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Global Medical and Health Communication is a journal that publishes medical and health scientific articles published every 4 (four) months. Articles are original research that needs to be disseminated and written in English.

The submitted manuscript must be an article that has never been published, and the author must ensure that all co-authors have agreed by signing a statement on the seal. For original research, we accept the study which is last then 7 (seven) years when the manuscript is submitted. The manuscript is an original article free from plagiarism. When the article is published in another journal then in the next journal, the article will be disallowed.

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Before writing the purpose of the study, there must be a clear and explicit Gap Analysis or statement of gaps (originality) or a statement of the contribution of novelty (novelty statement), or the unique difference of this research compared to previous studies, also in

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Methods

Methods contain 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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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. Suggestions are also written here.

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The conclusion is submitted by the results obtained by the researcher and written briefly and clearly in two or three sentences in one paragraph.

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All authors must make a formal statement at the time of submission indicating any potential conflict of interest that might constitute an embarrassment to any of the authors if it were not to be declared and were to emerge after publication. Such conflicts might include but are not limited to, shareholding in or receipt of a grant or consultancy fee from a company whose product features in the submitted manuscript or which manufactures a competing product.

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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.

Books and Other Monographs

Editor as Author

Nriagu J, editor. *Encyclopedia of environmental health*. Michigan: Elsevier BV; 2011.

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World Health Organization. *Guideline: neonatal vitamin A supplementation*. Geneva: WHO Press; 2011.

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Conference Proceeding

Nicholai T. Homeopathy. *Proceedings of the Workshop Alternative Medicines*; 2011 November 30; Brussels Belgium. Brussels: ENVI; 2011.

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RESEARCH ARTICLE

Effect of Training on Organic Waste Management in Neighborhoods of Pejanggik, Mataram, West Nusa Tenggara

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Abstract

Garbage is solid waste consisting of organic and inorganic substances that outlived their usefulness and must be adequately managed to prevent environmental harm. The amount and types of waste are strongly influenced by the lifestyle and the type of materials we consume, and increasing household income cause an increase in the variety of waste generated. Handling and managing organic waste requires community involvement and successful household organic waste management, contributing significantly to the zero waste program. This study aims to measure the effect of waste management training on knowledge and principles of reducing, reusing, and recycling in waste management. The study was conducted from April to June 2021 in the neighborhoods around Pejanggik, Mataram village, West Nusa Tenggara province. It is a pre-experimental study involving 50 households to analyze the effects of the waste management training provided using a one-group pretest-posttest method. Before the training, knowledge and waste management principles were 22 of 50 respondents and 32 of 50 respondents, respectively. After the provision of training, the increase in knowledge and waste management principles reached 50 of 50 respondents. In conclusion, the training activity shows increased knowledge and waste management principles in households involved. Waste processing with reduce, reuse, and recycle principles can help overcome household waste problems and convert waste into products with increased economic value. Therefore, we recommend that periodic community-based waste management training involving households be held to overcome increased organic waste in households.

Keywords: Knowledge, management, organic waste, waste management

Introduction

The population increase and rapid industrial growth impact the amount and types of waste produced, such as plastic, paper, and packaging products containing B3 (hazardous toxic materials).¹ Population growth in major cities in Indonesia with increasing opportunities to find work and education, affecting the amount of waste produced.² Daily waste production per person is estimated at 2.3 liters, and if the average number of family members per household is 4.5, the daily waste production in the home amounts to 13.5 liters.³ The Mataram City Environmental Service reported that 325 tons of waste were produced daily, with 274 tons going to Kebon Kongok's final disposal site that serves Mataram city and West Lombok regency.⁴

The city of Mataram consists of 6 districts, 50 urban villages, and 297 neighborhoods. Out of the 325 tons of waste produced daily by the town, the Kebon Kongok's final disposal site only received

80% of the trash, with 20% remaining in the households and often left on the roadside. Such areas affected by the accumulation of garbage are Pejanggik village, Mataram district, and Mataram city. The accumulation of organic waste in common living areas resulted in the community taking the most straightforward action to eliminate the waste by burning it. However, burning garbage only provides a temporary solution, and wastes remain accumulated. Moreover, organic waste left behind in common public areas can cause many problems such as environmental pollution, foul odors, road hazard, and health issues.⁴

The lack of public knowledge on household waste management methods causes waste to pile up. Responding to this condition requires knowledge in managing and utilizing organic waste in products with increased values.⁵ To support this movement, collaboration from all parties is needed, including the government, the private sector, and especially the community,

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to form a cross-sectoral partnership to increase community capacity in supporting sustainable development programs and improving the quality of life of the community.⁶

Community participation in household organic waste management can be generated through understanding and skills in processing household waste with the principles of reduce, reuse, and recycle, to reduce waste produced and convert waste into valuable goods.⁷ Providing training in zero waste and 3R training (reduce, reuse, recycle) to groups of households will develop the expertise in processing and utilizing household waste to achieve the goal of zero waste.⁸

Waste is often solid materials that are generated as a byproduct of household and industrial activities or objects that are no longer desirable or have no economic value.⁹ Waste management is regulated by Law no. 18/2008, and waste management efforts can be made using reuse, reduce, and recycle (3Rs). Reuse is an activity of direct use/reuse for the same function or other functions. Reduce is an activity to lessen all activities that cause waste. Finally, recycling is an activity to repurpose waste after being processed/reprocessed.¹⁰

This study aims to measure the effect of waste management training on knowledge and principles of reducing, reusing, and recycling in waste management.

Methods

The study was conducted from April to June 2021 in the neighborhoods around Pejanggik, Mataram village, West Nusa Tenggara province. This study is pre-experimental, aiming to analyze a treatment's results or effects. This study uses a one-group pretest-posttest design. This design did not have a comparison group (control). A total of 50 households are involved using the purposive sampling method with the inclusion criteria for heads of families who did not have a home yard. Data were collected through questionnaires measuring the variables of age, education levels, occupation, and each object of research were observed three times. The questionnaire also includes an organic waste management manual and multiple-choice questions about the knowledge of waste types and organic waste management. This questionnaire was adopted from the previous

research. This study is approved by the STIKes Yarsi Research Ethics Committee in Mataram, West Nusa Tenggara number 12/KEP/STIKES/Y. III/II/2021. For data analysis, interview results were recapitulated and given a score, and categorized as good, sufficient, and poor. Data presented in the form of tables, described by descriptive analysis and the difference in the average value of pre-test and post-test scores will be examined by using the dependent t test (SPSS version 24).

