allows us to broaden the health view of elderly populations with different lifestyles, seeking to understand which bio-psycho-social factors are inserted in the contexts in which they live, and how health polices can contribute to the promotion of new practices appropriate to each reality, in order to provide the elderly with a better quality of life and healthy long life within their means in their territory.

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Competing Interests Statement

The authors declare that there are no competing or potential conflicts of interest.

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Correlation between Uric Acid and Non-Alcoholic Steatohepatitis (NASH) Occurred in Obesity and Non-Obesity

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Abstract

Background/Aim: Non-alcoholic Fatty Liver Disease (NAFLD) is one of the main causes that promote chronic liver disease in developing countries. Uric acid is correlated to metabolic syndrome. Based on this issue, we studied the correlation between uric acid level and the occurrence of NASH in non-alcoholic fatty liver disease (NAFLD) with or without obesity.

Methods: The research subjects were 149 patients diagnosed with NAFLD. The data were collected from the medical record by purposive sampling method. The subjects were taken from inpatient and outpatient data from Wahidin Sudirohusodo hospital. The medical record included demography, clinical, radiology and laboratory records. Statistical analysis were performed through descriptive statistical calculations, Pearson Correlation and multinomial logistic.

Results: There was a significant correlation between NAFLD and uric acid level (p=.000). Based on gender, the correlation between NAFLD and uricemia was significant in female patients (with p=.000); but insignificant in male patients (p=.137). Based on age, in age of >40 years old, NAFLD was significantly associated with uric acid level (p=.000). There was a significant correlation between hyperuricemia and NASH in obese and non-obese patients (p <0.001) for which the higher the uric acid level the greater the NAFLD degree was.

Conclusion: There is a correlation between uric acid level and NASH occurrence in NAFLD with or without obesity.

Keywords: uric acid, Non-Alcoholic Steatohepatitis, obesity, Non-Alcoholic Fatty Liver Disease, Body Mass Index, uricemia

1. Introduction

Non-alcoholic Fatty Liver Disease (NAFLD) is one of the main causes of chronic liver disease in developing countries (Lefere et al., 2019; Younossi et al., 2018). The highest prevalence of NAFLD in western countries is found in obese individuals ranging from 80% -90% (Bellentani et al., 2010). Obesity [Body Mass Index (BMI) < 25] is associated with a spectrum of liver disorders, known as NAFLD, indicated by an increase in intrahepatic triglycerides so-called simple steatohepatitis (non-NASH) (without inflammation and fibrosis), or Non-Alcoholic Steatohepatitis (NASH) with or without inflammation and fibrosis, which can progress to cirrhosis (Fabbrini et al., 2010). Many studies have reported a relationship between NAFLD and metabolic syndrome (Souza de et al., 2012). Likewise, the correlation between NAFLD and uric acid is researched as well.

Serum uric acid (SUA) is the final outcome of purine metabolism in the human body, and it is derived from hypoxanthine after the double enzyme catalysis, which is performed by xanthine, oxidized in the liver. It is a metabolic product of endogenous (nucleoproteins originating from cellular metabolism) and an exogenous (dietary) precursor protein transferred to the liver, and is excreted by the kidneys. Elevated uric acid levels are able to induce the triglyceride accumulation by promoting the over-expression of pro-lipogenic enzymes so-called *sterol regulatory element-binding proteins* (Yang et al., 2018). Therefore, any impairment in this balance may lead to high level of SUA (Yang et al., 2017).

The increasing level of uric acid serum is closely related to visceral fat accumulation, as well as to the onset of hepatic histological that changes independently. In adipocytes, soluble uric acid (UA) stimulates an elevation in reactive oxygen species (ROS) production which has been recently recognized as a major factor that determines the obesity-related endocrine imbalance inflammatory. Therefore, as a high-risk factor, uric acid levels may develop as one of the predictive markers for the incidence and severity of NAFLD, implying that uric acid levels may be a potential therapeutic target for NAFLD, especially in patients with hyperuricemia (Zhang et al., 2018).

Uric acid is correlated to metabolic syndrome (Ali et al., 2020). Hence, this research was conducted to identify the correlation of uric acid levels and NASH in NAFLD (Non-Alcoholic Fatty Liver Disease) with and without obesity.

