p-ISSN 2301-9123 | e-ISSN 2460-5441

Global Medical & Health Communication

DEC 2018 VOL. 6 NO. 3

Global Medical & Health Communication

Editorial Team

Editorial Address
Jalan Hariangbanga No. 2, Tamansari, Bandung 40132, West Java, Indonesia
Phone/fax: (022) 4321213
E-mail: gmhc.unisba@gmail.com
Website: https://ejournal.unisba.ac.id/index.php/gmhc

Accredited by:
Ministry of Research, Technology and Higher Education of the Republic of Indonesia
(Kemenristekdikti) Number: 2/E/KPT/2015, 1st December 2015

This journal is indexed on:

Published by:
Faculty of Medicine Universitas Islam Bandung;
Pusat Penerbitan Universitas-Lembaga Penelitian dan Pengabdian kepada Masyarakat (P2U-LPPM)
Universitas Islam Bandung

Publish Every 4 Months
April, August, December

Global Medical & Health Communication

pISSN 2301-9123 | eISSN 2460-5441

Volume 6 Number 3, December 2018

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RESEARCH ARTICLES

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Table title is the typed center, font size 10 pt, bold, initial letter of each word written with capital letter, except conjunctions. The titles are numbered and written on top of the table. Example: Table 3 *Neisseria gonorrhoeae* Resistance to 8 Types of Antimicrobials in 20 Specimens. Table, no vertical dividing line, and there are only three horizontal borderlines. Created tables in sequence two spaces from the text. Table descriptions and abbreviations are placed in the table description, not on the table title.

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The abstract is typed using 12 pt font size and one spaces. The abstract is written in one paragraph, one space, maximum 250 words, and should describes the entire contents of the article. The abstract should be suitable for the format of introduction, methods (contain method, place, and time of study), results, and discussion. Abstract be equipped with key words consisting of 3–5 words.

Introduction

The introduction is written succinctly to stimulate the reader's interest include all the necessary information. At the end of the introduction was written the purpose of the study.

Methods

Methods contains the material under study, and the way described briefly by the order of operation as well as the location and time of the study. Explain statistical methods in detail. Consideration of ethical issues is included. If the protocol has been approved then the ethical clearance/approval letter number and the health research ethics committee must be written.

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The result is the core of scientific writing. This section presents data and information that will be used as

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Discussion of the article reveals, explains, and discusses the results of the study with an analysis by the research design, interpretation, and explanation of its synthesis. Also, the results obtained are compared with the results of previous research of others.

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Zhang B, Kunde D, Tristram S. Haemophilus haemolyticus is infrequently misidentified as Haemophilus influenzae in diagnostic specimens in Australia. Diagn Microbiol Infect Dis. 2014;80(4):272–3.

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King P. Haemophilus influenzae and the lung (Haemophilus and the lung). Clin Transl Med. 2012;1:10 [cited 2015 August 15]. Available from: https://clintransmed.springeropen.com/articles/10.1186/2001-1326-1-10.

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Online submission: http://ejournal.unisba.ac.id/index.php/gmhc
DOI: https://doi.org/10.29313/gmhc.v6i3.2841

GMHC. 2018;6(3):155–61
pISSN 2301-9123 | eISSN 2460-5441

RESEARCH ARTICLE

The Effect of the BC-MK15 Birth Chair on the Labor Pain Intensity in Multipara

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Abstract

Labor pain causes worry, anxiety, increases the secretion of the adrenaline, adrenocorticotropic hormone (ACTH), cortisol serum levels, catecholamines and the perception of pain. One method to decrease labor pain is through the mobilization and upright position during labor which is facilitated by the BC-MK15 birth chair to relax, decrease catecholamines, increase the release of β-endorphins and block the transmission of pain stimulus. This study aims was analyze the difference of the effect of using the BC-MK15 birth chair and the conventional bed on the intensity of labor pain in multipara. The design of this study was the posttest-only control group design in 60 samples of the first active phase of multipara at Public Health Centers Garuda, Ibrahim Adjie and Puter of Bandung city in April–May 2017. Each group consisted of 30 for treatment (using BC-MK15 birth chair) and control (using the conventional bed). Assessment of pain scores using the visual analogue scale (VAS) in cervical dilations of 4 cm (post 1), 7–9 cm (post 2) and 10 cm (post 3). The statistical test analysis uses the Mann-Whitney test and the chi-square test. There were significant differences among groups which are obtained by the treatment and control of post 2 and post 3 ($p<0.05$, RR=0.69 [0.531–0.896]). In conclusion, there is an effect of using the BC-MK15 birth chair and the conventional bed on the intensity of labor pain in multiparous mothers.

Key words: BC-MK15 birth chair, conventional bed, labor pain

Pengaruh Kursi Persalinan BC-MK15 terhadap Intensitas Nyeri Persalinan pada Multipara

Abstrak

Nyeri persalinan menimbulkan rasa khawatir, kecemasan, meningkatkan sekresi adrenalin, *adrenocorticotropic hormone* (ACTH), kadar kortisol serum, katekolamin, dan persepsi nyeri. Salah satu metode menurunkan nyeri persalinan adalah mobilisasi dan posisi tegak saat persalinan difasilitasi dengan kursi persalinan BC-MK15 sehingga menimbulkan relaksasi, menurunkan katekolamin, meningkatkan pelepasan β-endorfin, dan mengeblok transmisi stimulus nyeri. Penelitian ini bertujuan menganalisis perbedaan pengaruh penggunaan kursi persalinan BC-MK15 dan tempat tidur konvensional terhadap intensitas nyeri persalinan pada multipara. Desain penelitian eksperimen *posttest-only control group design* dengan jumlah sampel 60 multipara kala I fase aktif di Puskesmas Garuda, Ibrahim Adjie, dan Puter Kota Bandung pada bulan April–Mei 2017. Tiap-tiap kelompok berjumlah 30 untuk perlakuan (menggunakan kursi persalinan BC-MK15) dan kontrol (menggunakan tempat tidur konvensional). Penilaian skor nyeri menggunakan *visual analogue scale* (VAS) pada dilatasi serviks 4 cm (*post 1*), 7–9 cm (*post 2*), dan 10 cm (*post 3*). Pengujian statistik menggunakan analisis Uji Mann-Whitney dan uji *chi-square*. Didapatkan perbedaan bermakna antara kelompok perlakuan dan kontrol pada post 2 dan post 3 ($p<0,05$; RR=0,69 [0,531–0,896]). Simpulan, terdapat pengaruh penggunaan kursi persalinan BC-MK15 dan tempat tidur konvensional terhadap intensitas nyeri persalinan pada ibu multipara.

Kata kunci: Kursi persalinan BC-MK15, nyeri persalinan, tempat tidur konvensional

Received: 14 August 2017; Revised: 30 October 2018; Accepted: 23 November 2018; Published: 31 December 2018

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Introduction

Labor pain causes worry, strain, and anxiety so it increases the secretion of adrenocorticotropic hormone (ACTH), cortisol serum levels, catecholamines, decreases blood flow and increases abdominal muscle strain, this process will increase the perception of pain. Physiologically, work pain gets stronger along with the addition of the cervical opening and increased contractions of the uterus.[1,2]

The technique of reducing pain stimulation can be done through the mobilization and the upright position during labor. The birth chair is designed to facilitate the stage in the labor process which can facilitate a position change with a reclining design that can bolster the back firmly so it will cause relaxation, decrease catecholamines, increase the release of β-endorphins, block the transmission of pain stimulus and reduce the perception of pain. The upright position can reduce the pressure of the fetus which causes sores around and decreases abdominal muscle strain. The upright position is also utilizing the advantages of gravity effects through the decrease in aortocaval compression and the alignment of the fetus body with the birth canal so that intrauterine circulation will be better, preventing uterine ischemia and decreasing the pain sensations. Decreasing the intensity of pain during labor will affect the mother's psychological conditions, accelerate the labor process, and enhance the well-being of the fetus.[3–9]

The birth chair has been used to help the labor process for centuries. Various innovations of birth chair drafts have been conducted starting from the BirthRite to the AVE birthing bed that has already received an award from the Red Dot Design Award in 2003 and 2017. The draft of the birth chairs is changed in accordance with the changing times, but the principles and functions are still maintained.[8–12]

Study of Gizzo et al.[12] showed that the maternity groups with the upright position have a lower pain level compared to the maternity groups with the supine position on the average score of 3.7±1.2 and 7.1±1.6 ($p<0.001$). Rana's[13] study in Iran showed that during the first active phase with the upright position and supine position it indicates that there is a significant relationship between the position of women during labor to the level of pain in the lower back and abdomen ($p=0.000$). The upright position can reduce back pain and abdominal pain can change the pain from the severe level to the medium level, and the medium level to the mild level at the first active phase of labor.

The result of the preliminary study is carried out in the *Pelayanan Obstetri Neonatal Emergensi Dasar*/PONED (Basic Emergency Obstetric and Neonatal Care/BEONC) Puskesmas (Public Health Center) of Bandung city, the facility that is used to aid labor is the bed that cannot facilitate the set up of the tilt back buffer to the maximum and cannot facilitate position change during labor. The result of the study conducted on 95% of women with maternity stated that the labor bed cannot help them change their position during labor so that the perceived increasing the pain. The rationale of the researchers are to plan and develop a tool that can facilitate the setup position of labor, i.e. Birthing Chairs-Magister Kebidanan 2015 (BC-MK15) which is more simple but has the same principle and function as the AVE birthing bed so it can be used by maternity volunteers in the community.

This study is implemented to analyze the difference in the effect of using BC-MK15 birth chairs and the conventional bed against the decrease in the intensity of labor pain in multiparous mothers.

Methods

The layout of the study uses the post-test only control group design. The selection of the sample uses the technique of consecutive sampling. This study used two groups, which were the treatment group (using BC-MK15) and the control group (using a conventional bed) and randomized by random permuted blocks. The study was implemented in PONED Public Health Center Garuda, Ibrahim Adjie and Puter of Bandung city in April until May 2017 and executed in sequential with other research teams which examine the appropriate technology of the BC-MK15. The sample was 60 multipara in the first active phase, each group consisted of 30 to treatments (using BC-MK15) and control (using conventional beds) which were taken to meet the inclusion criteria, i.e. the age of 20–35 years old, a multipara opening of 4 cm, an aterm with singleton pregnancies, presentation of the head of the posterior fontanel in front, a pregnancy of 37–42 weeks, amniotic still intact, good uterine contractions, regular rhythm, frequency of 3 times in 10 minutes,

no induction of labor, having a normal labor history, a fetal weight interpretation of >2,500 g to <4,000 g and willing to be a respondent. Exclusion criteria: there were disproportions of the pelvic head, hemoglobin <11 g/dL, mothers with a body mass index (BMI) of <18.5 to ≥30, pregnancy with complications such as pre-eclampsia, eclampsia, antepartum hemorrhage and contraindications of pervaginam labor and no companion of labor. The criteria for drop out: the maternity that cannot hold the sense of labor pain, unable to continue pervaginam labor, partus presipitatus (precipitate labor), along labor and on the BC-MK15 or conventional bed ≤80% during labor. The pain score assessment used the visual analogue scale (VAS) in a cervical dilation of 4 cm (post 1), 7–9 cm (post 2) and 10 cm (post 3).

The analysis used in this study was the bivariate analysis. The characteristics of the data analysis used a chi-square test. Data normality is determined by the Shapiro-Wilk test and the see the box plot. The analysis of the difference between score posts 1, 2 and 3 in the treatment and the control group was performed by using the Mann-Whitney test because the data were in numeric form, abnormally distributed and presented in the median and percentile form. The effect of the birth chair on the intensity of labor pain in both groups was analyzed by using the chi-square test.

The protocol was approved by the Health Research Ethics Committee, Faculty of Medicine, Universitas Padjadjaran Bandung note number: 451/UN6.C.10/PN/2017.

Results

The subjects of the study were 60 respondents and divided into two groups, each group consisted of 30 respondents, i.e. Group A was a treatment group using the BC-MK15 and Group B used a conventional bed.

Table 1 determines the characteristics of two study groups, namely the education, economic status, parity, stations and birth weight. There

Table 1 Characteristics of the Study Subject

Characteristics	Groups		p Value*
	Treatment (n=30)	Control (n=30)	
Education			0.529
Elementary school	18	15	
Junior high school	10	14	
High school	2	1	
Economic status			0.573
≤regional minimum wage	22	20	
>regional minimum wage	8	10	
Parity			0.881
2	18	18	
3	9	10	
4	3	2	
Stations			0.618
0	9	6	
+1	16	17	
+2	5	7	
Birth weight (g)			0.371
2,500–2,999	13	8	
3,000–3,499	14	17	
>3,500	3	5	

*Chi-square test

Table 2 Comparation of VAS Pain Scores in Both of Study Groups

Pain Scores	Groups		p Value*
	Treatment (n=30)	Control (n=30)	
Post 1: median (Q)	3.5 (3.00–4.00)	4 (3.00–4.25)	0.184
Post 2: median (Q)	7 (6.00–7.25)	9 (8.00–9.00)	0.000
Post 3: median (Q)	10(9.00–10.00)	10 (10.00–10.00)	0.002

*Mann-Whitney test: post 1 (pain score cervical opening of 4 cm), post 2 (pain score cervical opening of 7–9 cm), post 3 (pain score cervical opening of 10 cm)

is no significant difference (p>0.05) between the groups.

The data normality test result with the Shapiro-Wilk data was abnormally distributed with a significance value of p>0.05 and it was observed that the box plot data distribution results were not symmetric, the median was not precisely in the center of a square, there were also outlier and extreme values.

Table 2 determined that the pain score of the VAS in the post 1 was insignificant (p>0.005), but in the post 2 and post 3 there were significant pain scores (p<0.005) between the treatment group (using the BC-MK15) and control group (using the conventional beds).

Based on observing Table 3 there was an influence of the BC-MK15 on the labor pain intensity of the post 3 (opening of 10 cm) with a value of p≤0.05. The relative risk calculation result obtained a value of RR=0.69, it means the chance of maternity of BC-MK15 users will be in a severe pain of 0.69 times during first active phase opening of 10 cm when compared to the control group.

Discussion

The characteristics of the two observed groups were education, economic status, parity, station (decrease of the head) and birth weight. The result of studying education characteristics, economic status, parity, station and birth weight in the treatment and the control group have no significant differences (p>0.05), so both groups are homogeneous and comparable.

Birth pain is a complex, subjective pain, uncorfortable sensation or pain during birth. The perception of pain in every individual is different, how individuals perceive and interpret pain is influenced by various factors of physical, emotional, psychosocial, socioeconomic, cultural, education and environmental factors.[1,14–18] In this study, the factors which affect the intensity of labor pain in addition to physiological factors such as education, social economy, and the parity of the study subject have no significant differences (p>0.005) in both the treatment or control group.

Statistically, the results of the study, the difference in labor pain of multipara on groups that used BC-MK15 and groups that used conventional beds showed that there were significant differences in both groups. In the BC-MK15 group, the statistical results of the Mann-Whitney test showed that there was no difference of the pain scale in the first post (p>0.05) this is due to many factors that influence the perception of pain including environmental factors, cultural and anxiety. At the opening of 4 cm, the respondents have not yet adapted to the environment of the maternity room and the BC-MK15. The environment can affect the

Table 3 The Influence of BC-MK15 on the Intensity of Labor Pain in the Post 3

Group	Post 3		p Value*	RR (95% CI)
	Very Heavy	Heavy		
Treatment	20	10	0.002	0.69 (0.531–0.896)
Control	29	1		

*Based on two proportions of the first test side (chi-square), weight: VAS score 7–9, very weight: VAS score 10

perception of pain, including the people in it, the room, and the facility where labor occurs. Women usually prefer to be treated by the health care personnel who are well known in a comfortable environment and remind them of their homes. The environment must be safe so that a woman can be herself while trying various things to improve her comfort. A comfortable environment will have an impact on the perception of pain during the labor process.[1] The maternity environment settings have the opportunity to not have an anxiety of 2.5 times compared with maternity without the environment settings. Labor environment settings can take effect psychologically against mood and emotion, creates calmness, decrease maternal concentration towards the negative stimulus so that the mothers do not experience anxiety.[17] In this study, the maternity are still in the latent phase carried out by observations in the same room with the maternity in the active phase so that the surrounding environment which is uncomfortable will affect the psychological and perception of respondents to the pain.

Cultural, racial and ethnical also factors also play an important role in pain tolerance and the nature of pain. Research data and clinical observations show the difference of race, cultures and ethnicities in the facing pain. Some races in the world show great pain expression, while other races do not show conduct that they are experiencing great pain. Certain cultures will affect a person's response to the pain. There are cultures that expresses the pain freely, but there are also cultures who consider pain as something that does not need to be overexpressed.[1,18]

On the second post (opening of 7–9 cm) and the third post (opening of 10 cm in diameter), there were differences in the pain scale of both groups ($p<0.05$). This state indicates that the BC-MK15 can decrease the labor pain in multipara by facilitating changes in the position of each stage in the labor process that raises relaxation and decreases pain perception to create an increased sense of comfort in maternity with reclining backs which can be supported firmly. The tilt angle of the chair is in accordance with the principle of the upright position (avoid the supine position) which is above 45° from horizontal. This position can facilitate relaxation because it can reduce abdominal muscular tension and improve ventilation through a dilation of the chest. Relaxation is believed to be able to increase the release of endorphins which block the transmission of pain stimulus and also stimulate large diameter A-beta nerve fibers thus reducing the transmission of pain through small fiber impulses of A-delta and C nerve fibers.[3–7,13,17]

This is corresponding with the study of Smith et al.[19] which stated that relaxation on patients can help reduce muscle tensions and emotional tensions as well as decrease the labor pain. The results showed that relaxation techniques can reduce the labor pain, in the first active phase, relaxation can relieve the pain and the pain level is very different in women who do not implement relaxation, relaxation is effective way to reduce the pain at all stages of labor.

The use of the BC-MK15 facilitates the upright position by utilizing the advantage of gravity effects through the decrease in aortocaval compression and alignment of the body fetus with the birth canal for better intrauterine circulation, preventing uterine ischemia. The upright position can also reduce pressure of the fetus and uterus in the nerve filaments to prevent the stimulation that will cause sores and reduce the sensation of pain.[3–5] This is corresponding with Gizzo et al.'s[12] study on two groups, the first group was the 69 maternities in the supine position and the second group was the 156 maternities in the upright position. The study shows that the maternity groups in the upright position have a lower pain level than the maternity in the supine position on an average score of 3.7±1.2 and 7.1±1.6 ($p<0.001$).

The results of this study are corresponding with Rana's[13] study of maternity in the first active phase with the upright position and a switch of every 15 minutes on the supine position which indicates that there was a significant relationship between the position of women during labor and the level of pain in the lower back and abdomen in the active phase of labor ($p=0.000$). The upright position can reduce back pain and abdominal pain, can change the severe pain to a moderate level, from a moderate to a mild level at one active phase of labor.

Results of this research also supports the research of Fitriani et al.[20] in 30 maternal mothers which shows that the maternity time in the first active phase of the BC-MK15 was 250.44 minutes shorter than the conventional bed at 271.61 minutes ($p=0.038$). The second phase of the BC-MK15 was 20.67±2(1.02) minutes shorter than the conventional bed at 26.06±2(1.08) minutes ($p=0.001$). The total maternity time of the BC-MK15 was 269.42 minutes shorter than the

conventional bed at 299.09 minutes (p=0.011).

The use of the BC-MK15 only managed to reduce the labor pain at the opening of 7–9 cm and 10 cm compared to using the conventional beds. The labor pain cannot be eliminated entirely because of many factors that cause the labor pain. The intensity of pain increases along with the increase of cervical dilation and much correlated with the intensity, duration and frequency of uterine contractions. The longer the perceived pain grows stronger, the stronger the peak pain that occurs on the active phase in the full opening of 10 cm.

For further study, labor pain is a subjective factor that influences the perception of pain. Therefore, further study is needed to examine other variables that can affect labor pain such as variables of cultural and anxiety factors.

Conclusion

There are different effects of using the BC-MK15 compared to the conventional bed to the decrease of the intensity of labor pain in multipara mothers.

Conflict of Interest

All authors stated that there was no conflict of interest in this article.

Acknowledgements

Thanks to the Center for Quality Improvement of Human Resources for Health, Board of Development and Empowerment on Human Resources for Health, Ministry of Health Republic of Indonesia who have helped scholars for the implementation of this study. Thanks to the Politeknik Manufaktur Bandung and PT Kramatraya Sejahtera Cimahi who assisted the design and production of the BC-MK15, and thanks to the BC-MK15 teams who have collaborated in this study.

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Global Medical and Health Communication

Online submission: http://ejournal.unisba.ac.id/index.php/gmhc
DOI: https://doi.org/10.29313/gmhc.v6i3.2897

GMHC. 2018;6(3):162–8
pISSN 2301-9123 | eISSN 2460-5441

RESEARCH ARTICLE

Reproductive Health Game (KEPO Game) to the Self-Concept and Adolescent Reproductive Health Motivation

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Abstract

The problem of adolescent reproductive health has not been adequately addressed, although there have been many tried attempts both formally and informally. Adolescents aged 12–15 years old are suitable for early reproductive health education, so the needed media that suits their needs and developments. Reproductive health/*kesehatan reproduksi* (KEPO) game contains information about reproductive health and moral messages in the formation of self-concept, healthy reproduction, health motivation, and responsibility. The purpose of this study was for knowing the effect of using the KEPO game to the self-concept and motivation of adolescent reproductive health. The study layout uses a quasi-experiment with a pretest-posttest with control group design. The treatment group received a KEPO game, while the control group received the Young Health Programme (YHP). This study uses a sampling technique using simple random sampling with a sample of 42 students for each group. The analysis used is the nonparametric test. This research was implemented in the work area of the Public Health Center Ujungberung in Bandung city on the April–May 2017. The results showed that there was an effect of using the KEPO game to self-concept and motivation of adolescent reproductive health ($p<0.001$). The increase in self-concept in the treatment group was 8.2%, while in the control group it was 2.2%. For reproductive health motivation, the treatment group experienced an increase of 9.5%, while the control group experienced an increase of only 0.8%. In conclusion, the KEPO game increased self-concept and reproductive health motivation in adolescents.

Key words: Motivation, reproductive health game, self-concept

Gim Kesehatan Reproduksi (KEPO) untuk Konsep Diri dan Motivasi Kesehatan Reproduksi Remaja

Abstrak

Masalah kesehatan reproduksi remaja belum teratasi dengan baik, meskipun telah banyak upaya yang dilakukan baik secara formal maupun informal. Remaja usia 12–15 tahun merupakan masa yang tepat untuk pendidikan kesehatan reproduksi secara dini sehingga dibutuhkan media yang sesuai dengan kebutuhan dan perkembangannya. Gim kesehatan reproduksi (KEPO) berisikan informasi tentang kesehatan reproduksi dan pesan moral dalam pembentukan konsep diri dan motivasi kesehatan reproduksi yang sehat serta bertanggung jawab. Tujuan penelitian mengetahui pengaruh penggunaan gim KEPO terhadap konsep diri dan motivasi kesehatan reproduksi remaja. Rancangan penelitian menggunakan *quasi-experiment* dengan *pretest-posttest with control group design*. Kelompok perlakuan mendapatkan gim KEPO, sedangkan kelompok kontrol mendapatkan Program Pelayanan Kesehatan Peduli Remaja (PKPR). Teknik pengambilan sampel menggunakan *simple random sampling* dengan jumlah sampel 42 siswa untuk setiap kelompok. Analisis yang digunakan adalah tes nonparametrik. Penelitian ini dilakukan di wilayah kerja Puskesmas Ujungberung Kota Bandung pada bulan April–Mei 2017. Hasil penelitian menunjukkan terdapat pengaruh penggunaan gim KEPO terhadap konsep diri dan motivasi kesehatan reproduksi remaja ($p<0,001$). Kenaikan konsep diri pada kelompok perlakuan 8,2%, sedangkan pada kelompok kontrol 2,2%. Untuk motivasi kesehatan reproduksi pada kelompok perlakuan mengalami kenaikan 9,5%, sedangkan kelompok kontrol mengalami peningkatan hanya 0,8%. Simpulan, gim KEPO meningkatkan konsep diri dan motivasi kesehatan reproduksi remaja.

Kata kunci: Gim kesehatan reproduksi, konsep diri, motivasi

Received: 28 August 2017; Revised: 27 October 2018; Accepted: 7 December 2018; Published: 31 December 2018

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Introduction

Based on data from *Proyeksi Penduduk Indonesia* (Indonesia Population Projection) 2000–2035, in 2010 more than 43 million or around 18.3% of Indonesia's population were teenagers.[1] This amount is so large, that it establishes teenagers as the nation's next generation which are needed to be prepared to become healthy people physically, mentally, and spiritually. Adolescence is a transitional period from childhood to adulthood characterized by the occurrence of physical, psychological, intellectual, and social growth and development. According to the World Health Organization (WHO), adolescents are between 10–19 years old.[2]

The age of 12–15 years old is the right time for information delivery about health, especially reproductive health because this age is the peak of puberty, immature physical growth, psychosocial development, and adult brain development.[3] These changes can cause problems that can interfere with the teenager's development, for example, reproductive health problems. According to WHO, adolescents have health threats that are dominated by their behavior and ignoring this population will cause serious health hazards to their reproduction.[4,5] Adolescent reproductive health problems in Indonesia generally occur in women, including sexuality, human immunodeficiency virus (HIV)/ acquired immune deficiency syndrome (AIDS) as well as narcotics, psychotropics, and addictive substances (NAPZA), low knowledge about adolescent reproductive health, and the median age of the first marriage for women, which is still relatively low.[2,6]

The low health information for adolescents faces several challenges such as it delivered by un-optimal reproductive health information, electronic information technology that is not educational, improper parenting, socioeconomic and cultural factors and limited access to reproductive health services. Young women need to be provided an early reproductive health education using media that is appropriate to their development and needs.

Games are one of the media that is suitable for teenagers who have great curiosity, love adventure, and challenges because games have challenges, are interesting, exciting, and more interactive.[7] Games are an integral part of teenage life. When teens play games, they do something different and have their challenges to complete the game. According to the Entertainment Software Association (ESA) in 2015, teenagers under the age of 18 play video games as much as 26% and the average duration of playing is 5 hours a week. As many as 33% of girls under the age of 18 play video games, while it is only 15% for boys under 18 years old.[8]

The game can train for making life goals, provide feedback and assistance, maintain habits, stimulate, and monitor individual characteristics, such as self-esteem, self-concept, and goal setting. Players will also gain experience and can express themselves according to what they want without feeling uncomfortable.[9] Games can help in shaping youth motivation, and self-concept.[10] Positive self-concept and motivation can improve health and responsibility of reproductive health behavior.

From the above phenomenon, researchers are interested in designing a game application for teenagers that contains information about adolescent reproductive health. Informal education through this game will make teenagers more interested in exploring information about reproduction. Reproductive health games which are named reproductive health/*kesehatan reproduksi* (KEPO) game consists of several questions in the form of knowledge, attitudes, and skills packaged in the form of animation, and there are several notes and health information videos so that teenagers are expected to be healthy and responsible about reproductive health. The material in this game contains information about the growth and development of adolescents, adolescent reproductive health, sexually transmitted infections (STIs) and HIV/ AIDS, drugs, the introduction of gender concepts and future preparation, education in healthy life skills, and mental endurance through social skills.

The purpose of this study was for knowing the effect of using the KEPO game to the self-concept and motivation of adolescent reproductive health.