Results

The results of the characteristics of the subjects are shown in Table 1. Based on Table 1, 24 of the respondent's age group is 36–45 years, and 42 of 50 are male. About 30 of 50 subjects finished high school, and 35 of 50 work in the private sector.

During the pretest, the parameters of knowledge about waste and aspects of waste management were measured before an intervention (training/counseling). A summary of the answers of the 50 respondents is shown in Table 2.

Based on the recap of the answers to the questionnaire on the knowledge aspect, the

Table 1 Respondents Characteristics

Characteristics	n=50
Age (years)	
25–35	12
36–45	24
46–55	14
Gender	
Male	42
Female	8
Education	
Junior high school	16
Senior high school	30
College	4
Occupation	
Government employees	4
Private	38
Trade	8
Income (million)	
<1.5	35
1.5–2.5	10
>2.5	5

Table 2 Responses to the Pre-test Questionnaire Aspects of Knowledge and Aspects of Waste Management

Questions	n=50	Questions	n=50
Pre-test questionnaire aspects of knowledge		How many times do you take out the trash in a week?	
The division of waste groups is based on whether or not it decomposes easily		a. Everyday	32
a. Inorganic and organic waste	16	b. Every two days	10
b. Dry and wet trash	12	c. Every three days	8
c. Do not know	10	Do you do waste segregation?	
d. No answer	12	a. Yes	18
Definition of organic waste		b. Not yet	32
a. The garbage from the rest of the kitchen like vegetables	16	Temporary garbage collection at home	
b. Plastic or glass waste	12	a. Crackle/plastic bag	15
c. Do not know	11	b. Simple trash	17
d. No answer	11	c. Land	9
What are the bad effects of garbage on society?		d. Etc.	9
a. Causes pain and disturbs the view	16	Is reusing the container/packaging for the same function?	
b. Shows the low social status	12	a. Yes	12
c. Do not know	13	b. Sometimes	20
d. No answer	9	c. Never	18
What are the positive effects of waste on society?		Do you sell/give waste to those in need?	
a. Can be processed into compost	16	a. Yes	0
b. Does not provide good benefits	12	b. Sometimes	18
c. No	11	c. Never	32
d. No answer	10	Do you use recyclable packaging?	
Another name for organic fertilizer		a. Yes	0
a. Chemical fertilizer	16	b. Sometimes	18
b. Fertilizer produced from the factory	12	c. Never	32
c. Fertilizers sourced from natural ingredients	8	Do you use recyclable and biodegradable products and packaging?	
d. Fertilizer that comes from living things that have died	14	a. Yes	0
Mention the materials used to make organic fertilizer		b. Sometimes	18
a. Plastic waste	10	c. Never	32
b. Drink's cardboard	10	Do you process organic waste into compost?	
c. Fruits' peel/fruits' leftover	16	a. Yes	0
d. Soap water	14	b. Sometimes	18
Pre-test questionnaire aspects of waste management		c. Never	32
How many garbage bags are produced per day?		Is it processing non-organic waste into useful goods?	
a. 1 bag every day	32	a. Yes	0
b. 2-3 bags daily	9	b. Sometimes	18
c. >3 bags daily	9	c. Never	32
When is the right time to take out the trash?			
a. Morning	10		
b. Noon	10		
c. Afternoon	10		
d. Evening	20		

Table 3 Knowledge Distribution and Processing Aspects of the Head of the Family in Organic Waste Management

Variables	Pre-test n=50	Post-test n=50
Knowledge		
Well	16	50
Enough	12	0
Not enough	22	0
Processing aspect		
Well	0	50
Enough	18	0
Not enough	32	0

Table 4 Dependent T Test Knowledge and Processing Aspects of the Head of the Family in Organic Waste Management

Variables	Mean	SD	p
Knowledge			
Pre-test	6.36	3.026	0.000
Post-test	11.04	0.841	
Processing aspect			
Pre-test	7.44	2.022	0.000
Post-test	15.12	1.424	

majority of respondents' answers were in the poor criteria (22 of 50 respondents), and only 16 of 50 respondents were in a good category. It is because elements of knowledge ideally correlate with aspects of waste management.

Based on the waste management aspects in Table 2, the overall assessment recap is in the poor category (32 of 50 respondents) and 18 of 50 respondents sufficient. No answers were found in the good category (0 respondents). However, after training was given to the respondents, significant results were found in the post-test.

Table 3 shows the change in the assessment of knowledge and waste management aspects from pre-test to post-test. Overall, an increase was found in the good category (50 respondents) regarding knowledge and waste management.

After being given the waste management training, all respondents achieved the good category (50 respondents). This organic waste management training activity aims to increase the

understanding of families regarding household waste management to support the zero waste program. In addition, data were analyzed using the dependent t test to assess the difference in the value of the knowledge and waste processing before and after the intervention (Table 4).

The test results in Table 4 show differences in scores before and after the intervention, indicated by the value of $p=0.000$ ($p<0.05$). It means a statistically significant difference in the average value before and after the intervention.

Discussion

Pejanggik village, with a population density of about 9,349, has the potential as one of the areas that highly contribute to the daily waste in Mataram city. There is garbage scattered on the side of the road and unorganized illegal landfills. In general, we found the following situations, the community has not separated wet and dry waste, so it isn't easy to reuse. Wet waste can be recycled into compost, but it will be difficult if mixed with other waste such as batteries, sanitary napkins, or chemical waste. Community participation is still meager. The number of sanitation workers who work to handle waste is much less than the number of office workers and the amount of waste that must be addressed. There was no public awareness to be directly involved in handling waste, as indicated by the dirty environment caused by the accumulation of garbage. The condition of the landfill is limited, and scavengers can only reduce a small part of the waste that comes in daily. Trash is scattered in the final disposal site location because of the limited capacity. The operational costs of transporting waste from the temporary to the final disposal site are continuously increasing.