2. Method

2.1 Sampling Procedures

This research was an observational study with a cross-sectional approach applied on 149 NAFLD patients. The samples were obtained from medical record data through purposive sampling. The study population was the entire medical records of patients diagnosed with NAFLD, treated outpatient, and inpatient at Wahidin Sudirohusodo Hospital and its Network from 2018 to 2019.

2.2 Inclusion and Exclusion Criteria

The inclusion criteria included the patients at > 18 years in age, no history of consuming alcohol nor alcohol intake in amounts deemed harmful to the liver (less than 20 grams of ethanol per week), while the exclusion criteria were the people with coronary heart, hepatitis A, hepatitis B, hepatitis C, and malignant diseases. The criteria for Non-Alcoholic Fatty Liver Disease were determined based on the image of fatty liver from abdominal ultrasound/CT-scan, Magnetic Resonance Spectroscopy (1H-MRS) or Magnetic Resonance Imaging (MRI).

The obese criteria were determined based on body mass index which was calculated based on body's weight (in kilograms) and height (in meters). The subjects were classified into normal weight (BMI, 18.5-22.9), overweight (BMI, 23-24, 9), Obesity I (BMI, 25-29,9), Obesity II (BMI,> 30). The uric acid levels were considered increased if the value was > 7 mg/dL for men and > 6 mg/dL for women.

2.3 Statistical Analysis

Data analysis was carried out by using SPSS version 22. Statistical analysis was performed through descriptive statistical calculations, Pearson Correlation and multinomial logistic. The test result would be considered significant if the p-value was <0.05. The results were displayed descriptively with tables, narration, and figures.

2.4 Ethical License

Ethical permission has been obtained from the Health Research Ethics of the Hasanuddin University Medical Faculty/ Wahidin Sudirohusodo Hospital.

3. Results and Discussion

A total of 149 subjects were diagnosed with Non-Alcoholic Fatty Liver Disease (aged ≥18 years).

3.1 Correlation Analysis: Between NAFLD and Gender, Uric Acid Levels and Age

Among the 149 subjects, 70 were male and 79 were female. The correlation between non-alcoholic fatty liver and gender was proven statistically. The Pearson correlation was significant (p = .000), indicating that men and women had a different likelihood in experiencing different stages of NAFLD (see Table 1). No correlation was found between NAFLD and age even though we used the same statistics. We divided the ages by the threshold of 40 years old and found no differences between both age groups, see Table 1.

The stage of NAFLD was highly correlated with uric acid levels. We used Pearson's chi-square correlation for the categorical variables. By using all of the samples, we found a significant relationship between NAFLD and patient's uric acid levels (p = .000), see Table 1.

Table 1. Correlation between NAFLD and Patient's Gender, Uric Acid Levels, and Age

Variable	NAFLD		Total
	NASH	Non-NASH	
Gender			
Male	12	58	70
Female	43	36	79
Total	55	94	149
Age			
<40 years old	10	12	22
>40 years old	45	82	127
Total	55	94	149
Normourisemia	11	63	74
Hyperuricemia	44	31	75
Total	55	94	149

Based on Table 1. We found that 45 NASH subjects were aged > 40 years old and the 10 subjects were aged < 40 years old. On other hand, we found that the number of non-NASH patients, with the age of > 40 years old, were 82, and it was 12 for the patients with the age of < 40 years old. There are 44 subjects suffering from NASH and hyperuricemia. Meanwhile, the other 11 subjects who were suffering from NASH also had normouricemia.

3.2 Correlation between NAFLD Degree and Uric Acid Levels to Obesity

Table 2 shows a significant correlation between NASH and hyperuricemia in obese and non-obese patients. The Pearson correlation (ρ) represents the correlation between NAFLD and uricemia for each obese group.

Table 2. Correlation between NASH and non- NASH patients and the Uric Acid Levels in Obese and Non-obese Patients

		Uricemia				*Pearson*	
		Hyperuricemia		Normouricemia		*Correlation*	*Prob.*
		n	(%)	n	(%)	(ρ)	
Obese	NASH	29	(19.5)	9	(6.0)	-0.41	0.000
	Non- NASH	22	(14.8)	43	(28.9)		
Non-Obese	NASH	15	(10.1)	2	(1.3)	-0.55	0.000
	Non- NASH	9	(6.0)	20	(13.4)		