Methods

The method used in this study is the quasi-experiment with a control group pretest-posttest design. Respondent divided into two groups, the treatment group, and the control group, both who were given questionnaires before and after the intervention. The treatment group exposed to the game, while the control group educate through the Young Health Programme (YHP) from the public health center. This research

was implemented in the work area of the Public Health Center Ujungberung in Bandung city on April–May 2017 period. The State Junior High School 50 has a treatment group population because it is a school where the YHP services are inactive, while the State Junior High School 8 is a control group population with the most active YHP. The sampling technique used is the simple random sampling with a sample of 42 people for each group.

The inclusion criteria consisted of female students aged 12–15 years old, have android-based smartphones with a minimum RAM capacity of 1 GB with installed reproductive health games and play games at least three times in a week with a duration of 60 minutes in each playtime (treatment group). While the control group provided with YHP services by the public health center, while the exclusion criteria were adolescents who were sick or absent at the pretest and posttest, had received training on reproductive health and became a reproductive health representative at school. The drop out criteria was if the respondent did not use the game according to the instructions given (treatment group) and not attending the YHP services from the health center (control group).

The first stage is to implement a preliminary survey, literature study and identify adolescent reproductive health problems, to design the game scenario. After the experts analyzed the scenario, the game was designed in collaboration with the informatics engineering team and tested again and on adolescents. Experts are from the Department of Social Pediatrics, Social Obstetrics, Community/Public Health, Psychology, Adolescent Psychiatry, Educational Psychology, Ministry of Religion, Informatics Technology (IT) Team, Professional Organizations, and Indonesian Planned Parenthood Association.

The research questionnaire tested for validity and reliability in 30 adolescents. The instrument of self-concept variable research used the Tennesse Self Concept Scale (TSCS). The TSCS has 100 questions consisting of 6 dimensions, namely physical, moral-ethical, personal, family, social and self-criticism.[9] The motivation questionnaire consists of 4 components, namely attention, relevance, confidence, and satisfaction. This motivation model is known as the ARCS Model term proposed by Keller.[11]

In the treatment group, this game was installed first and used for 30 days, every week when an evaluation of the game usage conducted. The control group obtained reproductive health services from the Public Health Center (YHP). The data normality test used was the Shapiro-Wilk test, and the results of the data not normally distributed, that data analysis used is a non-parametric test. The research protocol was approved by the Health Research Ethics Committee of Faculty of Medicine, Universitas Padjadjaran, Bandung with the letter of ethics approval number: 400/UN6.C.10/PN/2017.

Results

The results in Table 1 show that there were

Table 1 The Effect of Reproductive Health Game (KEPO Game) to Adolescence Self-Concept

Self-Concept	Groups		p Value*
	Treatment (n=42)	Control (n=42)	
Pretest			0.534
Mean (SD)	59.6 (6.8)	60.6 (7.8)	
Median	58.0	58.9	
Range	49.0–78.7	48.2–79.5	
Posttest			0.007
Mean (SD)	64.9 (6.3)	61.9 (7.6)	
Median	64.5	60.6	
Range	51.0–81.7	48.2–81.0	
Differences in pretest-posttest	p<0.001**	p<0.001**	
% increase (SD)	8.2 (4.5)	2.2 (1.2)	p<0.001

*Mann-Whitney test, **Wilcoxon test

Table 2 The Effect of the Reproductive Health Game (KEPO Game) to Adolescence Reproductive Health Motivation

Motivation	Groups		p Value*
	Treatment (n=42)	Control (n=42)	
Pretest			0.446
Mean (SD)	60.8 (12.1)	58.9 (9.7)	
Median	60.0	60.0	
Range	30.0–97.0	37.0–94.0	
Posttest			0.000
Mean (SD)	66.8 (9.2)	59.3 (9.5)	
Median	66.5	61.0	
Range	49.0–96.0	40.0–94.0	
Differences in pretest-posttest	p<0.001**	p<0.05**	
% increase (SD)	9.5 (9.2)	0.8 (5.1)	p<0.001

*Mann-Whitney test, **Wilcoxon test

no differences in self-concept at the pretest with p>0.05, while at the posttest there were differences in the self-concept with a value of p<0.05. Besides, there are also significant differences in adolescent self-concept before and after the treatment and control groups with p<0.001. The percentage increase in self-concept in the treatment group was higher than the control group (8.2>2.2).

The results of the analysis in Table 2 show that there were no differences in reproductive health motivation at the pretest with p>0.05, while at the posttest there were significant differences in reproductive health motivation with p<0.001. There was a significant difference in the reproductive health motivation before and after the treatment with p<0.001. The percentage of an increase in reproductive health motivation in the treatment group was higher than the control group (9.5>0.8).

Discussion

Self-concept is what someone knows about themselves, which composed through the experience of interacting with the environment. Self-concept is not an intrinsic factor but develops from a continuous and differentiated experience. The basics of an individual's self-concept inculcated at the beginning of the day[12] and if others want to know whether she will be able to do something or if she wants to keep trying to achieve what she wants. Teenagers who have a positive self-concept will be optimistic, confident and always act positively towards everything.[13]

Providing reproductive health information to adolescents through games can have many benefits. In addition to increasing the understanding of reproductive health material, it also helps in the formation of a positive self-concept.[10] Health games are one of the methods that are interesting, innovative, potential and very effective to improve knowledge, attitudes, and skills, convey persuasive messages, change behavior, reduce stress, increase motivation and self-efficacy, change the habits and behavior of the players, grow interactivity, feedback, foster the ability to manage, and the opportunity for players to become desired characters in the game.[14,15]

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Figure KEPO Game Display

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According to Atkinson and Shiffrin,[16] information is processed and stored in 3 stages, namely sensory registers, short-term memory, and long-term memory. The new information is stored in a buffer called a sensory register. The duration of the information stored in the sensory memory is very short. The duration of information stored in short-term memory is 18–20 seconds. The storage duration will increase for up to 30 seconds if there is repeated information. If the information in short-term memory continues to used, then over time the information enters the long-term memory stage.

Many studies have been conducted using games on smartphones for health, including the use of "Flowy" games in patients with anxiety problems. These game players are motivated to detect and overcome the anxiety problems.[17] Games have also designed for lung cancer patients. Players know about the problems that they will face and how to overcome them and can create an optimal self-management of patients to increase the confidence and motivation of sufferers.[18] Katsikitis et al.[19] also designed a game on a smartphone called "Knowing You, Knowing Me (KYKM)." In this game, a mother and daughter can discuss the positive abilities they have, build good relationships, and how to manage risky behaviors in the social environment.

This game is expected to help adolescents in assessing how their characteristics are, how they should behave, how to assess the results that achieved and analyze the suitability of their ideal behavior and form a series of behavioral attitudes, values, and goals expected by society. In other words, the games can help the formation of components of youth self-concept such as body image, self-ideal, self-esteem, role performance and identity.[12]

In the game, there are questions about the relationship, social, cultural, religion, and human rights, so that teenagers not only get information about reproductive health but also there are some moral messages that can be used as guidelines in interacting with other people and the environment.

Based on the results of interviews with several respondents, they stated that the KEPO game was more attractive and can be used at any time. Storylines and animations in the game are real and like everyday life. So that makes them prefer the KEPO game rather than other forms of reproductive health services that they have experienced.

There is an increase in reproductive health motivation in groups using KEPO game because respondents obtain information about reproductive health regularly and continuously for one month of research. Respondents have used this game three times a week with a duration of 60 minutes for each player. During use, respondents exposed to reproductive health, including the impact that would occur if they did not have a healthy and responsible reproductive health. The dangers displayed in this 3-dimensional animation form a deep impression on teenagers. Various questions in the storyline of this game look real and are like the daily lives of teenagers. Not only is the material/problem packaged in the form of animation, the addition of notes or information and animated videos in the game can also increase motivation. Notes and animated videos provide additional information for teenagers about their reproductive health, so they will be motivated to be better.

Health motivation/healthy life behavior divided into three domains, which are health knowledge, a healthy attitude, and health practice. Health motivation is a mental impulse that can

grow from within and a result of external stimuli. It acts to meet the need for reproductive health.[14] Components of motivation that measured consists of attention to reproductive health, relevance to the goals to achieve reproductive health, the existence of confidence and satisfaction that will arise when making appropriate health advice and information. According to Sardiman,[20] motivation will encourage individuals to act, determine the direction of their actions following the objectives to achieved and select the actions to be taken. Actions or behaviors related to reproductive health formed if there is motivation from within the individual. If the motivation is high, then the reproductive health behavior will also lead to the positive side, and vice versa.[21]

Motivation is a situation in a person that encourages him to carry out certain activities in order to achieve a goal. Santrock[22] defines motivation as a process that gives encouragement, direction, and persistence of behavior. Motivated behavior is a behavior that is full of energy, directed and lasting. According to Winkel,[23] motivation is the driving force that becomes active. The motivation will be more active if there is a need to achieve the goal. The need for reproductive health education is essential when teenagers motivated through the use of reproductive health games.

Jong et al.[24] revealed that one of the media for learning are games. Games are not only entertaining but can also increase knowledge. According to Bellotti et al.,[25] the game can achieve learning goals and awareness, cognitive, behavioral, affective, and also benefit its users. Granic concludes that games are crucial in cognitive formation, motivation, social and emotional formation in children. Children who play the right games can help themselves in their development.[6] Ozcelik et al.[26] also concluded that the use of games could have a positive impact on increasing motivation. Based on the results of Grimes's et al.'s[27] research, serious games can provide entertainment and provide opportunities for players to explore themselves. This game can provide positive results such as motivating a healthy lifestyle.

Rath et al.[28] concludes that games can also change teen behavior. After playing this game, male teenagers who participate with the respondents in the study have reduced their smoking habits. This game increases player knowledge, directs attitude and motivates players to improve their habits and increases players' trust in the health information that they obtain. Similarly, research implemented by Safitri et al.,[29] through the use of media in the form of SEHATI applications can increase children's knowledge and skills in brushing teeth.

Further development of the game, preferably in 3-dimensional form is needed to make it more attractive. Maximum effects of the game for adolescents in improving their self-concept and reproductive health motivation are important.

Conclusion

The KEPO game increased self-concept and reproductive health motivation in adolescents.

Conflict of Interest

All authors declare that there was no conflict of interest in this article.

Acknowledgement

Thank you to the Center for Quality Improvement of Human Resources for Health, Board of Development and Empowerment on Human Resources for Health, Ministry of Health Republic of Indonesia for providing scholarships during the study. Thank you to the IT Team from Telkom University, Bandung who have contributed to the creation of games and all experts who have provided input for the perfection of this KEPO game.

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Global Medical and Health Communication

Online submission: http://ejournal.unisba.ac.id/index.php/gmhc
DOI: https://doi.org/10.29313/gmhc.v6i3.2907

GMHC. 2018;6(3):169–75
pISSN 2301-9123 | eISSN 2460-5441

RESEARCH ARTICLE

Mixed Juice Consumption During Labor to the Mother's Blood Lactate Levels

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Abstract

Maternal nutritional aim to prevent fatigue marked by lactate accumulation. Mix juice is made for the needs of the mother's energy quickly and reduces the accumulation of lactate. The objective of this study was to find out the influence of mix juice during labor to the mother's blood lactate levels. This study used a randomized controlled trial pretest-posttest group design. This research was carried out at the *Pelayanan Obstetri Neonatal Emergency Dasar*/ PONED (Basic Emergency Obstetric and Neonatal Care/BEONC) Puskesmas (Public Health Center) Garuda, Puter, Pagarsih, Padasuka, and Ibrahim Aji in Bandung city in March–April 2017. Simple random sampling used with the number of samples were 60 mothers in treatment and control group. The treatment group received mix juice during labor, while the control group consumed regular food. The result was analyzed using comparative-numerical categorical analysis test, and the mean difference was analyzed using unpaired t test. The results showed the average increased in blood lactate levels in the treatment group (1.9 mmol/L) was lower than in the control group (4.0 mmol/L). Statistically, there was a significant difference in elevated blood lactate levels after intervention between the treatment and control group. Mothers who did not receive the mixed juice in labor have a risk of elevated blood lactate levels four times higher than the mothers who received the mixed juice. Conclusion, giving mix juice to the labor process affects the prevention of maternal blood lactate levels.

Key words: Labor, lactate level, mix juice

Konsumsi Minuman *Mix Juice* pada Persalinan untuk Kadar Laktat Darah Ibu

Abstrak

Kebutuhan nutrisi ibu bersalin bertujuan mencegah kelelahan yang ditandai dengan akumulasi laktat. *Mix juice* dibuat untuk memenuhi kebutuhan energi ibu bersalin secara cepat dan mengurangi penumpukan laktat. Penelitian ini bertujuan menganalisis pengaruh pemberian *mix juice* terhadap kadar laktat darah ibu. Penelitian ini menggunakan desain *randomized controlled trial pretest-posttest group*. Penelitian dilaksanakan di Puskesmas Pelayanan Obstetri Neonatal Emergensi Dasar (PONED) Garuda, Puter, Pagarsih, Padasuka, dan Ibrahim Aji di Kota Bandung pada Maret–April 2017. Populasi penelitian adalah semua ibu yang akan melahirkan di Kota Bandung. Penarikan sampel dilakukan secara acak yang berjumlah 60 orang pada kelompok perlakuan dan kontrol. Kelompok perlakuan mendapatkan *mix juice* selama persalinan, sedangkan kelompok kontrol dibebaskan untuk makan dan minum. Hasil dianalisis menggunakan uji analisis komparatif kategorik numerik dan perbedaan rerata dianalisis menggunakan uji t tidak berpasangan. Hasil penelitian didapatkan rerata kenaikan kadar laktat darah pada kelompok perlakuan (1,9 mmol/L) lebih rendah dibanding dengan kelompok kontrol (4,0 mmol/L). Secara statistik terdapat perbedaan bermakna dalam kenaikan kadar laktat darah setelah intervensi antara kelompok perlakuan dan kontrol. Ibu yang tidak mendapatkan *mix juice* pada persalinan memiliki risiko kenaikan kadar laktat darah 4 kali lebih tinggi dibanding dengan ibu yang mendapatkan *mix juice* pada persalinan. Simpulan, pemberian *mix juice* pada proses persalinan berpengaruh terhadap pencegahan peningkatan kadar laktat darah ibu.

Kata kunci: Kadar laktat, *mix juice*, persalinan

Received: 30 August 2017; Revised: 10 December 2018; Accepted: 12 December 2018; Published: 31 December 2018

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Introduction

Labor complications can increase mortality and morbidity for mother and baby. Childbirth is often followed by fatigue both physiologically and psychologically and has adverse effects in the delivery process, one of which is prolonged labor. Prolonged labor increases maternal and neonatal mortality and morbidity.[1] Labor fatigue is influenced by various factors that occur naturally, such as changes in body metabolism, changes in energy needs, activity patterns, sleep patterns, social status, lifestyle, psychological conditions, and environmental factors. A result of energy metabolism explained one of the causes of physiological fatigue in labor, in which there is an accumulation of lactate in muscle activity caused by lack of oxygen and a reduction in muscle glycogen levels. Tzeng et al.'s[2] study state that there is a relationship between lactate levels and the level of fatigue in labor. Increased fatigue during labor associated high blood lactate levels. Lactate levels are an indicator of fatigue.

High-intensity physical activity such as labor can cause an increase in lactic acid levels in muscles and blood. Increased levels of lactate can cause a decrease in pH which will inhibit the action of enzymes or chemical reactions in cells, especially in the muscles themselves, thus affecting the ability of the maximum muscle fibers to work, decreased physical performance and caused fatigue. There is an increase in energy requirements in labor so that sufficient energy needed during labor.[3,4] Lack of nutritional intake during labor can have a detrimental effect on the mother, baby, and the progress of labor.[5,6]

During labor, there is an increased oxygen demand along with the increase uterine contractions when oxygen is not sufficiently available there is anaerobic metabolism, and lactate produced as a by-product. The concentration of lactic acid increases in the first phase of the active phase and improvements in the second stage as a result of straining.[4] Lactic acid insufficient oxygen can be converted back to pyruvic acid and then undergo an oxidative system to produce energy. This process is called the Cori cycle which can only run if there is adenosine triphosphate (ATP) as the fuel for the procedure. Lactic acid buildup occurs when the amount of lactic acid produced is greater than the amount of lactic acid metabolized by the body or in other words the rate of lactic acid formation is higher than the speed of decomposition (recovery).[7,8]

Based on preliminary studies that have been carried out on 30 mothers giving birth to nutrition fulfillment patterns during the delivery process. It concluded that usually the mothers still consume food at the latent phase, entering the first phase of the active phase and when the second stage most mothers refuse to waste food due to taste more frequent pain. The average number of calories they consume during labor is only 30 kcal/hour.

Energy requirements in labor are assumed to be similar to energy requirements for moderate aerobic exercise. From several existing research journals, the energy needs of maternity women estimated at 50–100 kcal/hour.[9,10]

Maternity mothers still need all the nutrients that needed in general, but in labor, there are physiological changes such as the occurrence of inhibition of gastric emptying and decreased gastrointestinal motility so that the absorption of nutrients lasts longer. Besides, there are also psychological changes during labor such as anxiety facing childbirth so that the mother does not have the desire to eat and drink, and this also occurs due to the pain caused by contractions that are increasingly frequent. Nutritional needs of the mother fulfilled by providing an intake in the form of a liquid that easily digested and quickly absorbed into energy, delicious (does not cause nausea), practical, and suitable with the condition of the mother who will give birth.[11] One of them is by providing drinks in the form of mix juice, and ingredients used to make mix juice drinks such as honey, dates, dried red beans, oranges, mangoes, and guava. Mix juice is a mixture of several raw materials that have a complete nutritional composition to improve the taste and density of nutritional value so that all nutrients from various ingredients mixed.[5,12]

The main dietary content of these ingredients (such as honey, dates, and fruits) are mostly simple carbohydrates such as fructose and glucose are ketose and aldose sugars, each of which has a different chemical structure and metabolic pattern. Both become monosaccharides with a tendency to experience rapid burning. Glucose rapidly metabolized and absorbed into the circulatory system to provide energy, but it also burns quickly, while absorption of fructose travels slower (fructose is released slowly into the bloodstream to produce sustained energy, increase and maintain homeostasis), fructose

continue to sustain individuals with the power generated.[13,14]

Besides containing high carbohydrates, mix juice is also rich in protein and fat which can also be used as an energy source even though the absorption process is not as fast as carbohydrates. Mix juice is also rich in vitamins and minerals, especially vitamin B contained in fruits as ingredients for making mix juice, which functions to accelerate the metabolism of energy formation. Mix juice can provide a source of energy quickly so that it is easily absorbed by the body to produce energy, saves glycogen use and accelerates the return of glycogen used. Thus lactate levels that accumulate will decrease faster. The purpose of this study was to analyze the effect of giving mixed juice drinks during labor to prevent the increase of maternal blood lactate levels.[13]

Methods

This study was a randomized controlled trial (RCT) pretest-posttest group design, which was conducted on 60 women with gravida 4 who would give birth at the basic emergency obstetric and neonatal care/BEONC (*pelayanan obstetri neonatal emergensi dasar*/PONED) puskesmas (public health center) in Bandung city (30 treatment groups and 30 control groups). Sampling in this study was conducted randomly by block randomization with block permutation. This research was carried out at the PONED Public Health Center Garuda, Puter, Pagarsih, Padasuka, and Ibrahim Aji in March–April 2017.

Inclusion criteria were parturients aged 20–35 years, pregnant women with gravida <4 came with the latent phase, the results of obstetric examination of term infants, single, and healthy, normal body mass index (BMI) before pregnancy. Exclusion criteria have specific food allergies, experiencing complications during pregnancy and childbirth, having a history of gastritis, and a history of metabolic disorders. The requirements for dropping out were the total consumption of mix juice during labor less than the minimum dose of 100 kcal/hour, delivery with action, the presence of fetal distress during labor, prolonged labor, and the presence of his disorder (hypertonus).

The treatment group received mix juice during the first stage until the third stage of labor, while the control group was free to eat and drink during labor. Blood lactate levels were measured by looking at maternal capillary blood lactate levels using the Accutrend Plus brand lactate levels. The result of the test was analyzed using comparative-numerical categorical analysis test. The mean difference was analyzed using unpaired t test.

Mix juice formulation was carried out in the laboratory to get standard mixed juice drinks, conducted several trials (trial and error) so that there were three suitable formulations, then organoleptic tests were carried out to determine the best formulation. The wording is a mixture of ingredients such as dates, honey, red beans, oranges, and red guava/mango.

This research has received a permit from the Health Research Ethics Committee of Faculty of Medicine, Universitas Padjadjaran Bandung by ethics approval letter number: 309/UN6.C.10/PN/2017.

Results

The test on the quality of mix juice drinks was carried out in the Food Analysis Laboratory, Department of Food Technology, Faculty of Engineering, Universitas Pasundan. The quality test aims to assess the content of protein, fat, carbohydrates, water content, and ash content in

Table 1 Mix Juice Drinks Quality Analysis

Characteristics	Red Guava Mix Juice (per 100 mL)	Manggo Mix Juice (per 100 mL)	Quality Requirements (per 100 mL)
Water content (%, w/w)	76.6537%	77.2111%	–
Ash content (%, w/w)	1.273% or 0.0132 g	1.2331% or 0.0127 g	Max. 1.1 g
Carbohydrate (%, w/w)	20.872% or 83.490 kcal	19.967% or 83.063 kcal	Max. 11.4 g or 45.6 kcal
Protein (%, w/w)	1.862% or 7.449 kcal	1.723% or 7.171 kcal	3.2–4.4 g or 12.8–17.6 kcal
Fat (%, w/w)	1.7923% or 16.131 kcal	1.695% or 15.866 kcal	Min. 0.6 g or 5.4 kcal
Calories/energy (kcal)	107.07 kcal	105,01 kcal	Min. 56 kcal

Table 2 Characteristics of Research Subjects

Characteristics	Groups		p Value
	Treatment (n=30)	Control (n=30)	
Age (years)			0.149*
20–24	11	9	
25–29	11	6	
30–35	8	15	
x (SD)	26.3 (4.5)	28.3 (5.5)	
Range	20–35	20–35	
Work			0.573*
Yes	8	10	
No	22	20	
Body mass index (kg/m²)			0.407**
x (SD)	21.2 (1.8)	21.6 (1.8)	
Median	21.2	21.5	
Range	18.5–24.9	18.6–24.9	
Anxiety level			0.453*
There is no anxiety	23	26	
Mild anxiety	6	4	
Medium	1	0	
Gravida			0.602*
Primigravida	14	12	
Multigravida	16	18	
Duration of labor (minute)			0.066**
x (SD)	271.5 (81.9)	321.5 (121)	
Median	272.5	326.5	
Range	125–473	131–660	

*Chi-square test, **independent t test

labor drinks. Analysis of protein content used the Kjeldahl method, analysis of fat with the Soxhlet method, carbohydrates using the Luff Schoorl method, and determination of water content and ash content using the gravimetric method. Resolution of storability is to test the microbial contamination method with total plate count (TPC) and *E. coli*.

Table 3 Analysis of Differences in Blood Lactate Levels Before and After Interventions

Blood Lactate Levels	Groups		p Value
	Treatment (n=30)	Control (n=30)	
Before intervention (mmol/L)			0.296*
x (SD)	2.6 (0.8)	2.4 (0.7)	
Median	2.4	2.4	
Range	1.3–4.5	1.2–4.1	
After intervention (mmol/L)			<0.001**
x (SD)	4.6 (1.1)	6.5 (2.1)	
Median	4.6	5.9	
Range	2.9–6.8	3.5–10.5	
Comparison before vs after			
p value	<0.001*	<0.001***	
Increase in blood lactate level (mmol/L)			<0.001**
x (SD)	1.9 (0.8)	4.0 (1.8)	
Median	1.9	3.4	
Range	0.4–4.3	1.8–9.3	

*Independent t test, **Mann-Whitney test, ***Wilcoxon test

Table 4 Analysis of the Effect of Mix Juice on the Process of Childbirth Against Prevention of Increase in Mother's Blood Lactate Level

Groups	Increase in Blood Lactate Level		p Value*	RR (95% CI)
	>2.35	≤2.35		
Control	24	6	<0.001	4.0 (1.9–8.3)
Treatment	6	24		

*Chi-square test, RR: relative risk, CI: confidence interval

Table 1 shows that most of the values mix juice have standard requirements for quality drinks for pregnant women based on Indonesian National Standard (*Standar Nasional Indonesia*/SNI) 01-7148-2005, with several ingredients adjusted to the needs of the mothers.

Table 2 shows that there were no statistically significant differences between the two study groups regarding age, occupation, maternal BMI, anxiety level, gravida, and duration of labor (p>0.05). Based on the homogeneity of the characteristics of the two research groups, the two research groups are suitable for comparison.

Table 3 shows that at the beginning of the study mean blood lactate level of the treatment group was higher (2.6 mmol/L) than the control group (2.4 mmol/L) while at the end of the study the mean blood lactate levels of the treatment group was lower (4.6 mmol/L) than the control group (6.5 mmol/L). In the treatment and control groups, there were significant differences between blood lactate levels before and after the intervention p<0.05. Table 3 also shows that there were no significant differences in blood lactate levels before intervention between the treatment and control groups (p>0.05). However, there were significant differences in blood lactate levels after the intervention between the treatment and control groups p<0.05.

Table 3 shows the average difference in blood lactate levels in the treatment group (1.9 mmol/L) lower than in the control group (4.0 mmol/L). Statistically, there was a significant difference in the difference between blood lactate levels before and after the intervention between the treatment and control groups p<0.05.

Table 4 shows that in the control group the study subjects who experienced an increase in blood lactate levels >2.35 (80%) were more than in the treatment group (20%). While the study subjects who experienced an increase in blood lactate levels ≤2.35 more in the treatment group (80%) than in the control group (20%) so that mothers who did not get mix juice during labor had a risk of increasing high blood lactate levels (>2.35) by 4 times compared to mothers who received mix juice during labor. In this study, the number need to treat (NNT) values were 1.67 rounded to 2. The NNT value means that every two research subjects received mix juice an additional one research subject experienced prevention of increased blood lactate levels.