On the other hand, operational costs are needed to maintain waste transport vehicles. As one of the tourist destinations that impacts increasing waste production daily, this situation requires attention from the community and government. Unfortunately, the local government regulations that regulate waste management have not been found, including sanctions for community violators.

The results of our study show that the level of public knowledge about waste before interventions was in the poor category (22 of 50 respondents). The same thing was observed in the aspect of waste management. 32 of 50 respondents

are in the poor category. It means the problem of poor waste management in the environment of Majeluk Pejangik village, Mataram city, is influenced by the local community's level of knowledge and management behavior.

Based on this information, we provide training and counseling to increase public knowledge, which will ultimately affect their waste management behavior. We conducted mentoring, observation, and evaluation activities thrice from April to May 2021. Starting with providing education about the impact of waste on environmental health and family health, we continued with the practice of separating organic and non-organic waste. We also introduced a simple composting method to increase the utilization of waste. Our observations and evaluations are carried out to see the progress of achievements that all respondents have practiced. We found significant behavioral changes characterized by a much better environment than before the intervention. At the end of June 2021, we again held training to evaluate the achievement of activities and conduct an assessment through posttest. Furthermore, we found significant results, where the knowledge and waste management aspects increased to 100%.

Community-based integrated waste management is one of the solutions that we recommend through the results of this research. This program is a method of approaching waste management based on the needs and demands of the community. These activities are planned, implemented, monitored, and evaluated together with the local community.¹¹ This activity also requires the role of the government and other institutions as motivators and facilitators. The government provides encouragement so that the community is ready to find solutions to the waste problems they face.¹²

Urban waste accumulation has increased significantly every year (2.4%/year), which is not matched by the availability of adequate waste processing infrastructure and facilities, resulting in increased environmental pollution. In addition, the collection-transport-disposal pattern program that has been carried out so far has resulted in the burden of pollution constantly piling up at the location, and the waste management method is not following the required standards.¹³

Community-based waste management also

involves the active role of the general public in managing waste. They start from the stages of stockpiling, collecting, and processing to a final product. Community empowerment programs through organic and inorganic waste management are considered very important and strategic as an effort to develop community-based environments.¹⁴ The goal is not only to reduce the accumulation of waste but also to maximize the role of the community care about the state of the environment. Community empowerment in waste management such as processing organic waste into compost and recycling inorganic waste into reusable tools.¹¹

Several previous studies have reported on the success of family empowerment in waste management. For example, Ruhmawati et al.¹⁵ in Bandung reported that empowerment interventions significantly increased families' knowledge and attitudes toward waste management. Research on waste management was also conducted by Yang et al.¹⁶ in China, Bernardo¹⁷ in the Philippines, Ezparsa et al.¹⁸ in Spain, and Matsuto¹⁹ in several Asian countries.

Public understanding of the 3R concept, namely reuse (reusing used goods that can still be used), reduce (lessening waste production), and recycle (recycle waste so that it can be reused), has increased over the past few years. The concept of 3R is not new. Many of our literature studies have shown the success of introducing the concept to society.²⁰ In contrast, the waste produced by the community was getting higher and piled up in any place.²¹ Illegal and uncontrolled landfills are popping up and mushrooming everywhere. Community participation is needed to manage waste starting from the household so that later the waste disposed of at the landfill has been reduced quite a lot and does not cause piles in the landfill location.²²

The principle of reuse is the reuse of containers/packages for the same function or other functions, utilizing reusable containers/bags, using rechargeable batteries, and selling or giving sorted waste to people who need it.²³ The principle of reducing is to choose products with packaging that can be recycled, avoid using/buying products that produce large amounts of waste, use products that can be refilled, and avoid using single-use materials. The principle of recycling is to choose products/packaging that can be recycled and easily decomposed, for example, processing organic waste into compost

and non-organic waste into valuable goods.²⁴

Research reports that have reported the success of family involvement in waste handling with 3R principles, including Hernawati et al.²⁵ and Ediana et al.,²⁶ concluded that there is a relationship between attitudes and 3R waste management. The empowerment program is hoped to be further improved, so that community groups are fostered in processing the 3R waste. Setianingrum²⁰ provides solutions to some waste problems, including increasing public awareness in sorting waste and maintaining environmental health, raising public awareness in handling waste, and reducing the volume of waste generated from households. Wahyudin et al.⁵ reported that the waste management planning efforts with the 3R approach were able to take 80% of waste, and 20% of the residue was disposed of at the Pasar Dasan Agung Mataram city landfill. Armanda²⁷ examines the planning of household waste processing sites with the 3R principle in the Medan district area, Medan city.

Based on the results of the research that we have done, some of the recommendations we offer are as follows:

Efforts to involve the community in waste management would be a common concern from the sub-district government, the Mataram City Environment Agency, community leaders, and local religious leaders. However, we found that the community was motivated and moved when control, evaluation, and support came from other parties.

Community participation in playing an active role in waste management starts from the household by separating organic waste, inorganic waste, and B3 waste. The sorting of waste will help recycle organic waste into compost while inorganic waste into other forms so that it has economic value and can be used as waste briquettes.

The community should take advantage of existing inorganic waste, which can be recycled to become a source of income for business creativity, including making handicrafts from plastic, paper, cardboard, and wood (a variety of recycled creations).

Most people in Mataram city have plants in their yard, so we recommend making organic fertilizer from waste that can be used for fertilizer needs.

The need for continuous supervision from relevant agencies (government, community leaders, religious leaders) to monitor success in

community-based waste management.

Conclusions

The community partnership program activities to assist the management of organic waste in households are successful, as indicated by the increase in the knowledge and skills of the family heads who have managed household organic waste. However, the evaluation of the training program with the support of community leaders, the government from both the environment of the village and the Mataram City Environment Agency need further improvement.