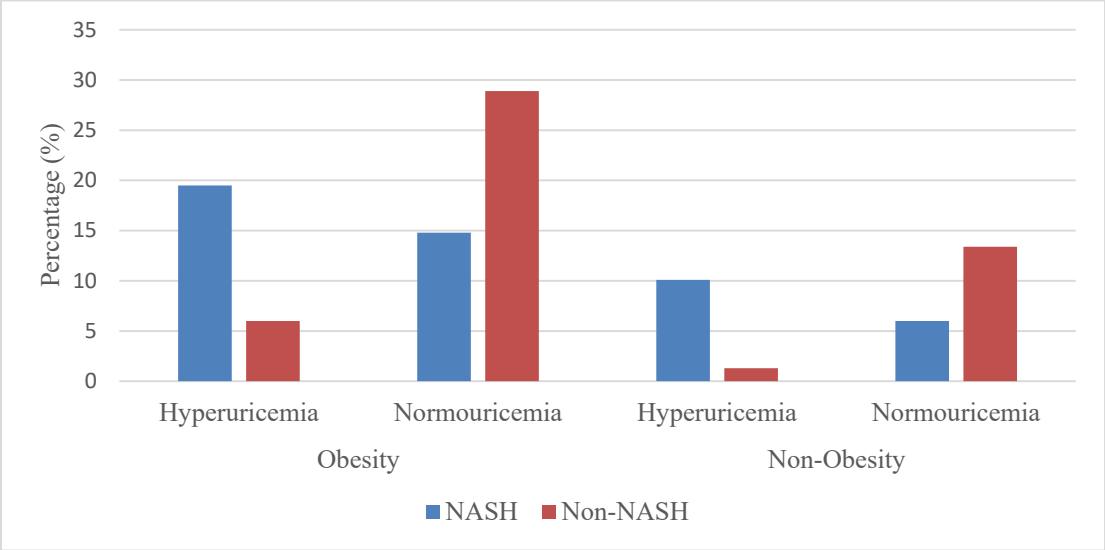

Figure 1. NAFLD Cases based on Uric Acid Levels and Obesity Status

As shown in Table 2, the number of obese patients with NASH and hyperuricemia (19.5%) was found significantly higher than that of the obese patient group with non-NASH and hyperuricemia (14.8%). The group of non-obese patients with NASH and hyperuricemia (10.1 %) had higher rate than the non-obese who suffered from non-NASH and hyperuricemia group (6 %).

Obese patients with NASH and normouricemia (6%) had lower rate than the obese group with non-NASH and normouricemia (28.9%). Non-obese patients with NASH and normouricemia group (1.3%) had lower rate than non-obese group with non-NASH and normouricemia (13.4%).

This study found a significant correlation between NAFLD and uric acid levels in female patients. Previous studies found a disparity between the two genders about the association between serum uric acid and NAFLD (stronger association was found in women rather than in men) (Jaruvongvanich et al., 2017). This result is in accordance with the study of Yang et al., stating that the independent effect of hyperuricemia on NAFLD was higher in women than in men (Yang et al., 2017). Gender difference concerning the relation between uric acid levels and NAFLD might lay in the fact that estrogen serves as a uricosuric agent, which can lower the uric acid levels through uric degradation and excretion. Some studies also suggest that insulin resistance may not only increase the uric acid synthesis but also decrease the uric acid excretion (Yu et al., 2017). The uricosuric action of estrogen has been suggested to be the mechanism which underlies the gender difference regarding SUA levels or the prevalence of gout (Park et al., 2018).

A study by Ballestri et al. revealed that increased liver injury and inflammation in premenopausal women generates a lower risk of liver fibrosis compared to men and women with the postmenopausal cases. The prevalence of NAFLD is globally higher in men than women, but, after menopause, women display a similar or even a higher NAFLD prevalence compared to men. The findings supported that it is related to the protective effect of estrogens. In some cross-sectional studies, it is stated that male gender and menopausal status have often been connected with the risk of NAFLD aside from the age and metabolic factors. The prevalence of NASH and advanced fibrosis were found to be higher in postmenopausal women than in men. However, other longitudinal studies were unsuccessful to support the role of gender in the progression of liver fibrosis (Ballestri et al., 2017).