Discussion

The development of drinks for maternity mothers is made to meet nutritional needs in the form of fluids contain nutrients that are high calories, high carbohydrates, and enough vitamins, minerals, and water.[6] Adequate energy requirements are the amount of food energy needed to balance total energy expenditure. Every individual needs substantial macronutrient intake to carry out physical activities, especially in labor. The body can break down carbohydrates, fats, and proteins as energy during physical activity. Although there is much potential energy stored in the body as fat, where fat can be broken down for fuel during intense exercise. Likewise, there is much protein in shape, but protein damage as energy is inefficient and supplies only a small portion of energy needs during exercise. Carbohydrates are the primary fuel needed during strenuous activity such as childbirth because these molecules can be broken down quickly as energy. The content of carbohydrates from ingredients that make mix juice drinks such as dates, honey, red beans, mangoes, oranges, and red guava is mostly glucose, sucrose, and fructose which are simple carbohydrates that can be used as a source of energy quickly.[13,14]

When food or drink chewed, it mixed with saliva, which consists of the enzyme ptyalin (an α-amylase) secreted by the parotid gland. This enzyme is useful for breaking down starch into disaccharides and disaccharides

into monosaccharides. The final product of carbohydrate digestion is monosaccharide. The small intestine absorbed monosaccharides and released into the bloodstream. Fructose, sucrose, and galactose must be metabolized to glucose by the liver. When excess energy in the form of carbohydrates, it will be stored in the skeletal muscle and the liver as glycogen with the help of the insulin hormone and will automatically maintain blood sugar balance. When the glycogen reserves are sufficient, excess glucose is oxidized and stored as fat. It is also important to remember that contraction of muscle fibers during strenuous exercise is very dependent on the availability of carbohydrates as energy because of their ability to use fat as limited energy.[14,15]

Carbohydrates circulated in the blood as glucose and stored in the muscles and the liver as glycogen. The process of glycogen formation in brief, namely the first stage is the formation of glucose-6-phosphate from glucose, with the help of glucokinase enzyme and get additional energy from ATP and phosphate. Furthermore, glucose-6-phosphate with glucoamylase enzyme becomes glucose-1-phosphate. Then, glucose-1-phosphate reacts with uridine triphosphate (UTP) catalyzed by uridyl transferase to produce uridine diphosphate glucose (UDP-glucose) and pyrophosphate (PPi). The last stage occurs condensation between UDP-glucose and number one glucose in the primary glycogen chain produce a new glycogen chain with one additional unit of glucose.[16]

During physical activity such as labor, the breakdown of glycogen triggered by hormones such as adrenaline (or epinephrine). Muscle glycogen used as a fast source of energy in muscle contraction. The liver releases glucose into the blood to help meet energy needs during exercise, which moves in the active muscle where used. Continuous training will gradually drain glycogen levels in the muscles and liver. Carbohydrate intake can delay the onset of fatigue and increase prolonged exercise performance like labor, this is done to maintain high levels of carbohydrate oxidation or in other words, keep energy fulfillment through the pathway oxidative.[17,18]

Mix juice drinks as a source of instant energy (additional energy from outside the body) that is easily absorbed by the body serves to maintain glucose levels and conserve glycogen use so that the body does not need to break down other energy sources, and accelerate the return of glycogen that used so that the accumulated lactate levels reduced faster.[5,19] Lactic acid buildup occurs when the amount of lactic acid produced is greater than the amount of lactic acid metabolized by the body or in other words the speed of lactic acid formation is higher than the rate of decomposition (recovery).[18] Lactic acid in conditions of sufficient oxygen can produce energy known as the Cori cycle. This process will only run optimally in the resting phase because oxygen from normal breathing is channeled maximally throughout the body and there is an opportunity to take simple carbohydrates that can be absorbed quickly in the digestive system.[18,19] This is similar with a study which mother was given mix juice for the first stage until the third stage during labor. The mixed juice consumed when the mother is not experiencing contractions so that the mother has the opportunity to get the maximum oxygen and get carbohydrate intake. It is to prevent lactate buildup caused by the occurrence of decomposition of lactate through the Cori cycle which has run optimally.

In the control group, mothers allowed the freedom to consumed regular food during childbirth. The researchers were unable to control the number of calories that had to be spent by mothers because each mother had different desires in consuming food and drinks. Most of the mothers did not have the desire to eat foods such as rice and side dishes that had been provided by the health center due to the pain caused by increasingly frequent contractions, so that the average calorie of food consumed in the control group in this study (45.87 kcal/hour) smaller than the intervention group (123.83 kcal/hour). Causes the intake of nutrients obtained by the control group so that the body breaks down other energy sources.

It is also consistent with research Khanna and Manna[13] about the effect of electrolyte drinks on blood lactate levels during exercise and recovery, blood lactate levels recorded during breaks at intervals every 10 minutes during exercise and recovery. Although most of the value is not significant, it was significantly lower ($p<0.01$) values were recorded after 70 minutes of exercise (without supplementation 3.4±0.6 mmol/L compared with 2.1±0.4 mmol/L with supplementation). However, no significant changes recorded for lactate levels at peak training (without supplementation of 3.7±1.2 mmol/L with supplementation of 3.2±1.0 mmol/L). At the

time of recovery of blood, lactate levels different significantly ($p<0.05$) (no supplementation 2.5±0.9 mmol/L; with supplementation of 1.5±0.4 mmol/L). From the study described this could occur due to consumption of carbohydrates can prevent a decrease in blood glucose and maintain oxidation of carbohydrates or for efficient use of muscle glycogen early.

Conclusion

Conclusions from this study there is the effect of giving mixed juice in the labor process to prevent the increase in maternal blood lactate levels.

Conflict of Interest

All authors state there was no conflict of interest.

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Global Medical and Health Communication

Online submission: http://ejournal.unisba.ac.id/index.php/gmhc
DOI: https://doi.org/10.29313/gmhc.v6i3.3034

GMHC. 2018;6(3):176–81
pISSN 2301-9123 | eISSN 2460-5441

RESEARCH ARTICLE

Clinical and Hematological Parameters as the Predictors of Shock in Dengue Infection

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Abstract

Dengue infection is one of the main health issues in the world and Asia has the highest incidence of dengue infection with most children aged 5–15 years affected. As World Health Organization guidelines recommend, the identification of warning signs at defervescence can detect patients who are at risk of progression to shock. This study aimed to determine the clinical and hematological parameters as the predictors of shock in dengue infection. This retrospective study collected medical records of pediatric patients suffering from dengue infection admitted to dr. Soediran Mangun Sumarso Regional Hospital in Wonogiri, Central Java in January–November 2016. Data was collected in December 2016. The studied predictor factors consisted of clinical and hematological parameters that represented the warning signs of dengue infection. Statistical analysis was performed using the logistic regression test. Of the 110 eligible subjects, 33 (30%) of them suffered from dengue shock syndrome. The multivariate analysis showed that gastrointestinal bleeding (OR=32.62), pleural effusion (OR=31.45), hematocrit >45% (OR=8.67), and thrombocytopenia ≤50,000/µL (OR=13) increased the risk of dengue shock syndrome. Clinical parameters as gastrointestinal bleeding and pleural effusion as well as laboratory parameters of hematocrit and thrombocytopenia became the predictors of shock in dengue infection.

Key words: Dengue infection, predictor factors, shock, warning signs

Parameter Klinis dan Hematologis sebagai Prediktor Kejadian Syok pada Infeksi Dengue

Abstrak

Infeksi dengue merupakan salah satu masalah kesehatan utama di dunia. Asia merupakan kawasan dengan insidensi infeksi dengue tertinggi dengan penderita terbanyak anak berusia 5–15 tahun. *World Health Organization* menyatakan bahwa tanda bahaya dengue pada fase kritis dapat mendeteksi kejadian syok pada pasien. Tujuan penelitian ini adalah menentukan parameter klinis dan hematologis yang menjadi prediktor syok pada infeksi dengue. Penelitian ini merupakan penelitian retrospektif dengan mengumpulkan data rekam medis pasien anak yang menderita infeksi dengue dan dirawat di RSUD dr. Soediran Mangun Sumarso Wonogiri Jawa Tengah pada Januari–November 2016. Pengambilan data dilakukan pada bulan Desember 2016. Faktor prediktor yang diteliti adalah parameter klinis dan hematologis yang merupakan tanda bahaya infeksi dengue. Analisis statistik dilakukan menggunakan uji regresi logistik. Dari 110 subjek penelitian yang memenuhi kriteria, 33 (30%) di antaranya menderita sindrom syok dengue. Analisis multivariat menunjukkan perdarahan saluran cerna (OR=32,62), efusi pleura (OR=31,45), hematokrit >45% (OR=8,67), dan jumlah trombosit ≤50.000/µL (OR=13) meningkatkan risiko sindrom syok dengue. Parameter klinis berupa perdarahan saluran cerna dan efusi pleura serta parameter laboratoris berupa hematokrit dan jumlah trombositopenia merupakan prediktor kejadian syok pada infeksi dengue.

Kata kunci: Faktor prediktor, infeksi dengue, syok, tanda bahaya

Received: 21 September 2017; Revised: 8 December 2018; Accepted: 13 December 2018; Published: 31 December 2018

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Introduction

Dengue infection is a serious health issue in the world. Approximately 2.5–3.6 billion of the world's population living in more than 125 endemic countries are at risk of suffering from this disease.[1] Each year, there are estimated 390 million cases of dengue infection and 96 million cases of clinical manifestations while the rest are asymptomatic cases.[2] Asia is the region with the highest incidence of dengue infection in the world with 5–15 years old children as the most sufferers.[3] In Indonesia alone, the number of dengue infection cases is increasing every year. In 2015, a total of 129,650 cases of dengue hemorrhagic fever (DHF) were reported with 1,071 deaths. The morbidity rate reached 50.75 per 100,000 people with a case fatality rate (CFR) of 0.83%.[4] In Central Java province, DHF remains a serious issue. In 2014, the CFR was 1.7%, which was higher than that in 2013 (1.21%) and even higher than the national target. The CFR of DHF of more than 1% occurred in 23 districts/cities in the province with the highest mortality rate of 9.3% in Wonogiri district.[5]

The clinical manifestations of dengue infection vary greatly from mild dengue fever (DF) to severe infection characterized by severe plasma leakage along with bleeding manifestations named dengue shock syndrome (DSS). To assist clinicians in diagnosing and determining the classification of dengue infection, the World Health Organization (WHO) recommends several criteria for clinical and laboratory diagnosis of dengue.[6] However, predictions of the course of dengue infection or shock in patients remain difficult to make due to the widely varied clinical manifestations among patients, complex pathogenesis, as well as differences in viral serotypes in different regions.[7] The 2009 and 2011 WHO guidelines state that in pediatric patients identification of dengue warning signs based on either clinical symptoms or laboratory findings in the defervescence phase/critical phase of infection has strong discrimination to detect patients who are at risk of severe dengue/shock or to determine whether patients need hospitalization.[6,8]

Studies to prove clinical and laboratory criteria as the risk factors or prognostic factors of the severity of dengue infection in children have been widely performed in Indonesia with varied methods and results.[7,9–13] In general, assessment of the predictors in those studies was conducted without considering the course of the disease/phase of dengue infection. In addition, some of the assessed parameters were not those obtained from routine examination results. Therefore, this study aimed to identify clinical and hematological parameters in the form of dengue warning signs as predictor factors of shock in dengue infection in children carried out in the critical phase of the disease.

Methods

This research was a retrospective study collecting medical record data of DHF patients treated in the pediatric wards of dr. Soediran Mangun Sumarso Regional Hospital in Wonogiri, Central Java from January 2016 to November 2016. Data was collected in December 2016. The inclusion criteria consisted of all patients aged 0–18 years who were diagnosed with dengue infection following the WHO 2011 diagnosis criteria (Table 1).[6] The research subjects were selected through consecutive sampling, and those diagnosed with DF, DHF grade I, and DHF grade II were included in the group of dengue infection in non-shock cases (dengue-NS). Meanwhile, the subjects diagnosed with DHF grade III and IV were categorized in the group of dengue with shock cases (DSS). Subjects were excluded if the medical record was incomplete and the patients had a comorbid infectious disease.

Data was collected from the medical records of dengue patients who were first admitted to hospital during the critical phase of the disease, which was day 3, day 4, or day 5 of fever. Days of illness/fever were calculated from the first day of fever complaint by the patients. The measured predictor factors of shock were the warning signs listed in the WHO 2009 criteria, including clinical parameters in the form of abdominal pain, persistent vomiting, >2 cm hepatomegaly, mucosal bleeding, gastrointestinal bleeding, and plasma leakage signs, as well as hematological parameters consisting of hematocrit level and platelet counts.

Chi-square test was used for the bivariate analysis among predictor variables with prognosis, in which variables with $p<0.25$ would be included in the multivariate analysis. To determine the predictor factors for DSS, the multivariate logistic regression analysis was employed.

This study has received the permit by the Medical and Health Research Ethics Committee, Faculty of Medicine, Universitas Islam Indonesia

Table 1 Classification of Dengue Infection and DHF Grade of Severity

Grades	Signs and Symptoms	Laboratory
DF	Fever accompanied by minimum 2 of the following symptoms: - headache, - retro-orbital pain, - myalgia, - arthralgia, - maculopapular rash, - hemorrhagic manifestations, - no signs of plasma leakage.	- Leucopenia (leukocyte count is ≤5,000 cells/μL). - Thrombocytopenia (platelet count is <150,000 cells/μL). - Hemoconcentration (5–10%). - No evidence of plasma loss.
DHF I	Fever and hemorrhagic manifestations (positive tourniquet test) and signs of plasma leakage.	Thrombocytopenia (<100,000 cells/μL); hemoconcentration (≥20%).
DHF II	Spontaneous bleeding in addition to the manifestations of grade I.	Thrombocytopenia (<100,000 cells/μL); hemoconcentration (≥20%).
DHF III	Manifestations of grade I or II along with circulatory failure (weak pulse, ≤20 mmHg pulse pressure, hypotension, restlessness, decreased diuresis).	Thrombocytopenia (<100,000 cells/μL); hemoconcentration (≥20%).
DHF IV	Profound shock with undetectable blood pressure and pulse.	Thrombocytopenia (<100,000 cells/μL); hemoconcentration (≥20%).

Yogyakarta by ethics approval letter number: 73/Ka.Kom.Et/70/KE/XI/2016.

Results

During the research period, 110 dengue infection patients admitted to the pediatric wards of dr. Soediran Mangun Sumarso Regional Hospital in Wonogiri, Central Java fulfilled the inclusion criteria. Characteristics of the subjects are presented in Table 2. Most of them were male (52%) with a proportion of 1.07:1 compared to female. The age of 49% of the research subjects ranged 10–14 years. The percentage of the subjects admitted to the hospital on 3rd and 5th day of fever was each 34%, while 33% of them were admitted on day 4.

Based on the final diagnosis, the subjects were divided into two groups, namely dengue patients with shock cases (DSS) of 33 people (30%) and dengue patients in non-shock cases (dengue-NS) totaling 77 people (70%). Table 3 shows that clinical manifestations of acral coldness, gastrointestinal bleeding, pleural effusion, and petechiae were more common in DSS patients than in non-shock dengue patients, with percentages

Table 2 Characteristics of the Subjects

Characteristics	Number (n=110)	Percentage (%)
Sex		
Male	57	52
Female	53	48
Age (years)		
0–4	12	11
5–9	29	26
10–14	49	45
≥15	20	18
Day of fever when first admitted to hospital		
3rd	37	34
4th	36	33
5th	37	34

Table 3 Clinical Parameters

Clinical Manifestations	Dengue-NS 77 (70%)	DSS 33 (30%)	p Value
Abdominal pain	38 (68%)	18 (32%)	0.617
Persistent vomiting	50 (68%)	23 (38%)	0.628
Hepatomegaly >2 cm	42 (59%)	29 (41%)	0.001*
Accumulation of fluid			
Ascites	46 (59%)	32 (41%)	0.000*
Pleural effusion	22 (43%)	29 (57%)	0.000*
Hemorrhagic manifestation			
Petechiae	21 (45%)	26 (55%)	0.000*
Gum bleeding/epistaxis	17 (63%)	10 (37%)	0.358
Gastrointestinal bleeding	2 (22%)	7 (78%)	0.003*

*p<0.05, statistically significant

Table 4 Hematological Parameters

Hematological Parameters	Dengue-NS 77 (70%)	DSS 33 (30%)	p Value
Hematocrit >45%	16 (42%)	22 (58%)	0.000*
Thrombocytopenia ≤50,000/µL	42 (58%)	31 (42%)	0.000*

*p<0.05, statistically significant

of 100%, 78%, 57%, and 55%, respectively. The most common clinical manifestations in non-shock dengue patients were abdominal pain (68%), persistent vomiting (68%), gum bleeding/epistaxis (63%), hepatomegaly (59%), and ascites (59%). Hematological abnormality in the form of hematocrit level of >45% was more commonly found in DSS patients than in non-shock dengue patients, reaching 58% as shown in Table 4.

The bivariate analysis using a chi-square test showed that clinical and hematological parameters based on warning signs that distinguish DSS from non-shock dengue were hepatomegaly >2 cm, ascites, pleural effusion, gastrointestinal bleeding, hematocrit >45%, and thrombocytopenia ≤50,000/µL.

The results of logistic regression analysis indicated that the clinical symptom parameters in the form of gastrointestinal bleeding (OR=32.62) and pleural effusion (OR=31.45) in a multivariate manner had a significant effect on shock cases with 5% significance level. In addition, the laboratory parameters as the predictors of shock in this study included thrombocytopenia ≤50,000/µL

Table 5 Logistic Regression Analysis for DSS Predictor Factors

Characteristics	Coef.	p Value	OR	95% CI	
				Min.	Max.
Clinical parameter					
Gastrointestinal bleeding	3.48	0.002*	32.62	3.50	303.95
Pleural effusion	3.45	0.000*	31.45	6.91	143.11
Constant	−3.35	0.000	0.04		
Hematological parameter					
Hematocrits >45%	2.16	0.000*	8.67	2.97	25.33
Thrombocytopenia ≤50,000/µL	2.57	0.002*	13.00	2.49	67.91
Constant	−0.48	0.219	0.62		

*p<0.05, statistically significant

(OR=13), and hematocrit >45% (OR=8.7).

Discussion

The cases of DSS were found in 30% of 110 patients with dengue infection who met the inclusion criteria. This is not much different from the DSS cases in several other studies ranging 30–40%.[7,12] In this study identified several DSS predictors indicating warning signs of dengue infection listed in WHO guidelines. Warning signs are a collection of signs and symptoms that precede shock manifestations, enabling them to be used as a prognosis for DSS cases. Such signs appear at the end of the acute phase because of increased capillary permeability.[8] Endothelial dysfunction leads to capillary permeability due to the release of inflammatory mediators triggered by proinflammatory cytokines. Such cytokines are produced by the cells infected with dengue virus.[14]

Accumulation of fluid in tissues, including ascites and pleural effusion, is a manifestation of plasma leakage due to increased capillary permeability. This clinical sign appears at the beginning of the critical phase.[8] In this study, pleural effusion had a highly significant correlation with DSS cases in children and was an important predictor factor (OR=31.45). These results are consistent with several previous studies.[12,13]

The incident of gastrointestinal bleeding in this study was more common in subjects with DSS than in non-shock cases, making it a strong predictor factor with OR=32.62. This finding is in line with other studies.[7,12,13,15] Gastrointestinal bleeding is closely related to thrombocytopenia in severe dengue infection.[16,17] The degree of severity of thrombocytopenia is directly proportional to the severity of hemorrhagic manifestations. In dengue patients, platelet counts of <50,000/μL have a significant association with severe bleeding.[18]

Hepatomegaly clinical manifestation is a fairly common prognostic factor of DSS.[7,11–13,15] Abdominal pain is an early indicator of increased capillary permeability and is a prognostic factor for predicting the severity of dengue infection.[11,16] It can be caused by gastrointestinal bleeding, hepatomegaly, or tissue hypoxia due to insufficient visceral blood supply during the condition of pre-dengue and dengue shock.[10] In this study, abdominal pain and hepatomegaly were more common in non-shock dengue patients than in those experiencing DSS, indicating that they were not the prognostic factors of DSS. This is likely due to the limitations in confirming complaints and examination results to the research subjects because the data was taken only from the patients' medical records.

In this study, the laboratory parameter, the hematocrit >45%, is a predictor factor for DSS cases (OR=8.67) similar to the finding of previous studies.[7,11–13,15] Increased hematocrit level above normal is one of the initial signs of plasma leakage. High hematocrit level is associated with the severity of plasma leakage. Such plasma leakage will reach its peak during a shock event.[8]

The platelet count of ≤50,000/μL in this study also increased the risk of DSS (OR: 13.00). Thrombocytopenia is a prognostic factor of shock in dengue as suggested by previous studies.[7,9,11–13,15] Thrombocytopenia in DHF patients results from a decrease in platelet production by the bone marrow, which is temporarily suppressed, as well as an increase in platelet destruction in the peripheral circulation. Bone marrow suppression is a direct result of damage to hematopoietic cells due to dengue virus attacks, or as a result of dengue virus infection in stromal cells that triggers the production of proinflammatory cytokines. Increased peripheral platelet destruction is caused by several mechanisms such as imbalance between coagulation factor and fibrinolysis factors, autoimmune processes that attack platelets, direct interaction between dengue virus and platelets, as well as interaction between platelets and endothelial cells or monocytes/neutrophils that cause activation and destruction of platelets at once.[19]

Gastrointestinal bleeding, pleural effusion, hematocrit level of >45%, and thrombocytopenia ≤50,000/μL are the clinical and laboratory parameters that become the predictors of shock in dengue infection. These predictor factors are expected to be the warning sign that can improve accuracy, alertness, and monitoring of patients with dengue infection.

Conclusion

Clinical parameters as gastrointestinal bleeding and pleural effusion as well as laboratory parameters of hematocrit and thrombocytopenia became the predictors of shock in dengue infection.

Conflict of Interest

The authors declare no conflict of interest.

Acknowledgement

Thank you to the Head of the Undergraduate Medical Education Program, Faculty of Medicine, Universitas Islam Indonesia, Yogyakarta that has provided the funding for this research through the Hibah Kinerja II program. We also thank you to the Director of dr. Soediran Mangun Sumarso Regional Hospital in Wonogiri, Central Java and all the staff who have given permission to and assisted the researchers during the study.

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Global Medical and Health Communication

Online submission: http://ejournal.unisba.ac.id/index.php/gmhc
DOI: https://doi.org/10.29313/gmhc.v6i3.3079

GMHC. 2018;6(3):182–7
pISSN 2301-9123 | eISSN 2460-5441

RESEARCH ARTICLE

Two Serial Hematocrit Level Just After Admission to Predict Dengue Hemorrhagic Fever Severity

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Abstract

Dengue hemorrhagic fever (DHF) is still the leading cause of hospitalization and death among children in Indonesia because of plasma leakage leading to shock syndromes. This study aimed to associate the hematocrit difference (first and second) from serial hematocrit (Hct) examination just after admission with DHF severity. A analytical cross-sectional study was involving medical records of pediatric patients with DHF admitted at the pediatric ward and the Pediatric Intensive Care Unit (PICU) of Dr. Hasan Sadikin General Hospital, Bandung in January–December 2015. The subjects excluded if other conditions also cause plasma leakage. The difference in first and second Hct (ΔHct) from serial Hct examination just after admission and DHF grade of severity (DHF I–IV) confirmed by a positive result in serologic tests (anti-dengue IgM/IgG), or detection of dengue virus antigen (NS1Ag test) obtained. Spearman association analysis test used for analysis. A total of 16 subjects with DHF I, 21 subjects with DHF II, 31 subjects with DHF III and two subjects with DHF IV included in this study. There was no significant correlation between positive ΔHct value (hemoconcentration) and DHF severity (r=0.247, p=0.394, CI=95%). In conclusion, the difference in first and second Hct from serial Hct examination just after admission has no significant association with the disease severity.

Key words: DHF severity, two serial hematocrit level

Dua Nilai Hematokrit Serial Sesaat Setelah Admisi sebagai Prediktor Keparahan Demam Berdarah Dengue

Abstrak

Demam berdarah dengue (DBD) merupakan penyebab utama hospitalisasi dan kematian anak di Indonesia disebabkan oleh kebocoran plasma yang berujung pada syok. Tujuan penelitian ini mengetahui hubungan perbedaan hematokrit pertama dan kedua pada pemeriksaan hematokrit serial sesaat setelah admisi dengan keparahan DBD. Penelitian merupakan *analytical cross-sectional study* menggunakan data sekunder berupa rekam medis pasien anak yang dirawat di ruang perawatan anak dan *Pediatric Intensive Care Unit* (PICU) RSUP Dr. Hasan Sadikin Bandung pada Januari–Desember 2015. Subjek penelitian dieksklusi apabila pada rekam medis terdapat diagnosis lain yang menyebabkan kebocoran plasma. Variabel penelitian ini adalah perbedaan hematokrit pertama dan kedua (ΔHct) pada pemeriksaan hematokrit serial serta diagnosis DBD (DBD I–IV) yang dikonfirmasi oleh hasil positif pada pemeriksaan serologis (IgM/IgG antidengue) atau deteksi antigen virus (NS1Ag). Terdapat 16 subjek DBD I, 21 subjek DBD II, 31 subjek DBD III, dan 2 subjek DBD IV. Dengan menggunakan Uji Analisis Spearman, tidak terdapat korelasi yang signifikan antara nilai positif ΔHct (hemokonsentrasi) dan tingkat keparahan DBD (r=0,247; p=0,394; CI=95%). Simpulan, perbedaan hematokrit pertama dan kedua pada pemeriksaan hematokrit serial tidak berhubungan dengan keparahan DBD.

Kata kunci: Dua nilai hematokrit serial, keparahan DBD

Received: 26 September 2017; Revised: 11 September 2018; Accepted: 13 December 2018; Published: 31 December 2018

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Introduction

Dengue hemorrhagic fever (DHF), a mosquito-borne viral disease, is still endemic and the cause of death in children aged <15 years.[1] Plasma leakage that leads to shock is the leading cause of death in patients with DHF.[2] Early clinical laboratory examination is needed to diagnose DHF so it can identify the clinical course of the disease and prevent the shock.[3]

The severity of DHF had been known to be related to the clinical characteristics of the disease and laboratory findings;[1] therefore, plasma leakage can identify by measuring the hematocrit (Hct). Serial Hct examination had been known as a marker to identify plasma leakage if the value increased ≥20%.[4] However, this following procedure had not indicated the course of disease yet, nor DHF severity. Since DHF can be a life-threatening disease,[5] efficient time between serial Hct examination is critical to be studied. Therefore, a fundamental notion about early serial Hct measurement related to DHF severity is needed. This study aims to correlate the difference in first and second Hct level from serial Hct examination just after admission with the severity of DHF.

Methods

A cross-sectional analytical study involving the clinical and laboratory medical records of pediatric patients diagnosed with DHF admitted at the pediatric ward and the Pediatric Intensive Care Unit (PICU) of Dr. Hasan Sadikin General Hospital, Bandung from January to December 2015. The diagnosis of DHF established by the clinician in charge based on WHO criteria (Table 1).[4]

Data included in this study should have the diagnosis of DHF confirmed by a positive result in serologic tests (anti-dengue IgM/IgG) or detection of dengue virus antigen (NS1Ag test), and the first and second Hct measurement result. The diagnosis of DHF used in this study was the working diagnosis established by the clinician at the time the subject discharged from the hospital. Any reports in medical record data informing plasma leakage caused by other diseases or conditions, i.e. severe dehydration, burns, polycythemia vera, diabetic ketoacidosis, and lung emphysema excluded.[6]

The first and second measurement of Hct level obtained through serial Hct examination of each patient just after admission. The time between first to second Hct examination also recorded—the difference of Hct defined as ΔHct. A positive value in ΔHct indicated an increase in Hct confirming hemoconcentration and increased vascular permeability, while negative value indicated a decrease in Hct confirming convalescence in DHF.

Data analyzed for their correlation using SPSS version 20.0. Normally distributed data were presented as mean (standard deviation/SD), while non-normally distributed data presented as median (inter-quartile range/IQR). Spearman analysis test was used to analyze the correlation between ΔHct and severity of DHF.

This research has received a permit from the Health Research Ethics Committee, Faculty of Medicine, Universitas Padjadjaran Bandung by ethics exemption letter number: 309/UN6.C.10/PN/2017.

Table 1 WHO Classification of DHF Severity Grade

Grades	Clinical Characteristics	Laboratory Findings
DHF I	Fever and hemorrhagic manifestation (positive tourniquet test) and evidence of plasma leakage (pleural effusion).	Thrombocytopenia <100.000/mm^3 and hemoconcentration ≥20%.
DHF II	As in Grade **I plus** spontaneous bleeding.	Thrombocytopenia <100.000/mm^3 and hemoconcentration ≥20%.
DHF III*	As in Grade **I or II plus** circulatory failure (weak pulse, narrow pulse pressure (≤20 mmHg), hypotension, restlessness).	Thrombocytopenia <100.000/mm^3 and hemoconcentration ≥20%.
DHF IV*	As in Grade **III plus** profound shock with undetectable blood pressure and pulse.	Thrombocytopenia <100.000/mm^3 and hemoconcentration ≥20%.