Conflict of Interest

All authors state whether there was a conflict of interest in this article or not.

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RESEARCH ARTICLE

Effect of *Katuk* Leaves (*Sauropus androgynus* (L.) Merr) on Breast Milk Production

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Abstract

Exclusive breastfeeding can reduce infant mortality in Indonesia. Lack of breastfeeding is one of the causes of the low achievement of exclusive breastfeeding. *Sauropus androgynus* (L.) Merr (*katuk*) leaves are believed to increase milk production. Most people process *katuk* leaves to make vegetable soup, while improper processing methods can reduce the beneficial effects. This study aimed to analyze the effect of *katuk* leaf soup consumption on breast milk production. The subjects in the study were postpartum mothers and their babies from October to November 2021 at the PONE Health Center in West Lombok regency who met the sample criteria. This research is a randomized controlled trial. The sample used is 32 respondents. *Katuk* clear soup was given to the intervention group and Asifit to the control group. The data collected was processed by a nonparametric test. The analysis showed no difference in *katuk* clear soup and Asifit on breast milk production ($p=0.105$). Therefore, breast milk production increased due to *katuk* clear soup and Asifit made from *katuk* leaves. This research concludes that *katuk* leaves are proven to increase breast milk production. Therefore, *katuk* leaf vegetables can be used as an effort to increase breast milk.

Keywords: Breast milk production, *katuk* leaves

Introduction

The Indonesian Health Demographic Survey (IDHS) in 2017 showed the infant mortality rate (IMR) was still high, at 24 deaths per 1,000 live births.¹ This figure is still high compared to the target set by the Sustainable Development Goals (SDGs), which is 12 per 1,000 live births.² The high IMR is mostly (53%) due to nutritional factors. Diseases caused by malnutrition include pneumonia (20%) and diarrhea (15%).³

Exclusive breastfeeding can reduce infant mortality.^{4,5} Exclusive breastfeeding can prevent under-five deaths and reduce deaths due to acute respiratory infections and diarrhea.⁶ Suboptimal breastfeeding causes 45% of neonatal deaths due to infection, 30% of deaths due to diarrhea, and 18% to acute respiratory distress.⁷

The percentage of children under six months who are exclusively breastfed has increased in the last five years, from 42 percent in the 2012 IDHS to 52 percent in the 2017 IDHS.¹ However, this percentage is still far from the national target of 80%. The coverage of exclusive breastfeeding for infants on average in West Nusa Tenggara (NTB) province in 2018 was above the national target of 82.68%. The lowest breastfeeding coverage in NTB is Mataram city at 70.30%.⁸ Previous studies

show the proportion of exclusive breastmilk in infants in rural areas higher than in urban areas.^{9,10}

One of the reasons for the low exclusive breastfeeding is the lack of milk production. A previous study shows that confidence and perception of little milk production are a factor for unsuccessful early initiation of breastfeeding.¹¹ Another study showed that as many as 51.1% of mothers experienced the perception of insufficient breast milk.¹²

In Indonesia, many plants are believed to increase breast milk production, including *katuk* leaves, turi, and moringa.¹³ Most of these ingredients have not been scientifically evaluated but are traditionally safe and effective.¹⁴ The results showed that most of the community (50.4%) used the clear vegetable *katuk* leaves to increase breast milk.¹³ However, the incidence of insufficient breastfeeding is still high in Indonesia.

Clinical trials showed that giving *katuk* leaf capsules for 15 days postpartum with a dose of 3×300 increased milk production by 66.7 mL (50.7%). Increase prolactin and oxytocin levels, and contain nutrients that are breast milk synthesis's main ingredients.¹⁵ Inappropriate processing and dosage methods can reduce the

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nutritional levels and function of *katuk* leaves.¹³

This study aimed to analyze the effect of *katuk* leaf soup consumption on breast milk production.

Methods

Katuk leaves used are light green to slightly dark green. *Katuk* leaves were taken from Berukelak hamlet, Sasake village, Praya Tengah subdistrict, Central Lombok regency. *Katuk* clear vegetable soup is made with a ratio of 150 grams of *katuk* leaves mixed with 750 mL of water, then cooked for 15 minutes over low heat.

The resulting *katuk* clear vegetable soup is then checked for the content of alkaloids and steroids. It was carried out at the Pharmacy Laboratory of the Universitas Muhammadiyah Mataram.

This research method is a randomized control trial post-test only control group design. The samples in this study were postpartum mothers and their babies with normal birth from October to November 2021 at the Basic Obstetric and Neonatal Emergency Service (PONED) health center in West Lombok regency, namely Gerung, Gunungsari, Kediri, Parampuan, Labuapi, and Dasan Tapen Health Centers. Before conducting the research, the researcher provided counseling about exclusive breastfeeding.

Respondents in this study were divided into two groups, each group of 16 respondents. The

treatment group received *katuk* clear vegetables soup two times a day, while the control group was given Asifit 3 times one caplet for four days. In addition, breast milk production was evaluated on the 5th day of the puerperium, using a weight test, with OneMed brand electric scale type OD231-B made in China. In addition, three students of the Midwifery Study Program assisted this research by distributing *katuk* clear vegetables soup and Asifit to respondents.

Processing for bivariate analysis used the chi-square test for education, Fisher's exact test for work, t test for no food for nutritional status, and Mann-Whitney test for age and milk production data. This research has received research ethics from the Research Ethics and Community Service Committee of the Faculty of Medicine, Universitas Islam Al-Azhar Mataram 39/EC-4/FK-06/UNIZAR/X/20.

Results

Table 1 shows that there are no significant differences in education and occupation between the treatment and control groups. There was also no significant difference in age and nutritional status between the treatment and control groups. Respondents' nutritional status on a normal scale.