Significant risk factors of the reported NAFLD will be obesity, diabetes mellitus (DM) and hypertriglyceridemia (Wong et al., 2019). Obesity, especially central obesity, is associated with insulin resistance through an inflammatory process (Hardy et al., 2012). According to the pathomechanism of NAFLD, based on the theory of “Two Hit”, “the first hit” is the occurrence of hepatitis steatosis in which there is an imbalance between the formation and overhaul of triglycerides (Fang et al., 2018). The existence of insulin resistance may have a major influence on the onset of NAFLD (Benedict et al., 2017).

The visceral fat component is metabolically active and regulates numerous adipocytokines, such as leptin and adiponectin, which have been associated with insulin resistance. Insulin resistance or hyperinsulinemia elevates the reabsorption of sodium and uric acid on the renal tubules, thereby decreasing the urinary excretion of uric acid,

and it may cause hyperuricemia (Kim et al., 2012; Fabbrini et al., 2010).

Uric acid promotes an escalation of the mRNA expression of monocyte chemotactic protein-1 (MCP-1) and decreases the mRNA expression of adiponectin. A strong positive association between serum leptin and UA has been demonstrated in both diabetic and healthy subjects (Zhang et al., 2018). In the patients with non-alcoholic fatty liver disease (NAFLD), hyperuricemia is related to a more severe degree of liver damage (Jaruvongvanich et al., 2017; Yu et al., 2017). High uric acid levels can lead to endothelial dysfunction, insulin resistance, oxidative stress, and systemic inflammation (Wang et al., 2018; Ali et al., 2020). All these factors are involved in NAFLD pathogenesis (Petta et al., 2011). Therefore, high uric acid levels are the cause of the progression from non-NASH to NASH (Jaruvongvanich et al., 2017). Another predictive factor of NAFLD, uric acid, was reportedly responsible for lipid metabolism impairment, including mitochondrial oxidative stress, sterol regulatory element-binding protein 1 (SREBP-1) activation which is induced by endoplasmic reticulum (ER) stress, and involvement of NLRP3 inflammation. Thus, there may be an interaction between high SUA levels and obesity in the pathogenesis of NAFLD (Yang et al., 2017). In addition, some studies have also revealed that insulin resistance may not only increase the uric acid synthesis but also decrease the uric acid excretion (Yu et al., 2017).

This study shows a significant correlation between NASH and hyperuricemia in obese and non-obese patients. The higher the uric acid level, the heavier the degree of NAFLD was. The details are shown in Table 2 and Figure 1. This study found a relationship between UA serum levels and clinically diagnosed NAFLD (ultrasound evidence or laboratory surrogates of steatosis).

This result is consistent with the study conducted by Petta et al. (a cohort study about patients with histological diagnosis of NAFLD) which shows an independent relationship between hyperuricemia and the severity of liver damage, implying that hyperuricemia was independently associated with lobular inflammation. These results indicate that hyperuricemia has an important role in inducing inflammation (Petta et al., 2011). Likewise, the study of Jaruvongvanich et al. shows that patients with NAFLD and hyperuricemia will be more commonly possessing a high NAS (defined as score of ≥ 5), in a significant way, rather than those without hyperuricemia with a pooled odds ratio of 2.17 (95% confidence interval: 1.51–3.12 (Jaruvongvanich et al., 2017). This study is consistent with the study undertaken by Yang et al. stating that uric acid level is significantly related to the prevalence of mild and severe steatosis ($p < 0.01$) (Yang et al., 2018). Zheng et al. reported that elevated uric acid level independently shows positive associations with the prevalence of Non-alcoholic fatty liver disease (NAFLD) and the severity of fatty liver (Zheng et al., 2017).

This study has some limitations, including the small number of samples, its nature as the cross-sectional study and the used diagnostic methods that could not show a relationship between the severity of NAFLD and uric acid levels. The exact role of uric acid in the pathophysiological mechanisms of NASH remains to be the thing that must be explored.

4. Conclusion

There is a correlation between uric acid levels and NASH cases in NAFLD (Non-Alcoholic Fatty Liver Disease) patients with and without obesity. A significant correlation was found between NASH and uric acid in obese results (19.5%, $p = 0.000$) and non obese results (10.1%, $p = 0.000$). In fact, NAFLD is also significantly associated with uric acid levels in female patients.

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Ethical Clearance

The protocol of this study has been approved by the Health Research Ethics Commission of the Hasanuddin University Medical Faculty/Wahidin Sudirohusodo Hospital in accordance with the ethical recommendations from the Helsinki Declaration of 1975.

Competing Interests Statement

No relevant potential conflict of interest to be declared.

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