*DHF III and IV are dengue shock syndrome (DSS)

Results

Seventy reports of confirmed DHF diagnosis with different severity grades recorded (Table 2). In one year, the majority of subjects in Dr. Hasan Sadikin General Hospital had DHF III (31 subjects). The mean ages of pediatric patients diagnosed having DHF I until DHF IV were 6, 7, 7, and 5, respectively. The median ΔHct values of DHF I to DHF IV were −3, −1, −3, and 4, respectively. The mean time between the first and second Hct of DHF I and IV were 15 and 5.5 hours, respectively. The median time between the first and second Hct of DHF II and III were 11 and 5.5 hours, respectively.

Reports of positive and negative Δhct value were distributed in each DHF severity grade (Figure). Fourteen cases of DHF had positive ΔHct value which indicated hemoconcentration confirming deterioration in DHF, while fifty cases had negative ΔHct value which indicated a decrease in hct confirming convalescence in DHF. Hemoconcentration occurred particularly in DHF II and III. Decrease in hct mostly occurred

Table 2 Distribution of Demography and ΔHct in Each DHF Severity Grade

Variables	DHF I (n=16)	DHF II (n=21)	DHF III (n=31)	DHF IV (n=2)
Sex				
Male	6	10	12	1
Female	10	11	19	1
Age (year)	6 (3.5)*	7 (4)*	7 (3.5)*	5 (1.4)*
ΔHct	−3 (0–[−4.3])**	−1 (0–[−2])**	−3 ([−1]–[−6])**	4 (6.5–1.5)**
Time between first and second Hct (hour)	15 (6.0)*	11 (12.5–8)**	5.5 (8–4)**	5.5 (0.7)*

*Data presented as mean (standard deviation/SD), **data presented as median (inter-quartile range/IQR)

Table 3 Correlation between Positive ΔHct Value and Severity of DHF

	Severity of DHF		Confidence Interval (CI)
	Correlation Coefficient	p Value	
Positive ΔHct value	0.247	0.394	95%

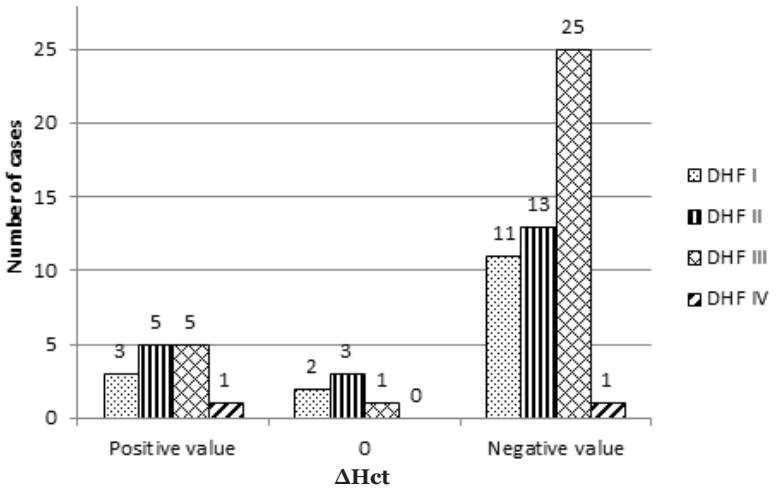

Figure Distribution of ΔHct Value in Each DHF Severity Grade

in DHF III followed by DHF II and I. There was no significant correlation between positive ΔHct value (hemoconcentration) and severity of DHF since p>0.05 (r=0.247, p=0.394, CI=95%) (Table 3).

Discussion

Based on WHO report, Indonesia is included in the most endemic country for DHF because of its leading cause of hospitalization and death among children.[4] Plasma leakage that leads to shock is the leading cause of death in DHF patients.[2] The increased capillary permeability allows extravasation of plasma into pleural or abdominal cavity then the patient will undergo hypotension, and therefore lead it to shock and death.[7]

A standardized classification system for the severity of dengue virus infections is crucial for optimal communication of scientific data to improve our understanding of the pathogenesis and treatment of the disease. Incorrect disease severity classification may lead to faulty decision-making in choosing the most appropriate treatment for the individual patient.[8] Therefore, WHO recommended criteria for DHF diagnosis based on clinical characteristics and laboratory findings. Grading the severity of the disease has been found clinically and epidemiologically useful in DHF epidemics in children especially in Indonesia. These criteria classified DHF severity into four grades (DHF I to DHF IV).[1]

The percentage increase in Hct is an accurate indicator of vascular permeability and plasma leakage; thus, serial Hct examination is a laboratory parameter which need to include as part of dengue patient management.[9–11] Early recognition and appropriate management reduce mortality to <1%, but if left untreated may rise to as high as 20%.[10] Previous studies reported that hemoconcentration correlate with DHF severity.[12,13] This study aims to correlate the difference in first and second Hct level from serial Hct examination just after admission with DHF severity. If there is a significant correlation, it would be a predictor for the clinician to establish the severity of DHF and to treat the patients based on its severity as soon as possible.

This study showed that the majority of subjects had DHF III. This data is relevant since Dr. Hasan Sadikin General Hospital is the top referral hospital in West Java province, so there were more DHF severe cases admitted in this hospital rather than non-serious cases. We noted that there was no statistically significant difference in gender among different DHF grades. The mean age range of pediatric patients with different DHF grades was 5–7 years. This data is relevant to the previous study that stated the maximum number of cases seen in the age group of 5–10 years.[14]

In this study, 50 cases of DHF had negative ΔHct value which confirmed the convalescence in DHF. This data is irrelevant with the natural course of DHF which stated that there should be deterioration in severity due to plasma leakage.[1] It is likely due to early fluid intervention that would have changed the natural course of the illness. It also reported in the previous study that in some cases the plasma leakage does not achieve a high degree hemoconcentration even if the patient is in shock.[15]

It also can be said that the hemoconcentration which is an indicator of plasma leakage did not occur in the first and second Hct of serial Hct examination. It is probably due to the lack of this study since we only collected the first and second Hct from serial Hct examination, of which the patient underwent this examination when he/she admitted to the hospital, not earlier when the patient got the symptoms for the first time. Therefore, the same study should be in primary health care facilities where the patients check their conditions for the first time they get the symptoms. Another limitation of this study includes a lack of clinical data such as bleeding, ascites, pleural effusion, and hepatomegaly that may potentially influence the predictors of plasma leakage.

The median ΔHct value in DHF III-diagnosed group was −3. This negative ΔHct value indicated a decrease in Hct confirming convalescence in DHF. While in DHF IV-diagnosed group, which were more severe cases, the median ΔHct value was 4. This positive ΔHct value indicated hemoconcentration which is an indicator of plasma leakage in DHF if the value ≥20%. In this study, however, we found no significant correlation between positive ΔHct value (hemoconcentration) and DHF severity. This result is incompatible with the previous study that reported that hemoconcentration correlate with DHF severity.[16] The results probably due to the small sample size since we only found 14 cases with hemoconcentration from the total of 70 DHF cases in one year. The previous study showed that Bandung city was one of the hyperendemic

cities in West Java with fluctuated cases number especially in the year 2009, 2012, and 2013.[18] Our study result originated from DHF cases distributed in 2015, which is most likely to be the reason of small sample size. This notion provides evidence of compliance in DHF reporting system. Other than that, the increased capacity of health workers in detecting dengue symptoms and the availability of treatment in the primary health facilities would probably decrease the number of dengue hemorrhagic fever fatality rate. Besides, Dr. Hasan Sadikin General Hospital is a teaching hospital; thus, the clinician established the working diagnosis of the patient step by step and recorded in the medical record at the time the patient discharged from the hospital. Probably hemoconcentration had not been occurring when the clinician established the working diagnosis. The limitation of this study was since we used the variable of working diagnosis instead of initial diagnosis (at the time of admission). Besides, the grading of DHF severity has been noted to have limitations regarding its complexity and applicability, particularly in patients with severe symptoms.[12,17]

The time between first to second Hct examinations in each subject was different and had many variations from 3–24 hours. We noted that in Dr. Hasan Sadikin General Hospital, patients with DHF I and II had clinical signs that were not specific to DHF; thus, the patients were being less monitored and not adequately treated based on WHO guideline.[4] Meanwhile, patients with DHF III and IV had clinical signs that were specific to DHF; thus, the patients monitored and treated based on WHO guideline.

Considering the importance of close monitoring of patients with DHF, the difference in two serial hematocrit level measurements just after admission has no significant association with the disease severity; thus, it cannot be used to predict the severity of DHF. Therefore, serologic confirmation provides crucial consideration in the management for DHF patients.

Conclusion

Hematocrit difference (first and second) from serial Hct examination just after admission has no significant association with the disease severity.

Conflict of Interest

There was no conflict of interests declared.

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Global Medical and Health Communication

Online submission: http://ejournal.unisba.ac.id/index.php/gmhc
DOI: https://doi.org/10.29313/gmhc.v6i3.3337

GMHC. 2018;6(3):188–92
pISSN 2301-9123 | eISSN 2460-5441

RESEARCH ARTICLE

Fecal Calprotectin in Preterm Infants Sepsis with and without Necrotizing Enterocolitis Symptoms

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Abstract

Necrotizing enterocolitis (NEC) is one of the severe gastrointestinal disorder that predominantly affects preterm infants with high morbidity and mortality. The initial clinical manifestations of NEC are non-specific and indistinguishable from sepsis which making delay in diagnosis. Delayed diagnosis might require surgery and even cause death. Calprotectin is a calcium-binding protein, abundantly present in cytosol fraction of neutrophils, also found in feces, and has been found to increase significantly in gastrointestinal inflammation. This study purpose to compare fecal calprotectin in sepsis preterm infants with symptoms of NEC to sepsis preterm infants without symptoms of NEC. The study was a comparative cross-sectional analytic study performed at the Neonatology ward of Dr. Hasan Sadikin General Hospital Bandung, from October 2013 to January 2014 on 40 sepsis preterm infants aged <28 days. Fecal calprotectin was analyzed using enzyme-linked immunoassay (ELISA) kit. Mann-Whitney U test was used to compare the difference of fecal calprotectin concentration in both groups. There were 20 sepsis preterm infants with symptoms of NEC compared to 20 sepsis infants without abdominal symptoms. The concentration of fecal calprotectin was significantly higher in preterm sepsis infants with symptoms of NEC (790.67 μg/g) than preterm sepsis infants without symptoms of NEC (247.93 μg/g, p=0.019). The increasing of fecal calprotectin might provide relevant clinical information to pediatricians for early warning signs of NEC in preterm sepsis infants. In conclusion, fecal calprotectin in preterm sepsis infants with symptoms of NEC is higher compared to those without abdominal symptoms.

Key words: Fecal calprotectin, NEC, necrotizing enterocolitis, neonatal sepsis

Calprotectin Feses pada Bayi Kurang Bulan Sepsis dengan dan tanpa Gejala Enterokolitis Nekrotikans

Abstrak

Enterokolitis nekrotikans (EKN) merupakan salah satu gangguan gastrointestinal yang serius terutama pada bayi kurang bulan dengan angka kesakitan dan kematian yang tinggi. Gejala klinis awal EKN yang tidak spesifik dan sulit dibedakan dengan sepsis menyebabkan keterlambatan diagnosis. Keterlambatan diagnosis dapat menyebabkan diperlukan tindakan pembedahan bahkan kematian. *Calprotectin* merupakan protein yang berikatan dengan kalsium banyak terdapat dalam sitosol neutrofil, dapat ditemukan dalam feses, dan diketahui meningkat signifikan pada keadaan inflamasi gastrointestinal. Penelitian ini bertujuan membandingkan kadar *calprotectin* feses pada bayi kurang bulan (BKB) sepsis dengan BKB sepsis tanpa gejala EKN. Penelitian ini merupakan penelitian observasional analitik dengan rancangan kasus kontrol yang dilakukan di ruang rawat Neonatologi RSUP Dr. Hasan Sadikin Bandung dari Oktober 2013 sampai Januari 2014 terhadap 40 BKB sepsis berusia <28 hari. Kadar *calprotectin* feses dianalisis menggunakan kit *enzim-linked immunoassay* (ELISA). Analisis data menggunakan *Mann-Whitney U test* untuk membandingkan kadar *calprotectin* feses antara kedua kelompok. Terdapat 20 BKB sepsis dengan gejala EKN yang dibanding dengan 20 BKB sepsis tanpa gejala EKN. Konsentrasi *calprotectin* feses pada kelompok BKB sepsis dengan gejala EKN lebih tinggi (790,67 μg/g) secara bermakna dibanding dengan kelompok BKB sepsis tanpa EKN (247,93 μg/g, p=0,019). Peningkatan kadar *calprotectin* pada feses dapat memberikan informasi klinis bagi dokter sebagai tanda awal EKN pada BKB sepsis. Simpulan, kadar *calprotectin* feses pada BKB sepsis dengan gejala EKN lebih tinggi dibanding dengan BKB sepsis tanpa gejala EKN.

Kata kunci: *Calprotectin* feses, EKN, enterokolitis nekrotikans, sepsis neonatorum

Received: 21 January 2018; Revised: 16 December 2018; Accepted: 18 December 2018; Published: 31 December 2018

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Introduction

Necrotizing enterocolitis (NEC) is one of the most common and devastating diseases in neonates, typically manifests with feeding intolerance, abdominal distention, and bloody stools. It predominantly affects preterm infants with the incidence of about 7% among very low birth weight (VLBW) infants with high mortality (20–30%).[1] The incidence of NEC continues to rise because recent advanced in neonatal medicine have resulted in the survival of preterm infants. Early clinical manifestations of NEC are non-specific and difficult to distinguish from other gastrointestinal disorders and neonatal sepsis which can present themselves which similar clinical features to "classical" NEC such as abdominal symptoms.[2] Diagnosis further hampered by limited diagnostic accuracy of laboratory tests and currently use imaging modalities.[3] The histopathology of NEC characterized by defects in the intestinal epithelial barrier and gut wall inflammation, while neutrophils are essential in this process.[4]

Calprotectin is calcium and zinc-binding protein found predominantly in neutrophils and macrophages that constitutes about 30–60% of soluble cytosol proteins in neutrophils.[5] Significantly increased level of fecal calprotectin (f-calprotectin) seen in a small group of infants with proven NEC.[2] However, the usefulness of this marker remains controversial in the neonatal period due to high levels in this age range.[6] The previous study showed that f-calprotectin increased in proven NEC, but not useful in early NEC.[2,7,8] This study aimed to compare the f-calprotectin level in sepsis preterm infants with symptoms of NEC to sepsis preterm infants without symptoms of NEC.

Methods

The study was a comparative cross-sectional analytic study in the Neonatology ward of Dr. Hasan Sadikin General Hospital Bandung, West Java, from October 2013 to January 2014. Preterm infants <37 weeks aged <28 days with sepsis included in this study.

Symptoms of NEC define as abdominal symptoms such as abdominal distension of more than 2 cm, the gastric residue of more than 30% of feeding, and occasion of blood in stools. Preterm sepsis infant with symptoms of NEC was enrolled consecutively and compared to those preterm sepsis infants without symptoms of NEC. Infants with severe congenital gastrointestinal malformation and those without defecation in 5 days after enrollment excluded. Sepsis diagnosed based on fetal inflammatory response syndrome (FIRS). Demography, clinical and laboratory data recorded in all patients. Fecal occult blood (FOW) and radiology imaging were done to confirm the diagnosis and determine the staging of NEC. Laboratory test currently in used as classic systemic inflammatory markers in the early suspect NEC are white blood cell (WBC), platelet counts, and C-reactive protein (CRP), were measured from blood sample upon suspicion of NEC. Radiology imaging was done in all infants with symptoms of NEC to confirm the diagnosis and determine the staging of NEC. All suspected NEC infants treated with broad-spectrum parenteral antibiotic including anaerobic coverage and gastric decompression for 5–14 days depending on clinical improvement.

Stool samples were collected from the diapers and frozen at −80°C until analyzing. The stool samples collected just after the time of abdominal symptoms appeared or for those who could not defecate at the time whenever possible, maximum five days after the antibiotic given. F-calprotectin levels were measured using immunodiagnostic kit enzyme-linked immunoassay (ELISA) for calprotectin in stool according to manufacturer's instructions. F-calprotectin concentration provided in mg per kilogram stool. Statistical analysis performed with SPSS version 17.0 for Windows. All data presented as median and range. Kolmogorov-Smirnov test was used to find out normality distribution. Mann-Whitney U test was used to compare between groups with $p<0.05$ was considered to be statistically significant.

This study approved by the Health Research Ethics Committee of the Faculty of Medicine of the Universitas Padjadjaran Bandung by ethical approval letter number: 369/UN6.C2.1.2/KEPK/PN/2013. The aim, risk, and possible benefits of the study ere explained to the parents, and informed consent obtained from each.

Results

Forty sepsis preterm infants were enrolled and all infants produced stool within five days of initial assessment with an average day of 1.25 days (range 0–4 days) after enrollment. Twenty sepsis preterm infants with abdominal symptoms of NEC, six infants developed NEC stage 2 (proven by pneumatosis intestinal on X-ray) and 14

Table 1 Characteristics of Sepsis Infants with NEC Symptoms and without NEC Symptoms

Characteristics	Sepsis Infants (n=20)	
	With NEC Symptoms	Without NEC Symptoms
Age at sampling time (days)		
Median	13.5	12.5
Range	5–29	3–25
Gender		
Male	11	10
Female	9	10
Birth weight (grams)		
Median	1,450	1,500
Range	1,100–2,100	1,100–2,200

Table 2 Laboratory Characteristics in Each Study Group

Laboratory Characteristics	Sepsis Infants (n=20)	
	With NEC Symptoms	Without Abdominal Symptoms
WBC (10^3/mm^3)		
Median	8.1	10.1
Range	2.7–44	2.6–38
Platelet (10^3/mm^3)		
Median	31	45
Range	4–295	3–249
C-reactive protein (mg/dL)		
Median	88.8	80.75
Range	15.4–226	15–398
Fecal occult blood		
Positive	7	3
Negative	13	17

defined as NEC stage I (suspected NEC) at final diagnosis, and there was no stage 3 of NEC. There were 11 males and nine females in symptoms of NEC group with median birth weight were less than 1,500 gram. The characteristics of the subject presented in Table 1.

The laboratory test for classic systemic inflammatory markers in the early suspected NEC is WBC, platelet counts and CRP. White blood cells were normal in both groups, platelet was more decreased in infants with symptoms of NEC infants, and C-reactive protein (CRP) were higher in symptoms of NEC infants compared to without symptoms of NEC infants. Fecal occult blood was negative in 7/20 infants with symptoms of NEC and was positive in 3/20 sepsis infants without symptoms of NEC (Table 2).

Age and gestational age were a possible confounding factor that has an association with f-calprotectin concentration. No significant difference observed in postnatal age and gestational age between both groups (p>0.05) as

Table 3 Factors Associated with Fecal Calprotectin Concentration in Both Groups

Variables	Sepsis Infants (n=20)		p Value
	With NEC Symptoms	Without NEC Symptoms	
Postnatal age (days)			0,635*
Median	12	12	
Range	5–27	2–25	
Gestational age (weeks)			0,143*
Median	33	34	
Range	29–35	31–36	

*Mann-Whitney U test

Table 4 Fecal Calprotectin Level in Sepsis Infants with and without NEC Symptoms

F-calprotectin (mg/kgBW)	Sepsis Infants (n=20)		p Value(95% CI Differences)
	With NEC Symptoms	Without Abdominal Symptoms	
Median	456.85	188.1	0.019*
Range	36.1–3212	38.60–724.9	(165.044–920.436)

*Mann-Whitney U test

presented in Table 3.

Median concentration of f-calprotectin in infants with symptoms of NEC were significantly higher than those in the reference (p=0.019, 95% CI 165.044–920.436) as shown in Table 4.

Discussion

Early and reliable diagnosis of NEC is crucial to provide adequate treatment. Clinicians usually rely on clinical signs and symptoms to diagnose NEC while laboratory test such as platelet, CRP, WBC, and imaging technique is used to confirm the diagnosis but not specific in the early stage of the disease. Moreover, sepsis infants can present themselves which similar clinical pictures to that of "classic" symptoms of NEC such as abdominal symptoms.[2,3]

This study found a significant elevation of f-calprotectin in a stool sample of sepsis infants with abdominal symptoms of NEC compared to sepsis infants without abdominal symptoms (p=0.019, 95% CI 165.044–920.436). This result was different with the previous study by Selimoglu et al.[8] that found f-calprotectin higher in suspect NEC infants without sepsis compared to healthy newborn but could not find a statistical difference, due to high numbers of newborns with an early stage of the disease. Reisinger et al.[7] found that calprotectin level in neonates with NEC was significantly higher compared with infants with another diagnosis (sensitivity 81%, specificity 79%). Another study showed that f-calprotectin level was higher among VLBW non-sepsis infants with NEC like symptoms.[9,10]

It was different from the previous study, in this study we found a significant elevation of f-calprotectin due to the different population in inclusion criteria since we used a sepsis population infant with systemic inflammation. Studies showed that serum calprotectin was increased significantly in sepsis infants but could not be found in stool if the mucosal lining was intact.[5] Our results were suggesting that intestinal inflammation with epithelial cell disruption has occurred in sepsis infants with abdominal symptoms, so neutrophils have migrated into the intestinal lumen and resulting from an increasing level of calprotectin in the stool. Early treatment should be started immediately in sepsis infants with abdominal symptoms to prevent worse outcomes.

We found six infants with abdominal symptoms of NEC developed stage 2 NEC at final diagnosis with a median f-calprotectin concentration higher than in suspected NEC. It could be another probable reason why f-calprotectin in this study was significantly higher than the previous study.

Calprotectin present in the cytoplasm of neutrophil granulocytes constitutes about 60% of soluble cytosol proteins.[5] It has a regulatory function in the inflammatory process as well as antimicrobial activity. In intestinal inflammation, increasing transepithelial migrations of neutrophils reflect the increasing level of calprotectin in the stool. Its measurement in the stool is now recognized as a reliable marker for detection of organic intestinal disease and is used to differentiate inflammatory bowel disease with irritable bowel syndrome.[11,12] Moussa et al.[13] found that fecal calprotectin increased significantly in neonates with feeding intolerance.

A few studies before have been performed to investigate the usefulness of f-calprotectin in preterm infants in the early stage of NEC.[7,10] Studies showed that there was a dynamic change of f-calprotectin in VLBW infants during the first week of life and no correlation between f-calprotectin with maternal and infants factors.[9,14] In this study we also found no statistical difference of postnatal and gestational age in both group (p>0.05).

We observed a wide range of off-calprotectin in all infants (36.1–3,212 mg/kgBW vs 38.6–724.9 mg/kgBW). This result may be due to other factors that influence the expression of calprotectin in the stool, such as mucosal permeability, the establishment of gut flora,

mode of feeding, and genetic factors, or may reflect true inter-individual and intra-individual variability in calprotectin excretion as has been reported.[6,9,14]

We found a high level of CRP and decreased level of platelets in suspect NEC and reference sepsis infant as a parameter of classic systemic inflammation, but there was no significant correlation between f-calprotectin and CRP in sepsis reference and sepsis suspected NEC infants. This result suggests that systemic inflammation does not affect fecal calprotectin in the absence of abdominal symptoms.

There were limitations of this study, first, since the calprotectin excretion in the stool is influenced by bacterial as a role of calprotectin in gut inflammation, the establishment of gut flora must also consider. Second, we did not measure f-calprotectin concentration in healthy preterm infants as a control for baseline concentration of f-calprotectin. Further cohort study with a large number of NEC should be done to clarify the role off-calprotectin to predict who will develop NEC in sepsis infants with abdominal symptoms. The increasing of f-calprotectin might provide a useful early warning sign of NEC in sepsis preterm infants with abdominal symptoms.

Conclusion

Fecal calprotectin in preterm sepsis infants with symptoms of NEC is higher compared to those without symptoms NEC.

Conflict of Interest

The authors declare no conflict of interests.

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Global Medical and Health Communication

Online submission: http://ejournal.unisba.ac.id/index.php/gmhc
DOI: https://doi.org/10.29313/gmhc.v6i3.3427

GMHC. 2018;6(3):193–201
pISSN 2301-9123 | eISSN 2460-5441

RESEARCH ARTICLE

The Effectiveness of Ultraviolet, Ozonization and Reverse Osmosis as Disinfection Method in Drinking Water Refill Stations

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Abstract

The number of drinking water refill stations (DWRS) was increased rapidly because high of mid-low urban community need to get affordable drinking water. Water treatment methods in DWRS are varying even many DWRS uses more than one disinfection method to increase the effectiveness. The quality of many DWRS productions was reported unstandardized, however not yet the study to evaluate the effects of the water treatment method used. This study aimed to compare the effectiveness of various water treatment methods in DWRS to identify which method is the most effective. The study used a cross-sectional approach conducted in 3 groups of water treatment methods, namely ultraviolet, ultraviolet + ozonization, and a combination of ultraviolet + ozonization + reverse osmosis with each group consisted of 40 DWRS. The survey was conducted in July–September 2017 in Bandung municipality by structured interview. Examination of microbiological parameters of raw and processed drinking water samples using membrane filter method. Water samples from raw water and drinking water from treatment process were taken from each DWRS to be tested for the microbiological parameter by using the membrane filter method. Comparison of the effectiveness was analyzed using the Wilcoxon rank sum test and assessment of log removal reduction. The result showed that there was significantly different in the effectiveness of coliform removal between the three groups. The improvement for controlling and training particularly for the procedure and maintenance of water treatment equipment to the owners/workers in DWRS is urgently needed as the concern of related authority. In conclusion, the water treatment method using ultraviolet is the most effective disinfection method compared to the combination with other methods. The usage of more that one method of water treatment at the same time relate to the lower percentage of the effectiveness compares to the usage of only one method.

Key words: Drinking water, ozonization, reverse osmosis, ultraviolet, water refill stations

Efektivitas Ultraviolet, Ozonisasi, dan *Reverse Osmosis* sebagai Metode Desinfeksi Depot Air Minum Isi Ulang

Abstrak

Perkembangan depot air minum isi ulang (DAM) melaju dengan pesat karena masyarakat menengah ke bawah perkotaan membutuhkan air minum dengan harga yang terjangkau. Metode pengolahan air baku menjadi air minum di DAM bervariasi bahkan tidak jarang digunakan lebih dari satu metode desinfeksi untuk meningkatkan efektivitasnya. Kualitas produksi DAM banyak yang dilaporkan tidak sesuai dengan standar, namun belum terdapat penelitian yang mengevaluasi pengaruh metode pengolahan air yang digunakan. Penelitian ini bertujuan membandingkan efektivitas berbagai metode pengolahan air di DAM sehingga dapat diketahui metode apa yang paling efektif. Penelitian ini menggunakan pendekatan *cross-sectional* yang dilakukan pada 3 kelompok metode pengolahan air, yaitu ultraviolet, ultraviolet + ozonisasi, dan kombinasi ultraviolet + ozonisasi + *reverse osmosis* dengan tiap-tiap kelompok terdiri atas 40 DAM. Survei dilakukan pada Juli–September 2017 di Kota Bandung dengan melakukan wawancara terstruktur. Sampel air baku dan air minum hasil olahan diambil dari setiap DAM untuk diperiksa parameter mikrobiologinya menggunakan metode filter membran. Perbandingan efektivitas dianalisis menggunakan *Wilcoxon rank sum test* dan penilaian *log removal reduction*. Hasil penelitian menunjukkan bahwa terdapat perbedaan efektivitas yang signifikan pada ketiga kelompok terutama efektivitas terhadap *coliform*. Perlu upaya pengawasan dan pelatihan khususnya mengenai teknis pemakaian dan pemeliharaan alat pada pemilik/pekerja DAM yang harus menjadi perhatian pemerintah dan pihak terkait. Simpulan, metode pengolahan air menggunakan ultraviolet merupakan metode desinfeksi yang paling efektif dibanding dengan kombinasi metode lain. Pemakaian lebih dari satu metode desinfeksi pada saat yang bersamaan menyebabkan persentase efektivitas menjadi lebih rendah dibanding dengan yang menggunakan hanya satu jenis metode desinfeksi.