Table 2 shows clear vegetables cooked over low heat containing alkaloids and steroids. Table

Table 1 Characteristics of Research Subjects

Characteristics	Groups		P
	Treatment (n=16)	Control (n=16)	
Education			
Elementary school	2	1	0.871 ^a
Junior high school	6	5	
Senior high school	6	8	
University	2	2	
Occupation			
Employe	3	4	0.50 ^b
Housewife	13	12	
Age			
Median (min–max)	21.5 (17–26)	22.5 (17–26)	0.457 ^c
Average±s.b.	22.62±3.033	21.94±2.79	
Nutritional status in terms of weight and height			
Median (min–max)	19.98 (16.23–28.89)	20.47 (15.63–24.65)	0.885 ^d
Average±s.b.	20.7±3.35	20.5 ± 2.36	

Note: ^achi-square test, ^bFisher's exact test, ^cMann-Whitney test, ^dindependent t test

Table 2 Results of Phytochemical Screening of Alkaloid Compounds and Steroids of *Katuk* Leaf Vegetable Cooked on Low Fire

Phytochemical Screening	Reactor	Observation Result	Conclusion
Alkaloid	Mayer	No yellow/white precipitate is formed	+
	Dragendorff	No orange precipitate is formed	+
Steroids/triterpenoids	Acetic acid, anhydrous, concentrated H ₂ SO ₄	Formation of a brownish-blue-green ring	+

Table 3 Effect of Giving *Katuk* Leaf Clear Vegetables on Breast Milk Production

Breast Milk Volume Day 5	Groups		p
	Treatment	Control	
Median (min–max)	71.5 (25–336)	103.5 (50–278)	0.105*
Average±s.b.	102.44±78.7	121.31±60.258	

Note: *Mann-Whitney test

3 shows that the treatment group that was given *katuk* leaf clear vegetables and the control group that was given Asifit was proven to increase breast milk production.

Discussion

Lactation is a process of forming to the expulsion of breast milk.¹⁶ The success of lactation is influenced by hormonal factors and characteristics of breastfeeding mothers, such as maternal age, parity, and gestational age.¹⁷ The results of the analysis of the characteristics and confounding variables, including age, education, occupation, and nutritional status, showed no significant difference between breastfeeding mothers in the treatment and control groups with $p > 0.05$.

The results of the study (Table 3) show that the treatment group given the clear *katuk* leaves soup while the control group given Asifit proved to be able to increase breast milk production with a $p = 0.105$ ($p > 0.05$). The increase in breast milk production is due to the *katuk* leaf containing alkaloids (papaverine) and steroids (phytosterols). Other clinical trials showed that giving *katuk* leaf capsules for 15 days postpartum with a dose of 3×300 increased milk production by 66.7 mL (50.7%). Increase prolactin and oxytocin levels, and contain nutrients that are breast milk synthesis's main ingredients.¹⁵

Papaverine is a secondary metabolite

compound of *katuk* leaves. This compound can increase the expression of oxytocin and prolactin genes. It is because papaverine can dilate blood vessels and relax muscles, resulting in the circulation of the hormones prolactin and oxytocin through the bloodstream.¹⁸ Papaverine acts on smooth muscle, blood vessels, and heart muscle. These compounds act on beta-adrenergic receptors by intermediary cyclic adenosine monophosphate (cAMP)—similarly, prostaglandins are a group of compounds in eicosanoids. Prostaglandins also have specific effects on the cardiac muscle, blood vessels, and smooth muscle, which can act as vasoconstrictors and vasodilators depending on where the prostaglandins are synthesized.¹⁹ Papaverine and prostaglandins can have a dilating effect on large blood vessels, such as arteries, and can reduce peripheral pressure.²⁰ Research in rabbits shows papaverine can prevent vasospasm of blood vessels.²¹

Dopamine can inhibit the release of prolactin with inhibits cAMP and binds to dopamine (D₂). Papaverine has a function in inhibiting phosphodiesterase 10A (PDE10A). PDE10A regulates cAMP/PKA signaling in both striatopallidal and striatonigral neurons. In striatopallidal neurons, inhibition of PDE10A by papaverine leads to increased phosphorylation of cAMP-dependent substrates resulting in activation of cAMP/PKA signals. It leads to the

inhibition of signal receptors dopamine (D₂) and simultaneous potentiation of the adenosine signal (A_{2A}). In striatonigral neurons, inhibition of PDE10A due to activation of cAMP/PKA signals by papaverine leads to potentiation of D1 receptor signals. PDE10A inhibition affects striatopallidal neuron signaling.²²

Papaverine blocks dopamine receptors so that it can stimulate the release of prolactin. Prolactin influences hypothalamic control secretion via feedback mechanism.²² Elevated serum prolactin levels increase dopamine synthesis by the hypothalamus and the concentration of dopamine in the hypothalamic-pituitary portal blood.²² This explains that the higher the dose of *katuk* leaf extract, the higher the papaverine consumed. If prolactin secretion increases, it will increase dopamine secretion. Dopamine secretion causes inhibition of prolactin secretion.¹⁹ In addition to papaverine, *katuk* leaves also contain sterols (phytosterols) to increase milk production.²³ Phytosterols and cholesterol are almost the same in the human body. Intestinal absorption is limited by ABCG5/G8 (ATP-binding cassette sub-family G members 5 and 8) and promotes biliary excretion of sterols.²⁴

Bile salts, when in high enough concentrations, tend to form mycelium. This state is formed because each molecule of bile salts is composed of a sterol nucleus, most highly soluble in fat, and a polar group highly soluble in water. The 20–40 sterol nuclei of bile salt molecules from the micelles adhere to each other, along with digested fat, to form tiny bubbles in the middle of the micelles, with the polar groups of bile salts protruding outward to cover the surface of the micelles. Because this polar group is negatively charged, it makes all the mycelium bubbles soluble in the water of digestive juices. It remains in the form of a stable solution despite the considerable size of the micelles. Therefore, micelles can help digestion and absorption of fat.²⁵ Fat is needed for the formation of breast milk.

Androstan-17-one,3-ethyl-3-hydroxy-5 alpha, is one of the compounds in *katuk* leaves that functions as a precursor or intermediate step in synthesizing steroid hormones (progesterone, estradiol, testosterone, and glucocorticoids).²⁵ Through the action of prostaglandins and steroid hormones (glucocorticoids, progesterone, estradiol) as a result of the biosynthesis of compounds eicosanoids and steroid hormones. This hormone acts directly through an increase in

population and synthetic activity on the secretory cells of the mammary gland.²⁶ The increased concentration of steroid hormones in the bloodstream indirectly stimulates anterior and posterior pituitary gland cells to release prolactin, oxytocin, and growth hormone (GH).²⁷ These three hormones are involved in the synthesis of milk.