Kata kunci: Air minum, depot air minum, ozonisasi, *reverse osmosis*, ultraviolet

Received: 19 January 2018; Revised: 8 December 2018; Accepted: 13 December 2018; Published: 31 December 2018

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Introduction

Water is very important for human life as a basic and fundamental human need to support all of the daily activities to get survive. The importance of water in daily life should balance between appropriate quality and quantity. On the other hand, the availability of water sources such as groundwater and spring becoming restricted due to the increase of anthropogenic water contamination from improper treatment of industries and domestic waste. The local water company in Indonesia (*perusahaan daerah air minum* or PDAM) as the main supplier of clean water in the urban area is not capable to provide the whole community because of the limitation of raw water availability.[1] Consequently, bottled water and drinking water refill stations (DWRS) had been more popular and increasing during the last decades to provide the community's need for drinking water supply.

Bottled water was produced for the first time in Indonesia during 1972 and during the progress of development the price of bottled water had been increasing significantly. The community started to find alternatives to provide their drinking water need. This condition had created the business of DWRS which offer an affordable price, particularly for mid-low income community. The drinking water refill stations are the small business that treat raw water into drinking water using refill container and started to be more popular during the economic crisis in 1998 as the alternative of cheaper drinking water supply compare to bottled water. Since 1999, DWRS were rapidly increasing in all over Indonesia particularly in the urban area. However, some studies from many cities had reported the quality of DWRS production were not always appropriate according to the guideline.[2–8]

West Java is the most populous province in Indonesia and Bandung as the capital city is also reported an increasing number of DWRS as the result of rapid urbanization. However, the result of annual inspection from the Bandung Health Office showed that in 2015 about 22.22% of DWRS production still contaminated by coliform/*E. coli*, and the result of contamination was even increasing to be 55.22% in 2016.[9]

Some factors that might influence the quality of drinking water from DWRS production are hygiene sanitation in the stations, the quality of raw water and the choice of water treatment method. During the process of water treatment from raw water into drinking water, the quality of the filtration unit and disinfection method are very essential to affect the result of drinking water production.[9] However, no previous study had evaluated the comparison of effectiveness from many water treatment methods that popular to be used in Indonesia. Filtration process intends to separate the suspended particles and also to colloidal contaminants like microorganism in the water, while disinfection aims to exterminate the pathogens. Some methods that usually employ in DWRS are ultraviolet (UV), ozonization using O_3 and reverse osmosis (RO) or the combination of these methods.[10]

Nowadays, RO as the ultrafiltration process is known as the most effective water treatment method. This process can eliminate 90–99% of the contaminants in water. Wimalawansa[11] reported that RO can decrease more than 95% of the potential toxic contaminants in water. This technology is widely used not only in big industries including bottled water but also more popular to be used as household water treatment. The osmotic pressure combine with other technology formulates this ultrafiltration becoming like the best filtration method to produce drinking water. However, besides the expensive of operational cost the other limitation of this process is the time of filtration. Since the diameter of the membrane was extremely small therefore the volume of water production is very small and need longer time, subsequently, additional power was needed to give more pressure so that the time to flow over the filter is faster.[12]

The ultrafiltration method or combination of ultrafiltration + ozonization are the most popular method that is used in DWRS since the operational cost is cheaper compare to RO. Until now, no study analyze the comparison of these water treatment method effectiveness in DWRS. This study aimed to identify which method as the most effective to eliminate the microbiological contaminants as the evidence to increase the quality control of DWRS production.

Methods

It was a quantitative study with a cross-sectional design, the analysis unit was registered DWRS in the Bandung Health Office. This study intended to compare the effectiveness of water treatment methods in DWRS to change the raw water into drinking water. The water treatment methods were determined into three (3) groups that were

ultraviolet, the combination of ultraviolet + ozonization, and the combination of ultraviolet + ozonization + RO.

Minimal samples to compare the effectiveness in each group was calculated with alpha 0.05 and power of 0.80 resulted in the number of 34 DWRS as minimum samples in each group. Data from the Bandung Health Office reported that there were 659 registered DWRS listed in Bandung city during 2017. In this study, a total of 120 DWRS or 40 DWRS in each group were involved with random sampling method using the name list of registered DWRS in Bandung city. Randomization number was obtained from www.randomization.com.

The survey was conducted in July–September 2017 with two types of data collection that were water quality test and structured questionnaire-based interview. In every selected DWRS, a set of the structured questionnaire consisted of demographical and characteristics data was interviewed to the owner of DWRS. Water samples from raw water and drinking water that produced in DWRS were collected using 200 mL sterile plastic container to examine the microbiological parameters (colony count of coliform and *E. coli* according to the guideline). Water samples were kept in the cool box before transported to the Microbiology and Parasitology Laboratory in Faculty of Medicine Universitas Padjadjaran.

Water samples were examined using the membrane filter method. This method grows the colony of coliform species by filtering 100 mL of water samples through a nitrocellulose membrane filter (diameter 47 mm with 0.45 µm micropores from Merck KGaA, Darmstadt, Germany). The membrane was incubated using Chromocult® Coliform Agar (Merck KGaA, Darmstadt, Germany) for 24–48 hours in 37±1°C. The growth of coliform colony was identified in red colonies and *E. coli* in purple colonies. These colonies were determined using colony forming unit or CFU/100 mL.

The comparison of effectiveness from 3 groups was analyzed using the Wilcoxon rank sum test with 95% confident of the interval. Moreover, the effectiveness also compares based on log removal reduction (LRR), a method recommended by the World Health Organization (WHO) to evaluate the capability of the disinfection method to eliminate pathogens in water. This analysis used a logarithmic number of log10, the drinking water categorize safe if the effectiveness reaches minimal 4 log10 or in other words the minimal of decimal elimination is 4. The calculation of LRR based on an assumption of decrease number of pathogens. 1 log10 means 90%, 2 log10 means 99%, 3 log10 means 99.9%, 4 log10 means 99.99%, and 5 log10 means 99.999%. The water treatment method is good if the effectiveness reaches 4 log10 and 5 log10 and recommend as safe drinking water to be consumed.

This study started after obtaining ethics approval from the Health Research Ethics Committee of the Faculty of Medicine, Universitas Padjadjaran Bandung with a letter-number: 239/ UN6.10/ PN/2017.

Results

Total of 120 DWRS was selected and consisted of 40 DWRS with ultraviolet, 40 DWRS with ultraviolet + ozonization, and 40 with the

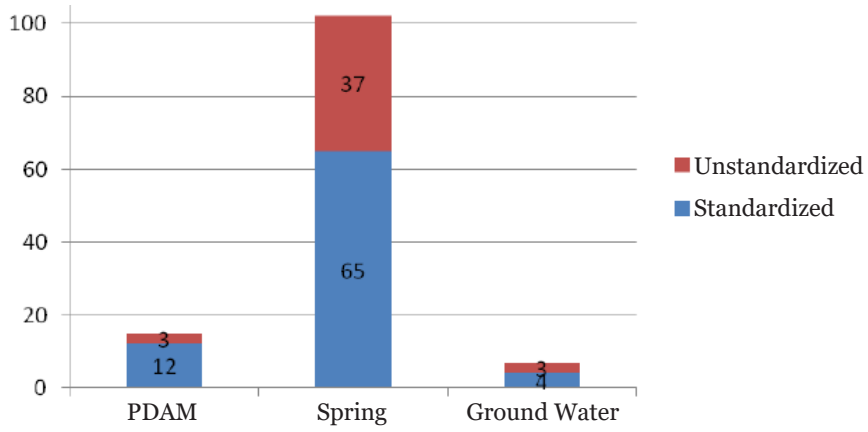

Figure 1 The Quality of Raw Water

Table 1 Characteristics of Drinking Water Refill Stations

Variables	Ultraviolet n=40 (%)	Ultraviolet + Ozonization n=40 (%)	Combination of Ultraviolet + Ozonization + RO n=40 (%)
Number of worker (person)			
1	20 (50)	14 (35)	6 (15)
2–3	17 (42.5)	23 (57)	27 (67.5)
>3	3 (7.5)	3 (8)	7 (17.5)
Duration of business (years)			
<5	21 (51)	12 (30)	19 (47.5)
5–10	13 (33)	21 (51)	16 (40)
>10	6 (16)	7 (19)	5 (12.5)
Raw water sources			
Tap water (PDAM)	2 (5)	1 (2.5)	8 (2)
Spring	36 (90)	37 (92.5)	29 (72.5)
Ground water	2 (5)	2 (5)	3 (7.5)
Legal document			
Business license			
Available	10 (25)	12 (30)	15 (37.5)
No available	30 (75)	28 (70)	25 (62.5)
Certificate of proper hygiene and sanitation			
Available	7 (17.5)	5 (12.5)	12 (30)
No available	33 (82.5)	35 (87.5)	28 (70)
Standard operating procedure			
Available	4 (10)	2 (5)	5 (12.5)
No available	36 (90)	38 (95)	35 (87.5)
Production protocols			
Available	11 (27.5)	8 (20)	15 (37.5)
No available	29 (72.5)	32 (80)	25 (62.5)
Laboratory test			
Last 3 months			
Yes	10 (25)	10 (25)	2 (5)
No	30 (75)	30 (75)	38 (95)
Last 6 months			
Yes	6 (15)	14 (35)	8 (20)
No	34 (85)	26 (65)	32 (80)
Source of information			
The owner of DWRS			
Yes	24 (60)	29 (72.5)	30 (75)
No	16 (40)	11 (27.5)	10 (25)
Training/workshop			
Yes	14 (35)	21 (52.5)	22 (55)
No	26 (65)	19 (47.5)	18 (45)
Employee coaching			
Yes	19 (47.5)	25 (62.5)	25 (62.5)
No	21 (52.5)	15 (37.5)	15 (37.5)

combination of ultraviolet + ozonization + RO. In particular, for the group of combination between ultraviolet, ozonization, and RO, only one DWRS that use only RO, 20 DWRS used ultraviolet + RO, 9 DWRS used ozonization + RO, and 10 DWRS used the combination of ultraviolet + ozonization + RO. The characteristic of these groups as described in Table 1.

Raw water source from spring water was dominantly used by DWRS, commonly it comes from foothill area near Bandung city, either in the north part or east part of Bandung area. The

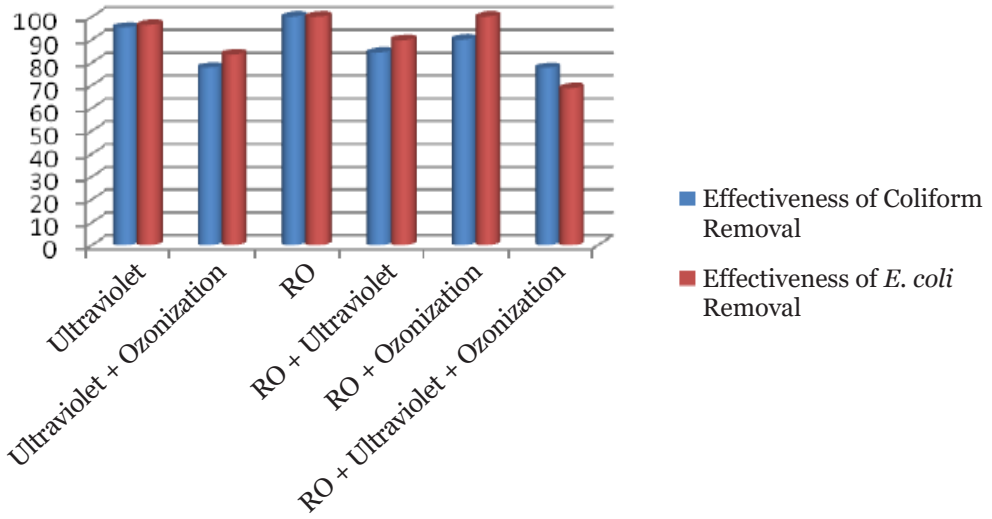

Figure 2 Percentage of Effectiveness in Various Disinfection Methods in Refill Drinking Water Stations

quality of raw water according to clean water guideline (based on Ministry of Health Republic of Indonesia Regulation number 416 the year 1990)[13] explained in Figure 1 according to the microbiological parameter.

The standard of Ministry of Health Republic of Indonesia and WHO guideline regulate that coliform and *E. coli* should be 0 (nil) in drinking water. WHO also divide the risk of having water-borne diseases due to consuming contaminated drinking water based on the number of fecal pathogens (*E. coli*). The classifications are low risk (1–9 *E. coli*/100 mL), moderate risk (10–99 *E. coli*/100 mL), and high risk (≥100 *E. coli*/100 mL).[14] The quality of microbiology parameter from 3 groups of water treatment methods in DWRS was illustrated in Table 2. Only 50% of ultraviolet + ozonization method produced drinking water according to the standard, and 10% of the water sample from this method had moderate and high risk. Ultraviolet as a single water treatment method showed better drinking production compare to combination with other methods.

The effectiveness of disinfection methods is determined by the percentage of coliform and *E. coli* removal number by analyzing the difference of the total number between the colony in raw water and drinking water production. The comparison of various disinfection method in DWRS illustrated in Figure 2. The average effectiveness of all type of combination RO method was 88% for coliform removal and 89.6% for *E. coli* removal, however, if we analyze in details we found that the effectiveness of RO decreased if we use it in combination with other methods, but the effectiveness of RO as single method could achieve 100%. Furthermore,

Table 2 The Quality of Microbiological Parameter of Water Treatment Method in Drinking Water Refill Stations

Indicator	Ultraviolet n=40 (%)	Ultraviolet + Ozonization n=40 (%)	Combination of Ultraviolet + Ozonization + RO n=40 (%)
Standardized	29 (72.5)	20 (50)	30 (75)
Unstandardized			
No risk	7 (17.5)	10 (25)	2 (5)
Low risk	4 (10)	6 (15)	6 (15)
Moderate risk	0	3 (7.5)	2 (5)
High risk	0	1 (2.5)	0

Table 3 Comparison of Ultraviolet, Ozonization, and Reverse Osmosis Effectiveness

Disinfection Method	Effectiveness of Coliform Removal				Effectiveness of *E. coli* Removal			
	Mean (SD)	95% CI	Mean Square	p Value	Mean (SD)	95% CI	Mean Square	p Value
Ultraviolet	95.3 (15.1)	90.5–100			96.3 (16.2)	91.1–100		
Ultraviolet + ozonization	77.1 (34.2)	66.3–87.9	3,353.4	0.019	84.1 (31.7)	74.1–94.1	1,651.9	0.120
RO + ultraviolet + ozonization	85.3 (31.9)	74.9–95.6			87.1 (31.9)	76.8–97.3		

comparison of effectiveness in 3 disinfection methods was analyzed by Wilcoxon rank sum, the result showed that significantly different found for coliform removal with p=0.019 as described in Table 3.

The comparison of effectiveness in various water treatment method can be analyzed using log removal with logarithmic scale since the number of colony removal were enormous. Comparison of between the three groups of disinfection methods explained in Table 4. Ultraviolet and a combination of RO + ultraviolet + ozonation have the highest percentage for LRR 5 log10 both in the removal of coliform or *E. coli*. The combination of ultraviolet + ozonization showed only 50% achieved 5 log10 to reduce coliform and only 75% to reduce *E. coli*. These result showed that the effectiveness of the combination in more than one water treatment method might be not efficient.

Discussion

Refill drinking water is popularly consumed by the lower middle-class community. Moreover, the phenomenon of rapid urbanization also influences the increase in DWRS in urban areas. Based on the characteristics in Table 1, the type of DWRS business is a small business with one or two workers. The compliance of the owners to gain the legal aspect such as business license and certificate of proper hygiene and sanitation was found low, moreover, only a few DWRS having the standard operating procedure with a clear flow of work for every step and maintenance process.

Even though the government had issued Ministry of Health Republic of Indonesia

Table 4 Comparison of Log Removal in Various Disinfection Method

Log Removal	Ultraviolet n=40 (%)	Ultraviolet + Ozonization n=40 (%)	RO + Ultraviolet + Ozonization n=40 (%)
Coliform			
0 log10	2 (5)	12 (30)	7 (17.5)
1 log10	5 (12.5)	6 (15)	1 (2.5)
2 log10	3 (7.5)	1 (2.5)	1 (2.5)
3 log10	0 (0)	1 (2.5)	0 (0)
4 log10	0 (0)	0 (0)	0 (0)
5 log10	30 (75)	20 (50)	31 (77.5)
E. coli			
0 log10	1 (2.5)	8 (20)	5 (12.5)
1 log10	3 (7.5)	2 (5)	3 (7.5)
2 log10	0 (0)	0 (0)	0 (0)
3 log10	0 (0)	0 (0)	0 (0)
4 log10	0 (0)	0 (0)	0 (0)
5 log10	36 (90)	30 (75)	32 (80)

Regulation number 43 the year 2014 about hygiene and sanitation in DWRS,[15] nevertheless the implementation had not been accomplished by all the owners of DWRS. The result showed that only 25% of DWRS routinely test the quality of drinking water production in the laboratory during the last 3 months, moreover only 5% of DWRS using the combination of RO tested the drinking water quality and only 15–35% of DWRS tested during the last 6 months. This fact provides evidence that in addition to low compliance with regulations, there is a mistaken belief among owners of the effectiveness of the disinfection method which may be caused by a lack of dissemination of information from the authorities regarding regulations to DWRS owners and workers. Lack of quality control from the government and no local regulation toward the law enforcement might also influence the quality of drinking water from DWRS production that consumes by the community.[16]

The selection of raw water is an important factor to be concerned by the DWRS owners, the better the raw water quality will produce a better quality of the drinking water. The examination from 3 types of raw water that usually use in DWRS showed that spring water had the highest percentage of unstandardized quality. Commonly, the community perception about the spring water quality was better compared to other water sources so that this type of raw water is customarily used by the community. All type of raw water that was used by DWRS should be in line with the health standard with the certificate of good quality from the standardized laboratory. Moreover, the transportation process should be noticed as a crucial phase that might influence the quality of raw water. Most of DWRS owners still not aware of this, even they do not know the name of the company that supplies raw water to their DWRS.

In practicality, many of DWRS owners combine more than one method to get more effectiveness. Figure 2 illustrated comparison of the various combination of disinfection method. DWRS that only use RO reach 100% effectiveness to remove coliform and *E. coli*, while DWRS that only use ultraviolet method reach 95%. Combination of more than one method in the same time resulting in lower effectiveness between 77–89%, even combination of 3 methods (RO + ultraviolet + ozonisasi) only reaches 77% of coliform removal and 68% of *E. coli* removal. This result contradictory with previous study that revealed combination of ultraviolet + RO effective to treat raw water from river or irrigation water to be drinking water with good quality with relatively low price of operational cost.[18] Low effectiveness of combination methods might be due to inaccuracy in technical step during installation or lack of the owners awareness to check and carry out routine maintenance since they already use more than one disinfection methods.

Many DWRS choose to combine ultraviolet and ozonization method to increase the effectiveness. The quality of ultraviolet is affected by the speed of water flow, capacity or volume of ultraviolet emission and the intensity of the lamp. The limitation of ultraviolet is ineffectiveness to remove a certain type of spores and viruses, furthermore, it needs a source of energy and no residue of ultraviolet might initiate recontamination to the water.[17,18] Disinfection process with ozonization takes place in the ozone mixing tank. Data in Table 2 illustrated that percentage of unstandardized drinking water quality using a combination of ultraviolet and ozonization was the highest, even 10% of water samples having the high number of *E. coli* and categorize of medium and high risk to transmit water-borne diseases.

The process of reverse osmosis uses high pressure to make raw water can pass the specific semipermeable membrane with extremely small pores (0.0001 microns). This small pores produce only H_2O could pass the membrane, while bacteria, viruses, and chemicals are filtered and removed through a certain channel as discharge out pipe.[21] Until now, reverse osmosis is known as the best disinfection method as ultrafiltration to produce drinking water with the highest purity, however this method need high energy to generate high pressure to push raw water passes through the semipermeable membrane, consequently this process also generate high volume of fluid waste with high concentrations of toxin and need high operational cost. The result in Table 2 showed that the percentage of standardizing drinking water between ultraviolet and combination of ultraviolet + ozonization + RO was similar. This result was not in line with the previous study that proved RO as the most effective method compare to others and ultraviolet still leave 31% of the pathogen in drinking water production.[19]

Table 3 revealed that effectiveness from various disinfection method significantly varies

in coliform removal. In Table 4, LRR of ultraviolet + ozonization that inline with standard or reach 5 log10 was only 50%. The previous study found many DWRS with other methods besides RO still produce coliform contaminated drinking water.[19,21] However, in this study, the usage of a single water treatment method is better compared to the combination of two or three methods. The percentage of DWRS that only used ultraviolet method reached higher 5 log10 LRR compare to other combination methods. This might be the effect of less maintenance process when two or more methods used in the same time since the owners of DWRS belief that more than one method should increase the effectiveness and this belief make them neglect the maintenance of each method.

The effort to increase quality control by the government in an integrated system in collaboration with the owners and consumers should be intensified. Training and supervision particularly regarding controlling and maintenance of disinfection unit should be scheduled regularly and accessible by all DWRS. Drinking water is essential for human life so any risk, although small should be prevented include ineffectiveness of disinfection methods.

Further development of trainings for owners and workers in DWRS is urgently needed in term of technical coaching about water treatment to prevent the production of unstandardize drinking water. The government should develop integrated supervision system to protect the consumers.

Conclusions

The water treatment method using ultraviolet is the most effective disinfection method compared to the combination with other methods. The operation of more than one method of water treatment in the same time in drinking water refill stations might decrease effectiveness of water treatment method.

Conflict of Interest

The authors declare no conflict of interests.

Acknowledgement

This study was part of Lecturer Competency Research Grant entitled “Prediction Model of Refill Drinking Water Station Production and Development of Integrated Surveillance System.” The researchers would like to thank the Directorate of Research, Community Services and Innovation, Universitas Padjadjaran, Bandung for the funding support from Internal Research Grant year 2017–2018. We also appreciate the support from all primary health care sanitarians, staffs of Bandung City Health Office and all staffs in the laboratory for the hard work of this study.

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Global Medical and Health Communication

Online submission: http://ejournal.unisba.ac.id/index.php/gmhc
DOI: https://doi.org/10.29313/gmhc.v6i3.2724

GMHC. 2018;6(3):202–8
pISSN 2301-9123 | eISSN 2460-5441

RESEARCH ARTICLE

Knowledge, Attitude, and Behavior of Indonesian Breastmilk Donors via the Internet

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Abstract

Breastmilk donors are increasingly widespread and can be done by mothers easily and rapidly through the internet. This study aims to analyze the correlation of knowledge and attitudes of breastmilk donors to the behavior of breastmilk donors via the internet in Indonesia. The study used a cross-sectional analytic design and using a total sampling technique by sending research instruments in the form of the Google form was conducted in January–April 2017. The study respondents were breastmilk donors who posted information on their breastmilk to be shared through Facebook Human Milk 4 Human Babies Indonesia in Jakarta, Depok, Indramayu, Bandung, and others were totaling 41 respondents. Statistical analysis using the Spearman test with confidence level was α=0.05. The study results showed that the correlation to knowledge and behavior of breastmilk donors had p value=0.080, while the correlation on attitude and behavior of breastmilk donors had p value=0.715. In conclusion, there was no correlation between the attitude of breastmilk donors and the practice of breastmilk sharing via the internet.

Key words: Attitude, behavior, breastmilk sharing, internet, knowledge

Pengetahuan, Sikap, dan Perilaku Pendonor ASI via Internet di Indonesia

Abstrak

Donor air susu ibu (ASI) semakin marak dan dapat dilakukan para ibu dengan mudah dan pesat melalui internet. Penelitian ini bertujuan mengetahui hubungan pengetahuan dan sikap pendonor ASI dengan perilaku donor ASI via internet di Indonesia. Penelitian ini merupakan penelitian desain analitik *cross-sectional* dan menggunakan teknik *total sampling* dengan mengirimkan instrumen penelitian dalam bentuk *Google form* yang dilakukan pada bulan Januari–April 2017. Responden penelitian adalah pendonor ASI yang mem-*posting* informasi ASI-nya untuk dibagikan melalui *Facebook Human Milk 4 Human Babies Indonesia* di Jakarta, Depok, Indramayu, Bandung, dan lain-lain yang berjumlah 41 responden. Analisis statistik menggunakan Uji Spearman dengan tingkat kepercayaan α=0,05. Hasil penelitian menunjukkan bahwa hubungan pengetahuan dengan perilaku pendonor ASI memiliki nilai p=0,080, sedangkan hubungan sikap dengan perilaku pendonor ASI memiliki nilai p=0,715. Simpulan, tidak terdapat hubungan pengetahuan dan sikap pendonor ASI dengan perilaku pendonor ASI via internet di Indonesia.

Kata kunci: Berbagi ASI, internet, pengetahuan, perilaku, sikap

Received: 21 July 2017; Revised: 27 August 2018; Accepted: 1 November 2018; Published: 31 December 2018

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Introduction

The number of breastmilk donors has multiplied, along with the development of internet technology, provided a choice of breastmilk donors accessible via the internet.[1] The demand for breastmilk donors in Indonesia increased by 3–5 fold from 2007–2012. It is increasingly effortless to do via the internet.[2] Currently, the number of mothers who are aggressively pumping breastmilk makes the production of breastmilk exceeds the needs of infants till this surplus offered as something "untested" and "unregulated" through the internet. About 60% of breastmilk donors via the internet do not show any screening for HIV, hepatitis, or syphilis in their posts, although it may be communicated privately to recipients using offline communication.[3] The behavior of breastmilk donors via the internet is not yet understood enhance by the absence of human milk banks in Indonesia that are capable of screening both breastmilk, and their donors make this topic interesting.[4] The Regulation of the Minister of Health Republic of Indonesia on Breastmilk Donors has not ratified till now.[5,6] However, knowledge of breastmilk as the best food for babies makes all mothers seek breastmilk. Breastmilk donors motivated to help others based on the trust between donors and recipients.[7] This knowledge and attitude shared without prior knowledge and consideration of the risks that can occur. Breastmilk donors are not without risk, for example, breastmilk can transmit various bacteria and viruses.[8] Dinger et al.[9] found breastmilk to transmit streptococcus infection. A study found that breastmilk found from internet donor as much as 74% of samples contained gram-negative bacterial colonization and 21% contained DNA-positive cytomegalovirus.[10] Transmission of the HIV via lactation described by WHO reached 5–20% and without antiretroviral risk doubled to 40%.[11] Case reports on "HIV transmission from surrogate breastfeeding" occurred in Spain.[12]

Based on these problems and risks, this study aims to determine the relationship between breastmilk donor health behaviors and factors influence the behavior, knowledge, and attitude.