Sterols also have specific functions in intracellular signal transduction. Like cAMP, sterols also act as secondary messengers, conveying signals from receptors on the surface of target cell molecules in the cell. Signals are relayed from hormones and growth factors and cause some changes in cell activity. Therefore, the sterol content in *katuk* leaves also helps to increase the signal transduction of the oxytocin hormone.²⁸ Phytosterols can stimulate EGF-R and PRL-R so that prolactin and EGF are needed for cell proliferation and maintenance.¹⁶

Conclusion

The results showed an effect of giving *katuk* leaf vegetables on breast milk production.

Conflict of Interest

There are no conflicts that occur in this study.

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RESEARCH ARTICLE

Correlation between Abdominal Circumference and Serum High-Sensitivity C-Reactive Protein Concentration at Age 35–64 Years

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Abstract

The prevalence of central obesity in Indonesia is increasing every year. Based on data released by *Riskesdas* in 2018, there were 31% of the population aged 15 years and over suffer from central obesity, where the highest was found in the 45–54 years group (42.3%), followed by 44 years (39.2%) and 55–64 years group (39.1%). Central obesity can be measured by waist circumference or abdominal circumference, and it plays an important role in the occurrence of cardiovascular disease. Examining C-reactive protein (CRP) at low levels using high-sensitivity CRP (hs-CRP) methods will help to predict the risk of coronary heart disease. This study aimed to find the correlation between waist circumference and hs-CRP serum levels between the ages of 35 and 64. The study was an analytical observational with a cross-sectional approach attended by 25 respondents at Bhayangkara Hospital Tingkat I Raden Said Sukanto, Kramat Jati, East Jakarta, from October to November 2019. The waist circumference was measured with a metlin roll, and Prodia Laboratory took the blood to measure hs-CRP serum levels using ELISA methods. The data were analyzed using the Pearson correlation test. The results showed a correlation between waist circumference and hs-CRP serum levels with Sig. (2-tailed)=0.000 ($p < 0.05$). There was a correlation between waist circumference and hs-CRP serum levels, which indicated that the greater the waist circumference, the higher levels of serum hsCRP would be.

Keywords: Abdominal circumference, central obesity, hs-CRP

Introduction

Central obesity is an accumulation of fat in the abdomen that may impair health. This accumulation is caused by excessive subcutaneous and visceral fat, caused by an energy imbalance between nutritional intake and lack of physical activities.¹ World Health Organization guidelines that alternative measures that reflect abdominal obesity, such as waist circumference, waist-hip ratio, and waist-to-height ratio, are superior to body mass index.² Waist circumferences are a method used to determine central obesity in Asian men who are more than 90 cm, and women who are more than 80 cm are declared to have central obesity.^{3–5} Recently, obesity has increased in Asia, along with rapid economic growth.⁶ In Indonesia, according to *Riskesdas* in 2018, there were 31% of the population aged 15 years and over suffering central obesity, where the highest was in the aged group 45–54 years old (42.3%), followed by 44 years old (39.2%) and in the aged group 55–64 years old (39.1%).⁷ This prevalence is higher if we compare it to 2013.⁸ Some studies showed that central obesity is essential to cardiovascular

disease.⁹ In Indonesia, data showed that stroke (21.1%) and coronary heart diseases (12.9%) were the most significant morbidity caused by obesity.¹⁰ C-reactive protein (CRP) is an acute-phase protein molecule produced by the liver in the acute phase. CRP production is affected by inflammatory cytokines, particularly IL-6. High-sensitivity C-reactive protein (hs-CRP) is a test capable of measuring elevated levels of low CRP, so it is more sensitive to measure the range between 0.1–2 mg/L. Several studies have shown that hs-CRP is used to predict the risk of coronary heart disease and can indicate recurrences.^{11,12} Research by Bennet et al.¹² showed a positive correlation between central obesity and hs-CRP examination. However, research by Kollathody et al.¹³ in India showed no correlation between central obesity and increased levels of hs-CRP.

The article analyses the correlation between waist circumference and hs-CRP serum levels between the age of 35 and 64 years.

Methods

This study is an observational analytic study using cross-sectional methods and was conducted

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in Bhayangkara Hospital Tingkat I Raden Said Sukanto, Kramat Jati, East Jakarta. The population in this study were all patients aged 35–64 who visited the hospital from October to November 2019 and were sampled using a consecutive sampling method. The inclusion criteria were patients aged 35–64 agreeing to be examined for waist circumference and hs-CRP serum level. The exclusion criteria were patients suffering infections such as fever, urinary tract infection, respiratory infection, gastroenteritis, pregnant or breastfeeding women, and smokers. The questionnaire in this study compiled sociodemographic data (age, gender, education level, and work) and anthropometry using metlin roll. The waist circumference for males >90 cm and females >80 cm are declared to have central obesity.^{2–4} The waist circumference was measured to the nearest 0.5 cm at the superior border of the iliac crest.¹⁴ Blood samples were taken to measure hs-CRP serum level and analyzed by Prodia Laboratory using ELISA methods. They were divided into three risk categories: low risk (<1.0 mg/L), average risk (1.0–3.0 mg/L), and high risk (>3.0 mg/L).^{8,10} This study was attended by 25 respondents who calculated using the relation coefficient with $\alpha=5\%$, $Z\alpha=1.96$, $\beta=20\%$, $Z\beta=0.842$, with $r=0.552$.¹⁵ Analysis used the Pearson correlation test with differences at $p<0.05$ that were considered significant.

This study was accorded to the Helsinki Declaration and approved by the Research Ethics Committee of the Faculty of Medicine, Universitas Trisakti, number 67/KER-FK/VII/2019.