Methods

The study used the cross-sectional analytic design with the sample of all breastmilk donors who posted donor information via Facebook community titled Human Milk 4 Human Babies (HM4HB) Indonesia from January to April 2017. The approval to use information in the HM4HB Indonesia has been granted by the community administrator. The sample uses the total sampling technique by sending research instruments in the form of Google form to respondents.

Before data collection, the designated respondents provided with information about this research and asked for their willingness to join by emphasizing ethical issues that include consent, anonymity, and confidentiality. The subject was breastmilk donors that upload information to donate on the HM4HB Indonesia, willing to become the respondent and answer the research questions on Google forms. During the data collection processed, there were 41 people responded from Jakarta, Depok, Indramayu, Bandung, and others. The results were analyzed statistically using Spearman analysis with confidence level α=0.05.

This study had been reviewed and approved by the Health Research Ethics Committee, Faculty of Medicine, Universitas Airlangga Surabaya by ethical clearance letter number: 011/EC/KEPK/FKUA/2017.

Results

The subjects of this study were 41 respondents. The characteristics of the respondents were the majority aged 26–35 years old (34 of 41), have a college education (39 of 41), working (25 of 41), and reside in Jakarta (14 of 41) (Table 1).

The results of respondents' knowledge on breastmilk and breastmilk donors showed in Table 2. Most respondents (34 of 41) have been able to correctly answer that a person with HIV disease and hepatitis B should not be a breastmilk donor.

Table 3 showed the results of filling out questionnaires about respondents' attitudes on breastmilk and breastmilk donors.

The behavior of the respondents in breastmilk donor via internet showed in Table 4. The most common reason for recipient breastmilk infants was that their breastmilk is not enough (23 of 41), followed by unspecified medical reasons for infants, infants incompatible with infant formula, and preterm infants younger than one month.

The results of this study indicate no relationship between knowledge of breastmilk donors and the behavior of breastmilk donors (p=0.080) and the correlation coefficient of 0.276. However, results show that respondents who are well behaved are

Table 1 Characteristics of the Respondents

Characteristics	n=41
Maternal age (years)	
20–25	4
26–30	14
31–35	20
36–45	3
Working status	
Not working	16
Working	25
Province (city)	
Jakarta	14
West Java (Depok, Indramayu, Bandung)	9
East Java (Surabaya, Malang, Sidoarjo)	7
Banten (Tangerang, South Tangerang)	5
North Sumatera (Medan, Nias)	2
South Borneo (Balangan, Banjarmasin)	2
East Bornea (Balikpapan)	1
Yogyakarta (Bantul)	1
Maternal education	
High School graduate	2
College graduate	39

Table 3 Attitude of the Respondents on Breastmilk and Breastmilk Donor

Question of Attitude	Answer	n=41
Felling on participate in the activities of breastmilk donors.	Common	1
	Happy	6
	Very happy	34
There is a baby who cannot get the opportunity to get breastmilk.	Very not sad	5
	Not sad	1
	Ordinary	3
	Sad	10
	Very sad	22
The donation of breastmilk should include the results of consultation or health laboratory results of donors.	Strongly disagree	1
	Disagree	1
	Less agree	12
	Agree	15
	Strongly agree	12
The role of health workers is very much needed.	Very not needed	1
	Not needed	1
	Less needed	4
	Needed	11
	Very much needed	24
Mother who decided to give formula milk compared to seek breastmilk donor?	Agree	3
	Less agree	15
	Disagree	11
	Very disagree	12
Breastmilk cannot transmit disease, virus or bacteria.	Strongly agree	3
	Agree	11
	Less agree	10
	Disagree	9
	Very disagree	8
Sick mothers donate breastmilk.	Less agree	7
	Disagree	8
	Strongly disagree	26

also well-informed (Table 5).

Attitudes of respondents also showed the same thing; there was no correlation of breastmilk donors attitude and breastmilk donors behavior (p=0.715) with the correlation coefficient of 0.059 (Table 6).

Discussion

The knowledge of mothers on breastmilk and breastmilk donors by Reeder et al.[13] suggested that the delivery of information on breastmilk by health workers is effective. The education on lactation management learning such as breastmilk nutrition, how to prevent and overcome common problems breastmilk in working mothers because they are also expected

Table 2 Knowledge of the Respondents on Breastmilk and Breastmilk Donor

Question of Knowledge	Answer	
	True	False
Can a person with cytomegalovirus disease be breastmilk donor?	24	17
Can a person with HIV disease be breastmilk donor?	34	7
Can a person with hepatitis B disease be breastmilk donor?	33	8
Can a person who has had a blood transfusion in the past year be breastmilk donor?	13	28
Benefits of the pasteurization process of flash heating on breastmilk	6	35

Table 4 Behavior of the Respondents in Breastmilk Donor

Behavior	Answer	
	Yes	No
Motivation to participate in breastmilk donor		
Compassion if surplus milk had to discard	33	8
Help others	38	3
Driven by religious orders	5	36
Habitual	1	40
Reason for recipient breastmilk infants		
Unspecified medical reasons for infants	15	26
Preterm infants younger than one month	6	35
Infants are incompatible with infant formula	15	26
Problem of breastfeeding	13	28
Not enough	23	18
Unspesific medical reasons for mothers	9	32
Working or travelling mother	7	34
Donated dairy breastmilk were		
<1 month postpartum	10	31
In 1–6 month postpartum	29	12
>6 months postpartum	16	25
>12–24 month postpartum	1	40
Involved health workers in donating breastmilk at	6	35
Do you consume alcohol?	0	41
Are you a smoker?	0	41
Do you use narcotics?	0	41
Have you ever had blood transfusions in the past year before donating breastmilk?	0	41
Has been screened for HIV	17	24
Has been screened for hepatitis B	24	17
Has been screened for hepatitis C	20	21
Has been screened for syphilis	12	29
Has been screened for cytomegalovirus	10	31

to breastfeed exclusively. This material does not convey the method of breastmilk to women with sexually transmitted infections (STIs) and breastmilk donor procedures and screening of potential breastmilk donors as well as the highly basic flash-heating pasteurization technique as an effort to prevent transmission of the disease.[14] Predetermined rules on exclusive breastmilk more widely disseminated, while further regulations on breastmilk were still under discussion.[6]

Donors feel pleased to help those in need.[15] Meanwhile, studies in the Kupang area showed that most mothers stated that they still preferred formula milk and did not accept the concept of breastmilk donors because of the risk of infection.[16,17]

Assessment of results regarding respondent behavior is inversely proportional to the

Table 5 Correlations of Knowledge and the Behavior of Breastmilk Donors

Knowledge	Behavior			p Value	α=0.05
	Good (n=12)	Fair (n=7)	Poor (n=22)		
Good	9	4	9	0.08	0.276
Fair	1	1	5		
Poor	2	2	8		

Table 6 Correlations on Attitude and the Behavior of Breastmilk Donors

Knowledge	Behavior			p Value	α=0.05
	Good (n=12)	Fair (n=7)	Poor (n=22)		
Good	3	1	5	0.715	0.059
Fair	9	5	15		
Poor	0	1	2		

assessment of knowledge. Both donors and recipients share breastmilk online are reportedly less likely to involve healthcare workers in making breastmilk decisions.[7,18] The American Academy of Pediatrics (AAP) provides rules on breastmilk and using breastmilk not from breastmilk sharing sources, but doctors may not discuss this topic and families are reluctant to inquire about these clues.[19] Health workers should be more vigilant because every baby has the possibility of receiving breastmilk from another mother and should be asked about the baby's intake. It is essential to know the risks involved in breastmilk activities, but also to educate the public on how best to use breastmilk.[1]

Research on breastmilk donors via the internet in the United States depicts more mothers donating their breastmilk at infants aged between 3–5 months (55%), then infants aged 6–8 months and infants >8 months with numbers of 26% of total 52%.[3] The Indonesian Pediatric Association states mothers who wish to donate breastmilk have to go through several screening stages. The first screening points are to have babies less than six months old.[20] The World Health Organization (WHO) explains the energy content in breastmilk of 6 months babies were less than breastmilk on less than six months babies. After the age of 6 months breastmilk no longer able to meet energy needs.[21]

Mannel et al.[22] revealed recipients' decisions to seek donor milk are common conditions that often coincide with or exacerbate lactation insufficiency. In addition to having a positive side, breastmilk donors also have a negative side, such as the risk of transmission of infection as well as being demotivators for recipients mother to breastfeed. A breastmilk donor is only a temporary solution and not a long-term solution, and the mother should also get counseling from a breastmilk counselor in the long run.[23]

Human Milk Banking Assessment of North America (HMBANA) receive breastmilk with criteria for infants aged <1 year.[24] In contrast to policies by Royal Prince Alfred (RPA) Hospital, Human Milk Donor (HDM) Program in Sydney, New South Wales, Australia. The hospital can only accept breastmilk donors from mothers whose children are treated in the NICU room or receive frozen donor breastmilk from mothers whose babies die in NICU RPA hospital by performing previous screening procedures. The mother who delivered and her baby died at another hospital, her breastmilk was not accepted, and they only received screening tests.[25] Preterm infants were noted to have high levels of nitrogen, total proteins, immune proteins, total lipids, total energy, some vitamins, and minerals. The content of electrolytes, protein and also breastmilk nutrition from mothers who gave birth to premature babies is higher than breastmilk from mothers who gave birth to mature babies. The composition of breastmilk from premature baby mothers will turn into similar breastmilk from mature baby mothers within 3–4 weeks. However, by that time the baby is also old enough so that the mother's milk is suitable for her/his needs.[26]

The information from donors stated that 40% had infectious diseases and only three donors stated specific illnesses, 2% of respondents described having screened hepatitis B and C, 1% for syphilis and 0% for HIV.[19] All types of diseases can be transmitted through breastmilk and infect infants who receive it. Mothers infected with HIV infection justified the reasons for not breastmilk permanently, mothers with cytomegalovirus who gave birth to premature babies are also unable to breastfeed. Although there is no reason not to breastfeed with infants for hepatitis B mothers, the acquisition of hepatitis B virus in small amounts in breastmilk remains a concern about the role of breastmilk in the transmission.[21]

The result of research related to the knowledge and attitude of the donor of breastmilk to the behavior of breastmilk donor has not yet compared with other research.

Researches by Palmquist and Doehler,[18] Keim

et al.,[19] and Reyes-Foster et al.[27] illustrate that breastmilk activities appear in the general public of the United States, especially in college-educated women. The better a person's knowledge, the better it is in applying the material he has acquired. Science is a vehicle for the underlying of a person behaving scientifically while its level depends on the science or primary education of the person,[17] whereas attitude is not yet an action or activity, but it is predisposing to action behavior. Attitude is a readiness to react to objects in specific environments as an appreciation of the object. Attitudes are also not automatically manifested in action (overt behavior).

Several studies have shown behavior adopted after passing through knowledge stages, attitude, and practice.[13,17] However, other studies also prove that the process is not always similar to the above phases, even in everyday practice it might go the other way around. That is, a person has behaved positively, although his knowledge and attitude are harmful or otherwise. Knowledge does not affect one hundred percent of the behavior in donating breastmilk.[15] External factors include environmental health professionals who have not educated on breastmilk donors, health facilities such as breastmilk banks not yet available in Indonesia.[16] Breastmilk donor units that can screen breastmilk donors and affordable health services by the broader community, as well as government regulation have not explicitly stated about breastmilk donors.[25]

Similarly, to make the attitude to be a real action required supporting factors or a condition that allows among other facilities or support factors (support) from other parties.[16] In the practice of breastmilk donors is one of them from the recipient itself that does not include a request about the current breastmilk safety conditions on the processed of pumped, stored, prevention of transmission of infection, as well as the content of the donor's milk itself. Breastmilk recipient does not know the risks of the breastmilk donor.[24] The above shows how the complex factors behind the formation of human attitudes and behaviors.

Recipients from 90% breastfeed donors do not explicitly require the health and safety of breastmilk practices from the donor. Health behaviors and disease screening affecting breastmilk security have not been a prominent topic in the donor posts.[19] Many discussions have already developed on the topic of possible risk and benefit events from breastmilk donors.[18] One approach to the security of internet-based breastmilk expressed by Walker and Armstrong[28] is four pillars supporting the security of sharing breastmilk that is informed consent, donor screening, safe handling, and home pasteurization.

The Prevention of Mother to Child Transmission Program (PMTCT) established since the issuance of Regulation of the Minister of Health of the Republic of Indonesia Number 51 of 2013 can at least be one of the solutions in screening for infectious diseases against HIV during integrated antenatal care.[29] If it is correctly applied, at least the health status of each mother can be known, and the risk of transmission of infection anticipated.

Conclusions

This study shows that there is no correlation between knowledge and attitude of breastmilk donors to their behavior.

Conflict of Interest

The authors declare no conflict of interests.

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Global Medical and Health Communication

Online submission: http://ejournal.unisba.ac.id/index.php/gmhc
DOI: https://doi.org/10.29313/gmhc.v6i3.3108

GMHC. 2018;6(3):209–19
pISSN 2301-9123 | eISSN 2460-5441

RESEARCH ARTICLE

The Peer Counseling Model in Adolescents Reproductive Health for Senior High School Students

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Abstract

Premarital sexual behavior in adolescents is at risk of sexual intercourse. One of the teenagers' factors in premarital sexual intercourse is a lack of knowledge about adolescent reproductive health. One method that can be given to increase knowledge about reproductive health is peer counseling. Peer counseling service improvement can be supported by the availability of modules or teaching materials to be used as a guide for peer counselors. The purpose of this study was to analyze the substance of the peer counseling module, analyze the perspective of the prospective module user on the development of peer counseling modules, and develop a model of the peer counseling module. The design of this study was the concurrent mixed method was divided into two stages, namely in-depth interviews with the experts and interviews and surveying with module users. The data was collected from the senior high school students in Cimahi and Bandung, West Java from March to July 2017. The result of this study showed that the substances developed in this module were the adolescents' reproductive health, adolescents' preparation in family planning, and adolescents' ethics. Based on results of the analysis using the Rasch model, in the module user's perspective, there is a need for the development of peer counseling modules. Evaluation of the module's model from participants showed that they mostly agreed with the module's model and the substances that were developed.

Key words: Adolescent, peer counseling, reproductive health

Model Modul Konseling Sebaya dalam Kesehatan Reproduksi Remaja pada Siswa Sekolah Menengah Atas

Abstrak

Perilaku seksual pranikah pada remaja berisiko melakukan hubungan seksual. Salah satu faktor remaja melakukan hubungan seksual pranikah adalah pengetahuan tentang kesehatan reproduksi remaja yang kurang. Salah satu metode yang dapat diberikan untuk meningkatkan pengetahuan tentang kesehatan reproduksi adalah konseling sebaya. Peningkatan pelayanan konseling sebaya dapat ditunjang oleh ketersediaan modul atau bahan ajar sebagai panduan bagi konselor sebaya. Tujuan penelitian ini adalah menganalisis substansi modul konseling sebaya, menganalisis perspektif pengguna modul tentang pengembangan modul konseling sebaya, dan mengembangkan model modul konseling sebaya. Desain penelitian yang digunakan *concurrent mixed methods* yang dibagi menjadi dua tahap, yaitu wawancara mendalam dengan para pakar serta wawancara dan survei dengan pengguna modul. Data dikumpulkan dari siswa SMA di Cimahi dan Bandung, Jawa Barat mulai Maret hingga Juli 2017. Hasil penelitian menunjukkan bahwa substansi yang perlu dikembangkan dalam modul konseling sebaya adalah kesehatan reproduksi remaja, persiapan remaja dalam perencanaan keluarga, dan etika remaja. Berdasar atas hasil analisis menggunakan model Rasch, perspektif dari para pengguna modul adalah perlu pengembangan modul konseling sebaya. Evaluasi model modul dari partisipan menunjukkan bahwa kebanyakan mereka setuju dengan model modul dan substansi modul yang dikembangkan.

Kata kunci: Kesehatan reproduksi, konseling sebaya, remaja

Received: 17 October 2017; Revised: 11 December 2018; Accepted: 13 December 2018; Published: 31 December 2018

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Introduction

The success of a nation's development can see from the quality of its human resources. Society is one of the essential components to realizing health development goals.[1–4]

Teenagers are a part of the community that has an essential role in constructing a nation. The young generation very needs information about reproductive health and family planning for a prosperous and quality life in the future. Lack of information about reproductive health in adolescents will trigger some problems such as premarital sex, HIV/AIDS and drug abuse, one of which will result in teenage pregnancy.[5]

Results of the Basic Health Research (*Riset Kesehatan Dasar*/Riskesdas) 2013 showed that there are still teenage pregnancies aged <15 years (0.02%), especially in rural areas. The percentage of adolescents who have drunk alcoholic drinks is 40% done by young men and 5% by young women. The United Nations International Children's Emergency Fund (UNICEF) estimates that 18% of HIV/AIDS cases occur in the younger age group.[6–8]

To ensure maternal and child welfare more comprehensive efforts are needed to reduce the unwanted pregnancy rate of reproductive age couples, unfulfilled needs, teenage pregnancy (15–19 years old), the unsustainable contraception (high discontinuation rates) and to increase participation in the use of contraception.[9]

The phenomenon of young marriage among teenagers is still a serious problem and requires special attention. Consequences of young marriage include lack of family harmony and lack of household sustainability so that it can lead to divorce.[10]

The information about family planning should be socialized during adolescence. The National Population and Family Planning Board (*Badan Kependudukan dan Keluarga Berencana Nasional*/BKKBN) revived the Family Planning (*Keluarga Berencana*/KB) program in adolescents to prepare for married life and increase marriage age. Adolescents are a target of BKKBN programmed at socializing family planning because of the high rate of early marriage. One determining factor of early marriage is premarital sex. Many teenagers have sexual intercourse without knowledge about the unsafe impact of having sexual intercourse.[11]

West Java is the province with a high young population in Indonesia. According to BKKBN, 100 out of 1,000 young women aged 15–19 years in West Java were married (10%), and 80 of them had unwed pregnancy.[12]

To respond to the complexity of adolescent problems, BKKBN created the Generation Planning (*Generasi Berencana*/GenRe) program to improve adolescent reproductive health, including family planning preparation. This program has existed for a long time, but it is reintroduced using a new term that is easier to memorize and suitable for teenagers. The GenRe program uses two approaches, both from the adolescents' view and the family's view. The approach to the view of the youth is carried out through the development of the Information and Counseling Center for Youth and College Students (*Pusat Informasi dan Konseling Remaja/Mahasiswa* [PIK R/M]). The approach from the family's or parent's view is carried out through the development of the Adolescents' Family Development (*Bina Keluarga Remaja*/BKR) group.[13,14]

The PIK R/M program prepares and plans adolescents for family life, and this program is performed from, by, and for adolescents to provide information and counseling services about adolescent reproductive health. This program has been carried out and developed in all provinces in Indonesia with a total of 8,673 PIK R/M.[15,16]

Based on the results of a preliminary study conducted by Harini et al.[16] about peer counselors are in the PIK R/M program, 50% of adolescents admitted that they still lacked confidence when their friend (counselee) consulted about his/her problem and 30% of said they had not received information and knowledge about adolescent reproductive health. Furthermore, 20% said that the media used in counseling such as leaflets, flipcharts, and modules are still limited.

Factors that can influence peer counselors in providing adolescent reproductive health (*kesehatan reproduktif remaja*/KRR) counseling based on results of Permatasari's[17] study are sources of information such as television, mass media, schools and training, the counselor's knowledge of the counseling process and the motivation/support of BKKBN officers and coaches. The last two were the most dominant factors.[18]

The purpose of this study was to analyze the required substances of peer counseling modules in adolescent reproductive health based on in-depth interview results with experts, investigating

the user's perspective about the module, and develop a model of the peer counseling module.

Methods

This study uses mixed methods, which are the combination of two stages of qualitative and quantitative research. The design of this study was the concurrent mixed method by combining quantitative and qualitative data at one time using concurrent embedded strategies.[19]

There were two stages in this research, first is the collection of data with qualitative methods to analyze the required substance in peer counseling modules then we improve with research instruments by consulting with experts. Secondly, data is collected using qualitative and quantitative methods. The qualitative method at the second stage is to analyze the development needs and substance of peer counseling modules from module users. The quantitative method in this second stage was to conduct a survey to peer counselors for analyzing the extent and depth of development needs and the substance in the module.

The data was collected from the students of Public Senior High School (*Sekolah Menengah Atas Negeri*/SMA Negeri) 1 Cimahi, SMA Negeri 2 Cimahi, SMA Negeri 5 Cimahi, Public Vocational High School (*Sekolah Menengah Kejuruan Negeri*/SMK Negeri) 3 Cimahi, and SMK Negeri 6 Bandung, West Java province from March to July 2017.

The consideration of ethical issues of this research was approved by the Health Research Ethics Committee of Faculty of Medicine of Universitas Padjadjaran Bandung the letter of ethics approval number: 107/UN6.C1.3.2/KEPK/PN/2017.

Results

The explanation of the qualitative substance of adolescent reproductive health in the peer counseling modules was adjusting to the characteristics of adolescent development. The material in the module must be attractive, challenging, and able to open up adolescents' insight, not informatively material.

The substance of this module includes several sub-modules, one of which is the adolescent reproductive health. Based on the transcript from informant 1, the adolescent reproductive health of the youth counseling information center (*pusat informasi dan konseling remaja*/PIK R) curriculum was already complete, which includes three concepts of adolescent reproductive health (sexuality, HIV/AIDS, and drug abuse). The reproductive health material that necessary to be given to high school adolescents did not explain in detail. Not all schools are willing to accept the reproductive health curricula because it was already in biology subjects. Responding to this problem, stakeholders, especially the BKKBN of West Java was integrating reproductive health material into the subject of biology.

In line with the stages of adolescent development, the necessary reproductive health material provided was the process of menstruation, wet dream, sexual disorders, etc. That revealed by informant 2:

"....menstruation process, wet dream, masturbation, that's all. It was not too detailed until the introduction of contraception." (T102R12)

The PIK R curriculum book has widely discussed adolescent reproductive health, but it did not include life skills. Life skills that were needed by high school students were revealed by informant 1:

"Actually in life skills, there is a discussion about how to knit. But it was more about mental endurance skills, ability to say no if, for example, her boyfriend asked her to have intercourse she must dare to say no." (T101R7)

The substance of reproductive health which necessary to be included in the peer counseling module was the reproductive period of adolescents; organs and reproductive functions; maintenance of reproductive organs; adolescent puberty and changes that occur; risks of sexual behavior; drugs abuse; and skills of adolescent life.

In the substance of adolescent preparation in family planning, information regarding the general description of marital life can providing to peer counselors, but it was must be provided when the teenager is about to get married because if it was provided too early by peer counselors, the information becomes not up to date.

The preparation of family planning is provided according to the needs of adolescents because not

all adolescents will marry right after graduating from high school. Information about the process of menstruation, conception, pregnancy, and childbirth must be knowing by young women. Substances of adolescent preparation in family planning include ideal marriage age, marriage preparation, family planning, concepts, pregnancy and childbirth, and prevention of complications. It was according to the statement from informant 3:

"Yeah... it is necessary to provide all of that knowledge before they turn 17. It can be provided in stages 2...at the beginning of the 2nd grade." (TI03R12)

The language used in the substance of family planning preparation should be adjusted to the characteristics of adolescents, as expressed by informant 9:

"....but the use of the language should be thought to make sure that they will not have misinterpretations about it." (T109R16)

Teenagers, in general, will set their mindset for the future after graduating from school, whether they will continue to college, work, or get married. The material about the ideal marriage age should be provided then adolescents can live in a healthy and prosperous household both physically and psychologically.

The substance of adolescent ethics must be able to teach ethical knowledge during their growth and development. It must be able to educate adolescents about healthy behavior. It can provide by parents at home and teachers at school.

Juvenile delinquency which occurs today is quite concerning. Teenagers are willing to experiment with new things that they have never done before. Once they try something new, it becomes a habit, and it will be difficult to remove. The development of science and technology and the influence of globalization will trigger various problems, especially among teenagers. These problems were the spread of moral issues such as narcotics and drug abuse, student brawls, pornography, rape, theft, abortion, fraud, persecution, gambling, prostitution, murder, etc. These problems have not been resolving thoroughly and fully.

The most common social problems in adolescents today are the low level of morals and ethics in their daily life, both at home, school and in the surrounding environment. Teaching ethics should begin when the child is familiar with the outside world. Good ethics will create good morals. Teenagers, in general, have been able to make decisions in determining their own lives, even though there are still contributions from parents.

The attention and support provided by the closest people to adolescents matter very much. Teenagers will have a determination to make decisions in their social life. Ethical teachings should include the basic concept of ethics, teenage ethics, and social manners.

During peer counseling, peer counselors must be able to provide information regarding reproductive health with real-life examples and adjusted to the characteristics of adolescent development. Language is constructed in a friendly way but must be inseparable from the norms, customs, and culture adopted by adolescents.

The peer counseling process divided into three phases. The first phase was building a relationship between peer counselors and adolescents. At this stage, the counselor must be able to understand the expressions of adolescents including their feelings and thoughts, explore adolescent problems, and encourage adolescents to make their own decisions. Counselors only explore the positive and negative side of each choice. Problem-solving was must base on the needs and characteristics of adolescents.

The counseling process can also be done based on the stages of greet, ask, tell, help, explain, return (GATHER). Dialogue is the most appropriate method during the peer counseling process because adolescents have creative and critical thinking potential. Characteristics of the adolescent that must be understood by peer counselors are the willingness to unite with their peers, and interest to the opposite sex.

Peer counselors have limited authority in providing counseling. Adolescent problems that are not resolved by peer counselors can be referred to a higher level, for example to the counseling teachers in school, psychologists, and health workers in public health services. The informant's expression in regarding the referral system in the peer counseling process was:

"Refer to the higher level...to the counseling

teacher, not to a peer counselor. She/he can be referred to as the professional counselor." (T105R7)

The peer counselor's skills during the counseling process were able to make peer clients feel comfortable. The counselor must able to analyze the needs of their teenage clients. Organizations in the school environment were can used as a facility for peer counselors. Reference schemes for peer counselors must be provided in detail, to facilitate peer counselors if they face a situation that they cannot handle. Peer counselors must be able to know the limits of their abilities.

In the qualitative phase II based on module users, the counselors still had some difficulties, especially in providing information regarding problems that occur. Access to obtain information about the management of adolescent problems is still limited; this is according to what is revealed by an informant during in-depth interviews:

"Sometimes I search through Google, sometimes from a friend who has the same problems. Sharing between peer counselors before we share it with our counselee...."

The practice of counseling provided by peer counselors does not have to be formal, but it can be simple and in a relaxed situation known as *curhat* (vent). Counseling is provided to help adolescents to solve their problems as expressed by an informant:

"In my opinion, it should be better to talk about it. It's better to be open to each other." (T201R2)

Problems in adolescents are very complex, and sometimes peer counselors find it difficult to access information regarding problems that occur in adolescents. Some teenage problems that often occur were free sex, drug abuse, and HIV/AIDS. Some cases that occur in schools were different from the problems of adolescents in general, as revealed by informants:

"....it was about illness, painful menstruation, and also about love." (T201R5)

During counseling, peer counselors must be able to build good relationships and listening of clients actively so that clients can trust them as friends to share their feelings (*curhat*). An informant stated that:

"....counseling is like fostering good relations, we must trust each other so they will be open to us." (T201R8)

Counselors must build a sense of trust in their clients. In the counseling process, peer counselors must record in a log book the peer clients identity containing the initial names, addresses, classes, problems, problem-solving, and follow-up/referrals. The records will report to their counseling teacher or mentor. They will analyze the resolved and unresolved problems and follow up the problems solving they have been giving.

The reproductive health substance needs to be provided and known by high school teenagers. The material includes the adolescent preparation in family planning that explained in broadly speaking and not be too detailed. The purpose of this substance is to find the ideal age of marriage, management of independent life and responsibility as expressed by this informant:

"It is necessary, for information purposes only...." (T201R6)

Usually, reproductive health information was already to provide at the junior high school in the subject of biology, but gradual repetition is required to maintain reproductive health until they reach adulthood.

The media used in providing information for high school adolescents must be adjusting to norms or culture and religion. As revealed by this informant:

"According to my mother, the media is too exposing for high school students. There are matters that must not be known by adolescents." (T202R3)

The informant revealed that the media that was provided by the government was not suitable for adolescents, for example in the pamphlet about HIV/AIDS there are procedures for using condoms before sexual intercourse. According to the informant, this is not suitable for adolescents; therefore the development of peer counseling modules must be adjusted to the needs of the module users.

Table 1 The Validity of the Instruments in Peer Counseling Modules about Adolescent Reproductive Health

Entry Number	Total Score	Total Count	Measure	Model SE	Infit		Outfit		PT-Measure		Exact Match		Item
					Mnsq	Zstd	Mnsq	Zstd	Corr.	Exp.	Obs%	Exp%	
2	74	30	1.63	0.35	0.87	−0.5	0.90	−0.4	0.79	0.35	80.0	62.2	b
4	74	30	1.63	0.35	1.28	1.3	1.23	1.1	0.33	0.35	56.7	62.2	d
3	75	30	1.50	0.35	0.74	−1.2	0.73	−1.3	0.46	0.35	70.0	62.0	c
5	79	30	1.00	0.35	1.23	1.0	1.21	1.0	0.06	0.34	56.7	62.4	e
8	79	30	1.00	0.35	0.75	−1.1	0.74	−1.2	0.37	0.34	66.7	62.4	h
9	79	30	1.00	0.35	0.70	−1.4	0.69	−1.5	0.44	0.34	73.3	62.4	i
13	83	30	0.49	0.36	1.18	0.8	1.22	0.9	−0.14	0.33	70.0	67.0	m
16	84	30	0.36	0.37	0.58	−1.8	0.56	−1.9	0.33	0.33	80.0	68.7	p
6	85	30	0.22	0.37	0.73	−1.0	0.72	−1.0	0.36	0.32	76.7	70.3	f
7	87	30	−0.05	0.37	0.97	0.0	0.97	0.0	0.48	0.32	70.0	72.7	g
14	89	30	−0.34	0.38	1.82	2.3	1.81	2.3	0.15	0.32	56.7	74.0	n
15	91	30	−0.62	0.38	0.61	−1.4	0.61	−1.4	0.37	0.32	83.3	74.2	o
12	96	30	−1.34	0.37	1.85	2.6	1.93	2.7	0.06	0.34	56.7	70.7	l
10	98	30	−1.61	0.37	0.78	−0.9	0.78	−0.8	0.57	0.34	73.3	68.5	j
11	100	30	−1.88	0.37	0.84	−0.7	0.83	−0.7	0.28	0.34	56.7	65.9	k
1	108	30	−2.98	0.38	0.99	0.0	0.99	0.0	0.55	0.31	83.3	64.5	a
Mean	86.3	30.0	**0.00**	0.37	1.00	−0.1	1.00	−0.1			69.4	66.9	
SD	9.8	0.0	1.33	0.01	0.38	1.3	0.39	1.3			9.7	4.4	

SE: standard error; Infit: an information-weighted statistic; Outfit: an unweighted statistic; Mnsq: mean-square; Zstd: z-standardized; PT-Measure: an observed point-correlation; Exp.: expected value of the point-correlation; Obs%: observed%, the percent of data points; Exp%: expected%, the percent of data points

The adolescent was needed information about family planning. These based on this informant's expression:

"It is necessary; we must know that someday we will be married. From that information, we must know that we have to be more responsible with ourselves." (T203R7)

Teenagers will face diverse life challenges, and every teenager has a life plan. Harmonious and prosperous family life is a dream of every individual. The material about family planning preparation can provide an overview of the roles and responsibilities of a person in the family lived in the future.

A person's quality of life influenced by their principles of life. The development of life principles needs support from the closest persons such as family. The risks and threats in life can overcome with a positive attitude.

The assessment of peer counselor perspectives on the development needs and substance of peer counseling modules in adolescent reproductive

Table 2 Reliability of Instrument Used in This Study

	Total Score	Count	Measure	Model Error	Infit		Outfit	
					Mnsq	Zstd	Mnsq	Zstd
Mean	86.3	30.0	0.00	0.37	1.00	−0.1	1.00	−0.1
SD	9.8	0.0	1.33	0.01	0.38	1.3	0.39	1.3
Maximum	108.0	30.0	1.63	0.38	1.85	2.6	1.93	2.7
Minimum	74.0	30.0	−2.98	0.35	0.58	−1.8	0.56	−1.9
Real RMSE=0.39		True SD=1.27		Separation=3.23		Item reliability=**0.91**		
Model RMSE=0.37		True SD=1.28		Separation=3.49		Item reliability=0.91		
SE of item mean=0.34								

Infit: an information-weighted statistic, Outfit: an unweighted statistic, Mnsq: mean-square, Zstd: z-standardized; RMSE: root mean square errors, SE: standard error

health from the survey results is strengthened by quantitative research methods, using instruments developed from the results of the stage I research (in-depth interview with the experts). Results of quantitative research obtain from providing questionnaires to 30 respondents (active peer counselors) in senior high schools in the Cimahi city and Bandung city.

Thirty respondents were included in this study, consisting of 7 male counselors and 23 female counselors. Active peer counselors were in the 11th-grade (2nd-grade in high school). We selected 11th-grade students because this class group already adapted to the school environment and peers and has not yet been scheduled to take the national examination.

Table 1 analyzes the level of reliability of the research instrument used by the researcher. The result the analysis showed that the instrument has a high level of reliability and can be accepted by respondents. Table 1 shows that all the items in the questionnaire meet the three Rasch modeling criteria so that all items in the peer counseling modules can be used in the study.

The instrument's reliability in this study was assessed based on the level of reliability. Reliable means can to be relied on and trustworthy. The reliability analysis in this study was conducted using the Rasch model by Winsteps software version 3.73. The criteria used to determine

Table 3 Person Measurement of Peer Counseling Modules about Adolescent Reproductive Health

Entry Number	Total Score	Total Count	Measure	Model SE	Infit		Outfit		PT-Measure		Exact Match		Person
					Mnsq	Zstd	Mnsq	Zstd	Corr.	Exp.	Obs%	Exp%	
3	52	16	3.08	0.53	1.33	0.9	1.28	0.8	0.32	0.55	62.5	72.5	CP
5	52	16	3.08	0.53	0.85	−0.3	0.82	−0.4	0.62	0.55	75.0	72.5	EP
10	51	16	2.81	0.52	0.43	−1.8	0.58	−1.2	0.58	0.55	93.8	72.0	JP
4	50	16	2.54	0.52	0.96	0.0	0.97	0.1	0.37	0.55	68.8	70.9	DP
2	49	16	2.28	0.51	1.36	1.0	1.33	0.9	0.72	0.54	43.8	69.7	BP
1	48	16	2.02	0.50	1.22	0.7	1.22	0.7	0.45	0.54	68.8	68.5	AP
22	48	16	2.02	0.50	0.67	−1.0	0.67	−0.9	0.58	0.54	81.3	68.5	WP
23	48	16	2.02	0.50	0.67	−1.0	0.67	−0.9	0.58	0.54	81.3	68.5	XP
8	47	16	1.77	0.50	1.51	1.4	1.45	1.3	0.77	0.54	56.3	67.0	HP
9	47	16	1.77	0.50	0.84	−0.4	0.84	−0.4	0.76	0.54	62.5	67.0	IP
14	47	16	1.77	0.50	1.62	1.7	1.61	1.6	0.32	0.54	62.5	67.0	NP
18	47	16	1.77	0.50	1.17	0.6	1.18	0.6	0.34	0.54	62.5	67.0	RL
20	47	16	1.77	0.50	0.62	−1.2	0.63	−1.1	0.47	0.54	87.5	67.0	TP
21	47	16	1.77	0.50	0.62	−1.2	0.63	−1.1	0.47	0.54	87.5	67.0	VP
16	46	16	1.52	0.50	0.62	−1.2	0.58	−1.3	0.78	0.54	75.0	65.7	PL
24	46	16	1.52	0.50	0.92	−0.1	0.93	−0.1	0.60	0.54	62.5	65.7	YP
17	45	16	1.28	0.49	0.79	−0.6	0.78	−0.6	0.75	0.54	68.8	65.2	QL
26	45	16	1.28	0.49	0.72	−0.9	0.71	−0.8	0.77	0.54	68.8	65.2	AP
27	45	16	1.28	0.49	0.91	−0.2	0.92	−0.1	0.67	0.54	68.8	65.2	BP
7	44	16	1.03	0.49	0.50	−1.9	0.47	−1.9	0.57	0.55	87.5	64.1	GP
12	44	16	1.03	0.49	1.21	0.7	1.26	0.8	0.73	0.55	62.5	64.1	LP
15	44	16	1.03	0.49	0.79	−0.6	0.81	−0.5	0.30	0.55	75.0	64.1	OP
29	44	16	1.03	0.49	0.97	0.0	0.98	0.1	0.68	0.55	62.5	64.1	DP
11	43	16	0.79	0.49	0.55	−1.6	0.53	−1.6	0.58	0.55	81.3	65.3	KL
25	43	16	0.79	0.49	1.17	0.6	1.20	0.7	0.59	0.55	68.8	65.3	ZL
28	43	16	0.79	0.49	1.17	0.6	1.20	0.7	0.59	0.55	68.8	65.3	CP
30	43	16	0.79	0.49	1.26	0.9	1.29	0.9	0.55	0.55	56.3	65.3	EP
6	42	16	0.55	0.49	2.06	2.6	2.11	2.6	0.37	0.55	56.3	65.8	FL
13	42	16	0.55	0.49	1.24	0.8	1.21	0.7	0.09	0.55	62.5	65.8	MP
19	42	16	0.55	0.49	0.98	0.1	1.00	0.1	0.30	0.55	62.5	65.8	SP
Mean	46.0	16.0	**1.54**	0.50	0.99	0.0	1.00	0.0			69.4	66.9	
SD	2.8	0.0	0.71	0.01	0.36	1.1	0.36	1.0			11.1	2.4	

SE: standard error; Infit: an information-weighted statistic; Outfit: an unweighted statistic; Mnsq: mean-square; Zstd: z-standardized; PT-Measure: an observed point-correlation; Exp.: expected value of the point-correlation; Obs%: observed%, the percent of data points; Exp%: expected%, the percent of data points

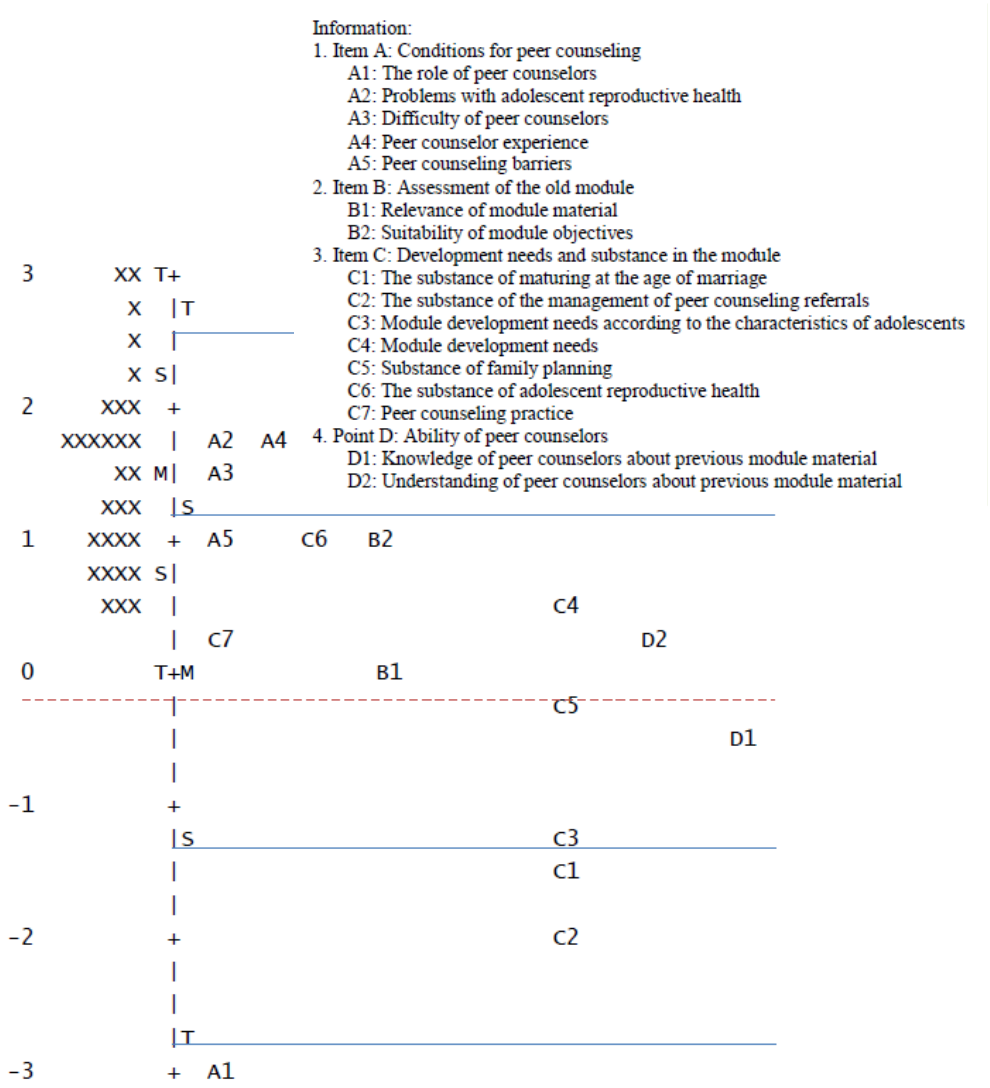

Figure Wright Map of the Needs and Substance of the Development of Peer Counseling Modules

the value of the person reliability and the item reliability are (a) weak:[20] <0.67, (b) adequate: 0.67–0.80, (c) good: 0.81–0.90, (d) very good: 0.91–0.94, and (e) special: >0.94.

Based on Table 2 it can be seen that the value of the reliability test was 0.91. Referring to the reliability criteria that included in a very good category, the instrument of the peer counseling module was sufficient and can be used for research. The grouping of items can be known from the separation value, if the greater the separation value, the better the quality of the instrument.

Table 3 assesses the needs of peer counseling modules from the respondents' answers. It can be seen that when the logical value is more than 0.00 (1.54), the respondent agrees and surely needs the development of peer counseling modules.

On the wright map above there is an X, which is the respondent who answers the research instrument, as a whole the respondents are above the 0 logical lines in the Rasch analysis model. All respondents agree and accept the statements contained in the instrument, meaning that the development needs of peer counseling modules are accepted. Points A, B, C, and D are items from the instrument, it can be seen in item C about the development needs and the substance

of the peer counseling module spread in each column, meaning that item C is the best item among other items. There were 30 respondents (100%) who agree to the items about substance in peer counseling modules consisting of the substance of adolescent reproductive health, the substance of maturing marital age, the substance of family planning, peer counseling practice, management of referrals in peer counseling, and module development needs according to the characteristics of adolescents.

The items about the previous module assessment seen in Figure are located above the 0 logical value marked letters B1 and B2. Based on the Rasch model, if there are items above the average value (0 logical) means that the items are difficult for the respondents to approve. Item B1 is an assessment of the relevance of the contents of the previous module, and B2 is an assessment of the suitability of the objectives of the previous module with the expected user of the module.

Discussion

The results of the research in stage I show that experts agree with the development of modules on the substance of adolescent reproductive health. The material on adolescent reproductive health recommended by experts is still largely similar to the curriculum issued by the BKKBN for peer counselors.

The adolescent reproductive health material is the primary priority required by high schools students according to the characteristics of adolescents, while the substance included in the peer counseling module is as the following: adolescent reproductive organs and functions, maintenance of adolescent reproductive organs, puberty in adolescence, risky sexual behavior, drug and youth life skills.

Education/information about reproductive health needs to be invested as early as possible in adolescents, in this case, BKKBN is implementing a GenRe program that can help adolescents in obtaining accurate sources of information about reproductive health through peer counseling. One of the contents of reproductive health information in the KRR module includes the substance of three basic threats (*tiga ancaman dasar*/Triad) KRR, including sexuality, HIV/AIDS, and drugs abuse.[18]

The user perspective of peer counseling modules on the need for module development in the substance of adolescent reproductive health organ can be seen from the results of the research which states that peer counselors agree with the development of modules on the substance of reproductive health. The results of the study using the Rasch modeling revealed a value of 0.54 logical in the personal measurement table. The need for the development of peer counseling modules is highly expected by module users, especially peer counselors.

The development of training and teaching material in the form of modules needs to be developed and updated according to the needs of the participants and stakeholders who provide training (trainer). The need for development is a must because it is adapted to the module users.[21]

Some experts agree with the substance of adolescent preparation of family planning in the counseling module. In adolescence (middle adolescent category), the possibility of life and the plan of life itself arises. After the graduation it varies, the general picture of family planning is provided when the teenager begins to show emotional development, one of the characteristics of emotional development is the attraction of the opposite sex that involves emotions (love, jealousy, and other emotions).[22]

Planning family life is based on an explanation of the ideal age of marriage (pendewasaan usia perkawinan/PUP). Teenagers are first provided information about the right age to get married. An explanation of the ideal age of marriage is listed in the curriculum prepared by the BKKBN.[18]

The development of other substances in this peer counseling module is related to adolescent ethics. Experts argue especially from the health department and obstetricians and gynecologists, that adolescents are faced with increasingly rapid technological developments. Adolescent behavior is much influenced by the environment and relationships both positive and negative. Improper use of technology will have an impact on adolescent behavior that is at risk. This risk behavior can be prevented by the existence of information about adolescent ethics in daily life at school and at home.

Conclusions

The substances developed in this module were the adolescents' reproductive health, adolescents' preparation in family planning, and adolescents' ethics. In the module user's perspective, there is

a need for the development of peer counseling modules. Evaluation of the module's model from participants showed that they mostly agreed with the module's model and the substances that were developed.

Conflict of Interest

The author states that there is no conflict of interest.

Acknowledgement

The author would like to thank the families who have contributed to this article.

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Global Medical and Health Communication

Online submission: http://ejournal.unisba.ac.id/index.php/gmhc
DOI: https://doi.org/10.29313/gmhc.v6i3.3748

GMHC. 2018;6(3):220–5
pISSN 2301-9123 | eISSN 2460-5441

RESEARCH ARTICLE

Perinatal *Al-Quran* Sound to Novel Object Recognition Memory and Hippocampal Cell Count

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Abstract

Al-Quran sound as auditory stimulation may influence the development of systems related to memory. This study aimed to investigate the effect of *Al-Quran* acoustic stimulation to novel object recognition (NOR) memory and amount of hippocampal formation cells at postnatal day (PND) 21 Wistar rats. This study was conducted in September 2016 to January 2017. Adult Wistar rats divided into intervention and control groups were bred at Faculty of Medicine Universitas Islam Bandung. Rat pups in the intervention group were exposed to Quranic sound from postcoital day 0 to the PND 20. Rats of PND 20 was involved in the NOR test by documenting the value of the duration of exploration of the familiar and novel object. The rats' brains were extracted and processed at Faculty of Medicine Universitas Padjadjaran for cell counting of hippocampal formation stained with hematoxylin-eosin. The results displayed a higher value of D_1 (exploration time difference) and a total number of hippocampal formation cells in the *Al-Quran* groups. These results can be related to the role of the Quranic voice in suggesting higher learning aspects, activating neurogenesis or cell survival transcription factors. However, there was no difference in discrimination index (DI) value between groups which could be indicating inadequate habituation period, interval, testing age, or stress factors. Numerous limitations from this field of research suggest that the biological role of sound stimulation is still in its early stages of development. In conclusion, exposure to perinatal *Al-Quran* sound may serve as stimulation which enhances learning, memory, neurogenesis or cell survival of hippocampal formation.

Key words: *Al-Quran*, hippocampal formation, memory, sound

Suara *Al-Quran* Perinatal pada Memori *Novel Object Recognition* dan Jumlah Sel Hipokampus

Abstrak

Suara *Al-Quran* sebagai stimulasi pendengaran diperkirakan dapat memengaruhi perkembangan sistem tubuh terkait memori. Penelitian ini bertujuan mengamati pengaruh stimulasi suara *Al-Quran* terhadap memori *novel object recognition* (NOR) dan jumlah sel formasi hipokampus pada tikus Wistar 21 hari setelah lahir (*postnatal day*/PND). Penelitian ini dilaksanakan pada September 2016 sampai Januari 2017. Tikus Wistar dewasa yang dibagi dalam kelompok perlakuan dan kontrol dibiakkan di Fakultas Kedokteran Universitas Islam Bandung. Anak tikus Wistar dipaparkan dengan suara *Al-Quran* sejak hari *postcoital* 0 sampai anak tikus lahir dan berumur 20 hari setelah lahir (PND 20). Tikus PND 20 dilibatkan dalam tes NOR dengan dokumentasi nilai durasi eksplorasi objek lama dan baru. Otak tikus diproses di Fakultas Kedokteran Universitas Padjadjaran untuk penghitungan jumlah sel formasi hipokampus dengan pewarnaan *hematoxylin-eosin*. Hasil penelitian ini menunjukkan nilai D1 (perbedaan durasi eksplorasi objek lama–baru) dan jumlah sel formasi hipokampus lebih tinggi pada kelompok perlakuan dengan *Al-Quran*. Hasil tersebut dapat terkait dengan peran suara *Al-Quran* dalam aktivasi faktor pertumbuhan atau transkripsi. Namun, tidak terdapat perbedaan bermakna pada nilai indeks diskriminasi antarkelompok yang dapat terkait dengan faktor stres atau kurangnya periode habituasi atau periode uji. Berbagai keterbatasan penelitian ini serta riset di bidang stimulasi embriologi mengindikasikan bahwa peran biologis suara *Al-Quran* masih harus diteliti lebih lanjut. Simpulan, paparan suara *Al-Quran* perinatal dapat berlaku sebagai stimulasi yang meningkatkan pembelajaran, memori, neurogenesis atau ketahanan sel formasi hipokampus.

Kata kunci: *Al-Quran*, formasi hipokampus, memori, suara

Received: 8 May 2018; Revised: 30 November 2018; Accepted: 7 December 2018; Published: 31 December 2018

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Introduction

Numerous studies indicate that environmental stimulation has influence in learning and memory through neuronal activity. Sound stimulation may affect neuronal response and amount of cells in the brain through increasing or activating elements of proliferation, growth, and survival.[1–3]

Al-Quran recitation as a form of sound has rhythmic and melodic aspects that may influence the brain through substances and patterns related to information coding, long-term potentiation, and retrieval in learning and memory. Related to auditory stimulation, *Al-Quran* sound may be capable of increasing the amount or activation of proteins such as calcium-binding protein (CBP), cyclic adenosine monophosphate (cAMP) response element binding protein (CREB) and its downstream transcription factor brain-derived neurotrophic factor (BDNF), each of which has stimulatory roles in of cell proliferation, synaptogenesis, and neuronal growth and survival.[4–7]

This study attempts to observe the effect of *Al-Quran* as a sound stimulation to novel object recognition (NOR) memory as one type of declarative memory, and the amount of cells in hippocampal formation as an important structure for memory functions at postnatal day (PND) 21 Wistar rats.

Methods

This study was conducted in September 2016 to January 2017. Eighteen (18) adult female Wistar rats the age of 8–9 weeks, with 200–250 grams of weight were randomized and divided into control and *Al-Quran* group. Each group was placed in separate rooms, conditioned into mating and breeding, with intervention group exposed to *Al-Quran* auditory stimulation (*Al-Fatihah*, *Al-Baqarah*, and *Ali Imran* respectively) in mp3 format for 3.5 hours once daily from post-coital day 0 to post-natal day (PND) 20 of the rat pups. The rat pups from both groups were then involved in NOR test for the NOR values to be documented. Breeding and NOR test commenced at the Faculty of Medicine Universitas Islam Bandung (Figure 1).

In NOR test, duration of exploring novel object (T_N) and duration of exploring familiar object (T_F) documented. The first value for NOR is D_1, which is a difference of exploration time studying the novel object substracted by the duration exploring everyday object ($T_N - T_F$). The second value is the discrimination index (DI), which calculated by $(T_N - T_F)/(T_N + T_F)$. The duration measured in seconds. Positive and negative values indicate a stronger preference for the novel object and the familiar object, respectively.[7]

The rats terminated, the brains extracted and put into formalin 10%-phosphate buffered saline (PBS) pH 7.4 and glutaraldehyde 2.5% overnight then dehydrated in increased concentration of ethanol of 70%, 80%, 90%, and 100% for 60 minutes each. Clearing procedure used xylol three times for 15 minutes each at room temperature, and the tissues were afterward infiltrated with liquid paraffin in the incubator with 60°C three times for 60 minutes each infiltration.

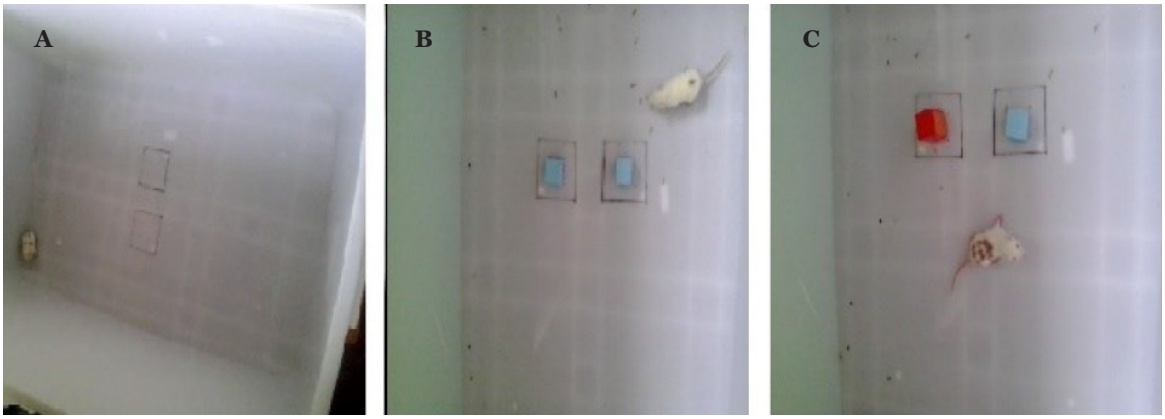

Figure 1 The Novel Object Recognition Test of Rat Pups after the Intervention
A. Habituation phase, empty arena; B. Training phase, arena with two identical objects; C. Test phase, arena with one familiar object and one novel object. PND 20 rats are exploring each arena in 3 phases consecutively with 3 minutes for each stage and 30 minutes for the interval between each step

Table Results of NOR Test and Hippocampal Formation Cell Counting

Variable	Groups		p Value
	Al-Quran	Control	
Exploration time difference (D_1)*			0.0491
Median	6.05	0	
Interquatile	0–7.19	0–0.415	
Discrimination index (DI)			0.1311
Median	0.355	0	
Interquatile	0–0.77	0–0.07	
Hippocampal formation cell count			0.0003
Mean	1,449.88	1,054.38	
Standard deviation	182.08	150.32	

*in seconds

The membranes were then embedded in liquid paraffin and cooled in room temperature to make paraffin blocks.[8]

Paraffin blocks were sliced coronally by rotary microtome with the thickness of 4 μm until reaching hippocampal formation. The targeted slices then put at warm water surface of 45°C, put in object glass coated by poly-L-lysine, dried vertically in room temperature before putting in slide warmer at 37°C horizontally overnight, and stored in a box at room temperature before stained with hematoxylin-eosin (HE).[8]

Tissue processing organized at Faculty of Medicine Universitas Padjadjaran. Cell counting of hippocampal formation is done using Optilab light microscope with a magnification of 400 times and Image Raster computer program. Data analyzed using Stata computer program with the significance of $p \leq 0.05$. From the Shapiro-Wilk test, NOR values analyzed by Mann-Whitney, and unpaired t test examined hippocampal formation cell count.