Results

Univariate analysis was used to determine the frequency distribution of subject characteristics in the form of age, gender, education level, and work. The subject characteristics can be seen in Table 1.

Table 1 shows that most of the subjects were females, the mean subject's age was 47.56 ± 6.63 years old, and most of the subjects had central obesity. Based on the level of education, the majority of the subjects were with higher education and still work.

Table 2 shows that the hs-CRP serum levels mean was 3.85 ± 2.39 mg/L and waist circumference means were 90.19 ± 9.96 cm.

The Kolmogorov test of normality of the data

Table 1 Characteristics of Research Subjects

Characteristics	n=25
Gender	
Male	6
Female	19
Age (years)	
Average±s.b.	47.56±6.63
Waist circumference	
Normal	5
Central obesity	20
Level of education	
Low (elementary–junior high)	2
Mid (senior/vocational)	7
High (D1–D3/college)	16
Work	
No work	8
Work	17

Table 2 High-Sensitivity CRP (hs-CRP) and Waist Circumference

	n	Mean±SD
hs-CRP serum levels	25	3.85±2.39
Waist circumference	25	90.19±9.96

distribution showed that the data were normally distributed, so this study was analyzed by the Pearson correlation test.

Based on bivariate analysis using the Pearson correlation test, there was a significant correlation between waist circumference with serum level of hs-CRP with Sig. (2-tailed)=0.000 ($p<0.05$) between ages 35 and 64 years old (Table 3).

Discussion

Being overweight and obese are commonly known as risk of cardiovascular risk factors. Central obesity can occur due the multifactor influence such as smoking habits, high consumption of fatty foods, low consumption of fruits and vegetables, lack of physical activity, lifestyle change, age increases, gender, ethnic and socioeconomic status.^{1,5,16,17} In this study, most subjects had central obesity with an average of 90.19 ± 9.96 cm, which showed an increased incidence of central obesity compared to *Riskesdas* 2018 data which showed only 31% had central obesity. This can be

Table 3 Pearson Correlation Test

		Waist Circumference (Central Obesity)	hs-CRP
Waist circumference (central obesity)	Pearson correlation	1	0.714*
	Sig. (2-tailed)		0.000
	n	25	25
hs-CRP	Pearson correlation	0.714*	1
	Sig. (2-tailed)	0.000	
	n	25	25

Note: *correlation is significant at the 0.01 level (2-tailed)

caused because, in the big cities, there has been a change from a traditional diet to a western diet which contains high calories, fats, sugar, and low fiber, which causes energy imbalance to trigger obesity.^{1,5,18}

This study result showed that the average hs-CRP serum level at age 35–64 years old was 3.85 ± 2.39 mg/L. Based on the America Heart Association recommendation regarding the cut-off value of hs-CRP serum level against the risk of cardiovascular disease, the average value in this study included high risk.⁹

This study shows a significant correlation between waist circumference and serum level of hs-CRP with Sig. (2-tailed)=0.000 ($p < 0.05$) at 35–64 years old. This finding indicated that the greater the waist circumference, the higher levels of serum hs-CRP would be.¹⁹

The mechanisms in the obese are excessive visceral fat accumulation, which causes adipose tissue dysfunction. Adipocyte hypertrophy and hyperplasia exacerbated inflammation, impaired extracellular matrix remodeling and fibrosis, and altered secretion of adipokines. Adipose tissue influences many other organs by releasing pro-inflammatory and anti-inflammatory bioactive molecules, known as adipokines. Adipose tissue can produce a huge variety of adipokines, pro-inflammatory factors (leptin), cytokines (TNF- α , IL-6, IL-10), acute-phase reactants like C-reactive protein, chemokines, damage-associated molecular pattern molecules, and anti-inflammatory (adiponectin, ghrelin). It is associated with impaired mitochondrial function, membrane protein changes, and higher cell death and inflammation.^{19,20} Intra-abdominal fat cells are more active than other elsewhere fat cells, so they are more atherogenic and easily cause inflammation in the blood vessels. Also, the IL-6 secretion induces the liver to produce acute-

phase reactants such as C-reactive protein.¹³ This similar finding was also found in some studies which said that is a positive correlation between central obesity and hs-CRP serum level.^{12,15,21}

The limitation of this study was the lack of possibility of subjects suffering from metabolic syndrome and cancer disease. Furthermore, no analysis was done to know the relationship between IMT and hs-CRP research.

Conclusion

There was a correlation between waist circumference with hs-CRP serum levels, which showed that the greater the waist circumference, the higher the hs-CRP serum levels would be.

Conflict of Interest

The authors do not have any conflict of interest to declare.

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RESEARCH ARTICLE

Effect of ESAT-6 on Phagocytosis Activity, ROS, NO, IFN- γ , and IL-10 in Peripheral Blood Mononuclear Cells of Pulmonary Tuberculosis Patients**Dicky Santosa,^{1,2} Dida Achmad Gurnida,³ Herri S. Sastramihardja,⁴ Anas Subarnas⁵**¹Doctoral Study Program of Medical Sciences, Faculty of Medicine, Universitas Padjadjaran/Dr. Hasan Sadikin General Hospital, Bandung, Indonesia, ²Department of Child Health, Faculty of Medicine, Universitas Islam Bandung, Bandung, Indonesia, ³Department of Child Health, Universitas Padjadjaran/Dr. Hasan Sadikin General Hospital, Bandung, Indonesia, ⁴Department of Pharmacology, Faculty of Medicine, Universitas Islam Bandung, Bandung, Indonesia, ⁵Department of Pharmacy and Clinical Pharmacy, Faculty of Pharmacy, Universitas Padjadjaran, Sumedang, Indonesia**Abstract**