This research was carried out by considering the ethical issues of 3R (replacement, reduction, and refinement) principles. The animals underwent adaptation, regular light-dark cycle, and given intervention during the late period to provide comfort and minimize stress factor of the experimental animals. This research had approved by the Health Research Ethics Committee of Faculty of Medicine Universitas Padjadjaran with the ethical clearance number: 839/UN6.C1.3.2/KEPK/PN/2016.

Results

Mann-Whitney analysis displayed the difference in D_1 in rat pups exposed to *Al-Quran* sound stimulation, yet no significant difference in DI. Cell counting results by t test showed the higher

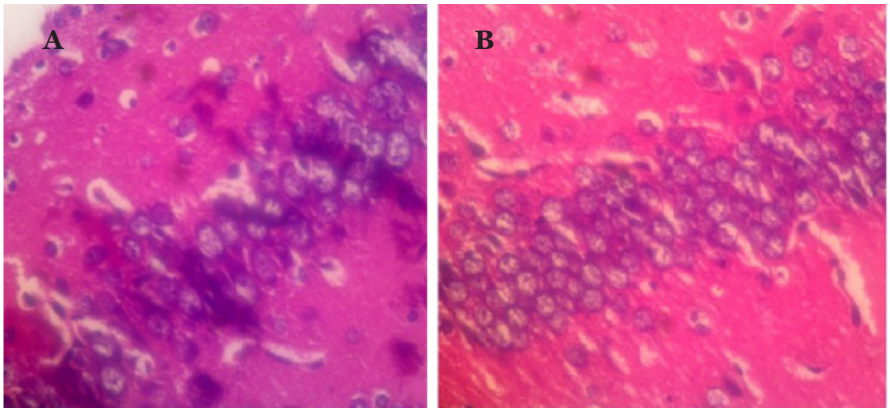

Figure 2 Hippocampal Formation of PND 21 Wistar Rats Stained with Hematoxylin Eosin
A. Control group, B. Intervention group exposed to *Al-Quran* sound stimulation

amount of cells in the hippocampal formation of rat pups exposed to *Al-Quran* sound (Table).

Images from the Optilab light microscope and the Raster Image computer program showed a higher cell count in the hippocampal formation of an animal group with exposure of *Al-Quran* sound stimulation (Figure 2).

Discussion

Al-Quran sound may affect brain growth and development through numerous mechanisms such as perceptual processing of its acoustic features such as pitch, timbre, melody, rhythm, intensity, and texture. Rhythmical sound stimulation was reported to activate cortical, subcortical and intermodal areas, which may relate to higher performance in tasks involving declarative memory.[9–10]

This study involved intervention by the sound of *Al-Quran* recited by specific rules affecting specific anatomical sites for verbal accuracy and length of pronounced letters in each part of recitation. One study resulted in higher alpha and theta oscillations in groups listening to *Al-Quran*, whereas alpha and theta power are related to retrieval, cognitive, and memory process. The recitation rules emphasized *Al-Quran* sound as rhythmic auditory stimulation. The result of this study supports the notion from previous observations that rhythmic sounds displayed influence toward learning and memory.[1–3,11]

Conscious recollection of facts and conditions termed declarative memory, which includes recognition memory. Recognition memory is closely related to the function of the medial temporal lobe, including hippocampal formation. Recognition memory in experimental animals observed through various neurobehavioral tasks, such as NOR task commenced in this study.[7,12]

The NOR task has the concept of exploration as an essential aspect. Animals can learn by exploring objects, with the term of exploration defined as directing the snout towards the object by the distance of 2 centimeters or less, sniffing or touching object using the snout. Activities of running around, climbing or sitting at the object excluded from the terminology of exploration. The duration of the animal's exploration of the novel object (T_N) and the length of the animal's exploration of the familiar object (T_F) documented as two distinct components used for two central values of NOR task.[7]

D_1 is total time spent by the animal to explore the new object, substracted from the full time devoted to examining familiar object (T_N–T_F). A positive value indicates a stronger preference for the novel object, and a negative value shows stronger inclination towards familiar object.[7]

In this study, we observed the higher value of D_1 in the group exposed to the sound of *Al-Quran*, noting shorter learning time of objects explored. During the NOR procedure, exposure of animals to novel objects can trigger labile phase that required the stabilization of memory, which is closely related to the reorganization of memory to open the access for new information to blend with the previous memory structure. The display of longer exploration time of novel object implied a shorter time required for memory stabilization of familiar object previously explored, enabling the experimental animals to switch the exploration from familiar to novel object more quickly. These may also relate to increased alpha and theta power in the brain associated with *Al-Quran* sound exposure, oscillation patterns which indicate the process of encoding new information and long-term potentiation (LTP) that participates in memory aspects.[3–5,7]

However, we observed no significant difference of DI between intervention and control group, indicating lack of distinction in the discriminating capacity of new and old information. DI is the value of D_1 divided by the amount of time spent exploring novel and familiar object [(T_N–T_F)/(T_N+T_F)]. Various factors may contribute to this result, one of which is olfactory stress factors experienced from the previous batch of animals tested. Another factor which possibly affected the test is a relatively long interval between each phase may be followed by memory degradation. An analysis stated that NOR memory might reduce as a result of interval duration between each stage reaching 10 minutes or more, which could contribute as an inhibiting factor.[14,15]

Another factor which may influence this result is the organ and cellular development. One study involving NOR procedure to PND 18 rat pups, resulted in lower NOR values compared to adult animals. Previous researchers showed that optimal NOR procedure could be displayed starting from PND 25–30, older than the ones in this study. Thus, a lack of difference in intervention and control groups in this study may also be related to sub-optimal growth processes in the brain such as neurogenesis, synaptogenesis,

and maturation of structures connected to memory.[14,15]

Hippocampal formation is a bilateral neuronal structure within the medial temporal lobe, which plays a substantial role in declarative memory. It receives afferent pathways from the entirety of cortical association areas and processes the information through various aspects such as encoding, intermodal sensory association, convergence, and memory consolidation.[16]

Sound stimulation from the prenatal period is recognized to have a role in brain function. Previous reports stated that sensory stimulation from early lifespan is capable of inducing long-term plasticity and also elevates proteins related to neuronal development, activation, and stabilization such as calcium-binding protein (CBP), cAMP response element binding protein (CREB), and brain-derived neurotrophic factor (BDNF). This study displays a higher cell count in the hippocampal formation of an animal group with exposure of *Al-Quran* sound stimulation, which supports those reports from previous researches. Higher cell count in Quran-stimulated pups may relate to the effect of rhythmical and melodious aspects of *Al-Quran* sound toward various factors of brain growth and development, such as proneural genes and transcriptional mediators of neurogenesis or survival of hippocampal formation cells.[1–5,13,16,17]

There was a shorter time of novel object recognition learning and neurogenesis or cell survival reflected in higher values of exploration time difference (D_1) and amount of hippocampal formation cells after *Al-Quran* auditory stimulation since prenatal period. However, there was no difference in discrimination index (DI) which may imply inhibition of discrimination capabilities or memory degradation related to the small age of intervention onset or interval duration, stress factors, and limitations in time documentation of NOR procedure. Nevertheless, the research field regarding *Al-Quran* auditory stimulation and its biological consequences is still in its early phases of development, opening itself for further scientific exploration.

Conclusions

Exposure to perinatal *Al-Quran* sound may serve as stimulation which enhances learning, memory, neurogenesis or cell survival of hippocampal formation.

Conflict of Interest

The authors declare no conflict of interests.

Acknowledgement

The author's thanks to the Educational Fund Management Institution (*Lembaga Pengelola Dana Pendidikan*/LPDP) Ministry of Finance Republik of Indonesia for financial support and Faculty of Medicine of Padjadjaran University and Faculty of Medicine of Bandung Islamic University for permission and facilities of this study.

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Global Medical and Health Communication

Online submission: http://ejournal.unisba.ac.id/index.php/gmhc
DOI: https://doi.org/10.29313/gmhc.v6i3.3618

GMHC. 2018;6(3):226–32
pISSN 2301-9123 | eISSN 2460-5441

RESEARCH ARTICLE

Antibiotics Used for Upper Respiratory Tract Infection: a Case Study at the Primary Health Center Bogor Indonesia

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Abstract

Acute upper respiratory tract infection (URTI) is one of the health problem in a community with high prevalence and healthcare cost. At the primary health center (PHC), URTI is one of the most common diseases with a prevalence 45.64% in Bogor city on 2015, while Basic Health Research 2013 data showed the prevalence of URTI in Indonesia by 25%. This study analyzes the antibiotic prescription for URTI patients, factors influencing the rationale of antibiotic prescriptions, and the rational use of medicine (RUM) program management at Primary Health Centers at Bogor city. The research was analytic descriptive cross-sectional study by collecting data from medical records of patients diagnosed with non-pneumonia URTI, observation for outpatient health care, and interview with all responsible persons. The data were collected on 16 April–20 May 2018 from primary health centers at Bogor city. The samples were 359 oral antibiotic prescriptions of three physicians and antibiotics were prescribed for 122 (34%) cases from 359 cases of which 102 were evaluated for rationality according to local guidelines issued by the Ministry of Health Republic of Indonesia. The URTI diagnosis is classified into few categories with the prevalence of nasopharyngitis (62.9%), pharyngitis (30.6%), tonsillitis (5.3%), and sinusitis and acute otitis media (0.6%). Most antibiotics used were amoxicillin and cefadroxil. This study revealed that antibiotics prescribed 88% inaccuracy of antibiotics duration, 12% incompatibility with the guidance of antibiotic, 3% incompatibility with guidance and imprecise duration, and 1% inaccuracy of dose. Some factors that influencing rationality of antibiotics prescription was lack of physician's adherence to the clinical guideline, pharmacist role was not optimal, and lack of monitoring evaluating.

Key words: Antibiotics, acute upper respiratory tract infections, rational use of medicine

Penggunaan Antibiotik untuk Infeksi Saluran Pernapasan Atas: Studi Kasus di Pusat Kesehatan Primer Bogor Indonesia

Abstrak

Infeksi saluran pernapasan atas (ISPA) akut adalah salah satu masalah kesehatan dengan prevalensi dan biaya perawatan kesehatan yang tinggi. Di pusat kesehatan masyarakat (puskesmas), ISPA adalah salah satu penyakit yang paling umum dengan prevalensi 45,64% di Kota Bogor pada tahun 2015, sementara data Riset Kesehatan Dasar 2013 menunjukkan prevalensi ISPA di Indonesia sebesar 25%. Penelitian ini menganalisis resep antibiotik untuk pasien ISPA, faktor yang memengaruhi dasar pemberian antibiotik, dan penggunaan manajemen program pengobatan rasional di puskesmas di Kota Bogor. Penelitian ini adalah penelitian deskriptif analitik *cross-sectional* dengan mengumpulkan data rekam medis pasien yang didiagnosis nonpneumonia ISPA, observasi perawatan kesehatan rawat jalan, dan wawancara. Data dikumpulkan pada 16 April–20 May 2018 dari puskesmas di Kota Bogor. Sampel adalah 359 resep antibiotik oral dari tiga dokter dan antibiotik diresepkan untuk 122 (34%) kasus dari 359 kasus yang 102 di antaranya dievaluasi untuk rasionalitas sesuai dengan pedoman yang dikeluarkan oleh Kementerian Kesehatan Republik Indonesia. Beberapa penyakit yang termasuk ISPA menunjukkan prevalensi nasofaringitis (62,9%), faringitis (30,6%), tonsilitis (5,3%), serta sinusitis dan otitis media akut (0,6%). Mayoritas antibiotik yang digunakan adalah amoksisilin dan sefadroksil. Penelitian ini mengungkapkan bahwa antibiotik yang diresepkan 88% tidak tepat durasi, 12% tidak cocok dengan panduan, 3% tidak cocok dengan panduan dan tidak tepat durasi, serta 1% tidak tepat dosis. Simpulan, faktor yang memengaruhi rasionalitas resep antibiotik adalah kurangnya kepatuhan dokter terhadap pedoman klinis, peran apoteker tidak optimal, dan pemantauan evaluasi yang kurang.

Kata kunci: Antibiotik, infeksi saluran pernapasan atas akut, penggunaan obat rasional

Received: 22 March 2018; Revised: 25 October 2018; Accepted: 28 November 2018; Published: 31 December 2018

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Introduction

Antibiotics use in developing countries is very high due to infectious diseases still the main health problems. Antibiotic resistance occurs when antibiotics are no longer able to inhibit or kill bacteria that cause infection because resistant to antibiotics.[1–3]

The national prevalence of non-pneumonia upper respiratory tract infection in Indonesia in 2013 was 25.0%. This figure is not much different from 2007 results was 25.5%.[4] Acute upper respiratory tract infection (URTI) is the most common diseases in the community, most of URTI have mild symptoms like cold, coughs caused by viruses and it doesn't need antibiotics treatment. In practice, many antibiotics are prescribed to treat this infection. Administration of antibiotics in patients that were not accompanied by adherence to drug consumption rules will increase the risk of side effects of drugs and antibiotics resistance.[5] The scope on URTI in this study refers to ICD-10 version: 2016 defined by World Health Organization (WHO) as an acute upper respiratory infection.[6]

The rational use of drugs is associated with several factors, including health care workers, patients, patient load and health care facilities.[7–10] Factors associated with increased drug prescription rationally by health workers include knowledge, training for rational drugs, and dissemination information of rational use of medicine.[7,8] The rational prescription of drugs is also associated with the characteristics of health care facilities, including the availability of treatment guidelines and the availability of drugs, policy, program management, monitoring and evaluation of implementation for rational use of medicine.[8–10]

The report of the Directorate General of Pharmaceutical and Medical Devices, the Ministry of Health of the Republic of Indonesia in 2016 on monitoring of the rational use of medicine (RUM) at the primary health center (PHC) showed the average use of antibiotics for non-pneumonia URTI in 2015 was 66.24% and in 2016 was 72.71%. These results indicate that the use of antibiotics is still high, above the established indicator of 20% of antibiotics for non-pneumonia URTI. The report also mentioned several challenges faced in implementation of RUM, among others lack of training and technical guidance to health workers at health centers in the absence of specific policies and strict sanctions on the use of antibiotics rational.[11]

The Ministry of Health Republic of Indonesia has developed strategies and interventions including a rational drug use course, an essential medicine list, Module for Rational Use of Medicine, Clinical Practice Guideline for Physician in Primary Health Center, and Standard for Pharmacy Services at Primary Health Center. The guidelines contain systematically developed statements that include recommendations and information to assist physicians and other health care practitioners in PHC to make decisions about appropriate health care for the patient.[1,2,12,13]

Bogor is a city bordering Jakarta, the capital of the Republic of Indonesia, with an area of 118.50 km^2, a population of 1,064,687 and Bogor has 24 primary health centers (PHCs) and 32 primary health sub-centers.[14] Bogor City Health Profile 2015 stated that group of URTI for age between 5–44 years is the highest percentage of disease, consist of non-specific acute respiratory infection of 22.78%, common cold 12.12 %, acute pharyngitis 4.56%, acute tonsillitis of 2.52%, while the lowest disease is acute laryngitis of 1.85%. Total of acute URTI in Bogor city on 2015 reached 45.64%. A large number of non-pneumonia acute respiratory cases occurring in Bogor city shows that non-pneumonia URTI is a public health problem.[15]

The rationality of the prescriptions in dose accuracy, choice of drug, and frequency and duration of administration are unknown. However, research evaluating the factors that influence the use of antibiotics by health providers in low-income countries is still rare. In the absence of research on prescribing antibiotics in primary health centers for URTI patients in Bogor city, it was necessary to conduct a study to evaluate whether antibiotics were prescribed rationally and research aimed to analyze the rationality of antibiotic prescriptions, analyzing factors influencing rationality, and management of rational use of medicine program.

Methods

This study is descriptive analytic research using cross-sectional research design with a quantitative approach, that is by doing the measurement of the medical record and qualitative data with observation and in-depth interview at the same time.

Outpatient medical record data of non-pneumonia URTI patient was taken prospectively

in 16 April to 20 May 2018 at primary health centers in Bogor city. Medical record data is used to analyze the rationality of antibiotics used for the patients. The data used in this study are (a) Patient data: gender and age; (b) Diagnosis: non-pneumonia URTI, non-specific URTI, common cold, cough, nasopharyngitis, sinusitis, and pharyngitis; and (c) Treatment given: the number of items/types of drugs given in each prescription, type of antibiotics, doses of antibiotics, frequency/interval of consumption per day, and duration of antibiotics (in days).

Direct observation was conducted to get the description of physician service process which made the diagnosis as supporting data of rationality evaluation of antibiotics. These observations were carried out on three physicians who provided services at the outpatient clinic.

Observation is not only conducted for non-pneumonia URTI, but also to other diseases so that researchers have a complete description of the service process. Observation variables in this study were medical history interview, physical examination, information and education for patients about the disease and its treatment, completeness of the medical record. Observations were carried out for ten working days for 150 patients at the outpatient clinic.

In-depth interviews were conducted with informants to obtain confirmation about the results of the medical record review. Furthermore, conducted interviews with some informants selected purposely (purposive sampling) according to the needs of this study. The informants were three physicians to obtain factors influencing rationality of antibiotics; two pharmacists to get information implementation of monitoring use of medicine; and head of primary health center and two stakeholders at the health district office to obtain information about policy, implementation, and program management of rational use of medicine.

The study already had ethical approval from the Research and Community Health Services Ethics Committee of Faculty of Public Health Universitas Indonesia with letter-number: 200/UN2.F10/PPM.00.02/2018.

Results

Medical record data in primer health centers at Bogor city during 16–30 April 2018 were 359 patients of non-pneumonia URTI. One hundred twenty-two (34%) non-pneumonia URTI patients had antibiotics treatment and 102 patient data were used to analyze the rationality of non-pneumonia URTI antibiotic treatments.

The rationality of antibiotics obtained through the assessment of the accuracy of antibiotics selection, the accuracy of dosage, the accuracy of frequency, and antibiotics duration compared to the Clinical Practice Guidelines for Physicians in Primary Health Center from Ministry of Health Republic of Indonesia.

Acute nasopharyngitis is the most amount of non-pneumonia URTI reaching 226 patients (62.9%) and the second is acute pharyngitis of 110 patients (30.6%). Other non-pneumonia URTIs are acute tonsillitis 5.3%, acute sinusitis and acute otitis media of 0.6% each.

The average number of drugs per prescription was 3.5 in the overall situation. Analgesics were the most commonly prescribed drug followed by antibiotics and antihistaminics. Amoxicillin

Table Evaluation of Rationality of Antibiotic Prescription for Non-pneumonia Upper Respiratory Tract Infection Patients

URTI	Rationality (n=102)							
	Clinical Guideline		Doses		Frequency/ Interval		Duration	
	Conform	Unconform	Accurate	Inaccurate	Accurate	Inaccurate	Accurate	Inaccurate
Acute nasopharyngitis, acute rhinitis, common cold	8	5	13	–	13	–	2	11
Acute pharyngitis	64	7	71	–	71	–	8	63
Acute tonsillitis	16	–	15	1	16	–	1	15
Acute otitis media	2	–	2	–	2	–	1	1
Total (%)	90 (88)	12 (12)	101 (99)	1 (1)	102 (100)	–	12 (12)	90 (88)

is the most widely used antibiotic in patients with non-pneumonia URTI, reaching 85.3%. Other antibiotics used for the treatment of non-pneumonia URTI include cefadroxil 12.3%, ciprofloxacin 0.16%, and thiamphenicol 0.8%.

Out of 122 patients with antibiotic treatments, 102 patients were fit to inclusion criteria and evaluated for the rationality of antibiotic use. The study revealed 99 (97%) of the 102 patient prescriptions were not according to the clinical guideline and 3 (3%) unconformity of guidance and inaccuracy of duration. The Table showed that 12 (12%) of the prescriptions was unconformity with guidance, 90 (88%) inaccuracy of duration, and 1 (1%) inaccurate of dose.

The process of diagnosis performed by the physicians appropriates with the stages in the treatment guidelines. Examination of vital and physical signs was performed in a limited time so that most physicians didn't give information about disease and treatment. Information on patient treatment will give when the physician needs to emphasize patients on specific medications. Most medical records in information system were not written completely. The average medical consultation time for every patient at the primer health center was 2.3 minutes.

Discussion

The Ministry of Health of the Republic of Indonesia assigned 2.6 as an indicator of the average number of drug per patient. The medication level for each patient is quite high compared to other countries such as Cambodia 2.35, Saudi Arabia 2.4, Sudan 2.5, and India 2.8.[16–19] However, compared to the WHO standard that suggested the average number of prescribed medications per patient was 1.6,[20] the above results indicated the presence of polypharmacy.

Polypharmacy is a large number of drugs in a prescription (with or without a prescription) for inappropriate clinical effects.[1] The factors that cause polypharmacy are the physician's focus on providing therapy for symptoms, not disease diagnoses.[19,20]

The issue of excessive drug administration in non-pneumonia URTI patients is a common problem in Indonesia; some studies suggest that the amount of drug administered tends to be excessive especially antibiotics and steroid drugs. The economic impacts of polypharmacy are not directly felt by patients at PHC, as patients only pay 3,000 Indonesian rupiahs (IDR) for all medical services including medication. The increasing number of polypharmacy leads to an increase in the number of drugs to be provided at PHC. Finally, this has an impact on increasing costs for drug procurement. Increased drug procurement costs using national/district budgets indirectly increase the economic burden of the community through increased tax revenue target of the government.

Excessive drug use can stimulate patient demand for multiple drugs. If the patient is accustomed to getting large of drugs, they will tend to choose a physician who will prescribe that. Patients will have a belief that there is a cure for all diseases so they will demand different drugs for the various symptoms they complain.

The proportion of antibiotics of non-pneumonia URTI patients were 34%. This proportion is lower than the national average in 2016 of 72.71% but has not reached the national indicator set at 20%.[11]

The results of research conducted by Hermawan and Kartika Sari[21] showed that antibiotics in URTI patients reached 93.8% in Sukasada II Primary Health Center of Buleleng regency. Meanwhile, the various studies showed that non-pneumonia URTI generally caused by a virus and can be self-healed so that the use of antibiotics is not needed.

Amoxicillin is the most antibiotic administered to non-pneumonia URTI patients. This finding is consistent with the study that conducted in PHC at Depok city which stated that amoxicillin mostly used for acute pharyngitis (46.6%) and non-specific (26.9%); erythromycin for bronchopneumonia, acute pharyngitis, and acute tonsillitis (33.3%); and cotrimoxazole for non-specific (30.7%) and acute pharyngitis (24.8%).[22]

The physicians of PHC stated that amoxicillin administration was in accordance by the standard operating procesude (SOP) established by the PHC, while the alternative antibiotics chosen by physicians was cotrimoxazole. However, in this analysis, the study was not found administration of cotrimoxazole and erythromycin recommended in treatment guidelines.

The other study had shown that high antibiotic use associated with increased bacterial resistance to antibiotics. A study in Health Service Unit of Universitas Jember by taking laboratory samples of URTI patients showed significant differences between amoxicillin and erythromycin. Eighty-

five percent of bacteria are resistant to amoxicillin and 40% against erythromycin. Logarithmic regression result obtained minimum inhibitory level (MIL) amoxicillin was 7.48–9.02 mg/L and erythromycin 0.23–4.95 mg/L. So it can be concluded that was a significant difference between the two drugs. The bacteria that cause secondary infection is no longer sensitive to amoxicillin.[23]

Rational use of the drug according to the WHO is if the patient received a drug that suits his needs to an adequate period at an affordable price for him and the community. The irrational use of drugs is an important issue that can have a substantial impact on the deterioration of the quality of health services which can result in increased resistance to the use of irrational antibiotics. Use of the drug said not rational if cannot be accounted medically (medically inappropriate) both regarding the accuracy of the type, the dosage, and how to administer the drug.[1,2]

The findings of 99 (97%) of the 102 patient prescriptions not in accordance to the clinical guideline, largely due to the duration of drug administration that was inconsistent with the guidelines even most antibiotics were given for only 3 days of treatment. In addition to the duration, the irrationality of antibiotics due to the selection of antibiotics and inappropriate dosage. Selection of cefadroxil which is cephalosporin group are second-line antibiotics for URTI and are used when there is suspicion of resistance. Muhlis's[24] study in one of PHC at Yogyakarta resulted not much different, all prescriptions met the accuracy of dosage and frequency, except cotrimoxazole dose 98% and ampicillin dose 49%. All prescriptions (100%) did not meet the exact duration of antibiotic use. The duration of administration of antibiotics according to the Regulation of Ministry of Health of the Republic of Indonesia is given for 6–10 days.[25]

The process of diagnosis is an important factor in RUM, the accuracy of disease diagnosis will determine the treatment that will be given by the physicians so that this study carried out the observation of the diagnosis enforcement process according to the Indonesian Good Medical Practice.[26]

The average length of medical consultation at PHC is 2.3 minutes. The medical consultation time is the time provided by the family physician to the patient is sufficient for the patient to express his or her complaint and wishes, sufficient for the physician to explain what he has gained in the history and physical examination, and enough to foster the patient's participation in carrying out the management he or she chooses as long as 10 minutes for each patient.[27] The research at 3 PHC in Cambodia resulted in medical consultation time of 4.43 minutes. This time is still far from Cambodia's national standard >10 minutes.[16]

Physicians of PHC explain that they have very high outpatients visit reached 150–200 patient visits, while PHC only has 3 doctors or sometimes only 2 doctors serve all patients without any assistance to call out the patient or measure the blood patients. And outpatient services have to be finished at 1 or 2 o'clock, so if the doctors did not work fast, not all the patient would get the outpatient services.

The researcher saw that the whole process of diagnosis by physicians in accordance with the stages in the guidelines, starting from probe the history of the diseases, physical examination and additional examination or appropriate action and refer the patient if necessary, but short medical consultation time causes inadequate information about the illness and treatment given to the patient. Patients have few opportunities to obtain information about their care.

Conclusions

Some factors that influencing rationality of antibiotics prescription were lack of physian's adherence to clinical guideline, pharmacist role for the rational use of medicine program were not optimal, and lack of monitoring evaluating for the rational use of medicine program.

Conflict of Interest

The authors declare no conflict of interests.

Acknowledgement

Thank you to the puskesmas doctors, nurses, administrative staff, and patients for good supports and collaboration in this study.

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