Tuberculosis (TB) is an infectious disease caused by *Mycobacterium tuberculosis* (MTB) that lives intracellularly. MTB can inhibit lysosomal enzymes and phagolysosomal fusion, which is challenging to eliminate. These are due to ESAT-6/CFP-10 originating from the RD1 region genome that expresses the Esx-1 type VII secretion system. Esx-1 encodes Esx-A (ESAT-6) and Esx-B (CFP-10), potential vaccine candidates still under research and development. ESAT-6/CFP-10 is predicted to affect macrophage phagocytic activity, IFN- γ , ROS/NO, and IL-10 levels. Several studies have begun to focus on the ESAT-6 antigen due to the high levels of ESAT-6 antibody found in pleural effusion and granuloma fluid. They can last up to 1 year compared to CFP-10 in experimental animals. This study aimed to analyze the effect of ESAT-6 on the phagocytic activity of macrophages, ROS/NO, IFN- γ , and IL-10 in peripheral blood mononuclear cells (PBMCs) cultures of pulmonary TB patients. It is experimental laboratory research with a post-test-only control group design with PBMCs from October 2019 to December 2020 in the Aretha Laboratory Bandung. There were two groups: the negative group (without ESAT-6) and the positive group (with ESAT-6). Six subjects were sampled at the Pindad Hospital in Bandung, and the research was carried out at the Aretha Laboratory in Bandung. Statistical analysis using paired t test. There was a significant difference between the negative and positive groups ($p < 0.05$). ESAT-6 can decrease macrophage phagocytic activity, intracellular ROS/NO, and IFN- γ but increase IL-10 levels.

Keywords: ESAT-6, IFN- γ , IL-10, macrophages, *Mycobacterium tuberculosis*, NO, ROS**Introduction**

Tuberculosis (TB) is an infectious disease caused by *Mycobacterium tuberculosis* (MTB), which usually affects the lungs.¹⁻⁴ *Mycobacterium tuberculosis* is an intracellular bacteria that lives and reproduces in macrophages cells and can withstand lysosomal enzymes and inhibit phagolysosomal fusion—making it difficult to eliminate due to the presence of early secretory antigenic target-6 (ESAT-6) and culture filtrate protein-10 (CFP-10). In a dormant state, they can hide in cells for long periods without being tracked by the immune system, making the global eradication of MTB very difficult.⁵ Prevention efforts in the form of BCG immunization are the most effective intervention in controlling TB disease. However, it has not been able to provide an optimal protective effect. The weakness of BCG is the loss of the genome region RD1 which

expresses the Esx-1 type VII secretion system, causing the protective effect is not maximal. Esx-1 encodes Esx-A (ESAT-6) and Esx-B (CFP-10), which are potential vaccine candidates that are still being researched and developed, and are used as markers of diagnostic of TB disease. ESAT-6 and CFP-10 are also virulence and pathogenicity factors for MTB which are predicted to cause cytolysis of alveolar epithelial cells and macrophages. The virulence mechanism and pathogenicity between ESAT-6 and CFP-10 are still being investigated but are predicted to drive the cytolysis of alveolar epithelial cells and macrophages.⁶ Several studies have begun to focus on the ESAT-6 antigen due to the high levels of ESAT-6 antibodies found in pleural effusions⁷ and granulomas.⁸ ESAT antibody levels can last up to 1 year compared to CFP-10 in experimental animals infected with MTB.⁹ Several studies using the ESAT-6 antigen in vitro on peripheral

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blood mononuclear cells (PBMCs) patients with TB showed an increase in IL-10 levels, while IFN- γ levels were still disputable.^{10,11} ESAT-6 is predicted to cause phagosome rupture so that MTB avoids elimination and translocates to the cytosol of macrophages.¹² ESAT-6 is predicted to be an MTB virulence factor that can inhibit macrophages in phagocytosis activity and inhibits the production of ROS/NO in eliminating MTB.¹³ ESAT-6 is an antigen that is predicted to induce IFN- γ but can inhibit the production of IFN- γ .¹¹ ESAT-6 can increase the production of IL-10.¹¹

This study aims to determine whether ESAT-6 can affect phagocytosis activity of macrophages, intracellular ROS/NO levels, IFN- γ levels, and IL-10 levels. The object used is peripheral mononuclear blood cells (PMBCs) cultures of adult active pulmonary TB patients *in vitro*.

Methods

This research is an experimental laboratory study with a post-test-only control group design with peripheral blood mononuclear cells (PBMCs) cultures in adult active pulmonary TB patients *in vitro* from October 2019 to December 2020 in the Aretha Laboratory Bandung. Subjects used in this study were adult active pulmonary TB patients from a national hospital in Bandung, Indonesia, who met the inclusion criteria. The inclusion criteria for this study were patients with active pulmonary TB aged >18 years, diagnosed for the first time, had not been able to receive anti-TB oral therapy, and had never been used as study subjects. Exclusion criteria were TB patients with severe malnutrition, liver disease, kidney disorders, heart disease, diabetes, malignancy, and HIV. The diagnosis of TB is made by a specialist in internal medicine based on clinical symptoms, chest x-ray, sputum, and rapid molecular tests. After establishing the diagnosis, we asked the patient to participate in the study. The subject data was recorded in the checklist, and a blood sample of ± 10 mL from the vein was taken. A total of ± 60 mL of blood from 6 patients from Pindad Hospital Bandung were brought to the Aretha Laboratory Bandung for research. The samples were divided into two groups: a negative control (NC) group (without induction) and positive control (PC) group (induced by ESAT-6). The PC group was induced by ESAT-6 first, then macrophages phagocytosis activity, intracellular ROS/NO, IFN- γ , and IL-10 levels were measured. The blood samples suspended into PBMCs were

cultured in RPMI 1640 media for five days, followed by phorbol 12-myristate 13-acetate (PMA) brand Biovision 1544-5 so that monocytes proliferate into macrophages. Into the 5-day-old PBMCs culture, added 5 $\mu\text{g/mL}$ ESAT-6 brand Abbexa/abx 169018 (except NC), incubated for 24 hours, and laboratory tests were carried out. ESAT-6 dose of 5 $\mu\text{g/mL}$ was determined based on reference and preliminary studies, which provide the most optimal proliferation of PBMCs cultures. In the macrophages phagocytosis activity test, latex beads suspension was added. They were incubated for 1–2 hours, then counted the number of macrophages cells that phagocytized latex particles. Intracellular ROS levels were measured using a DCFDA-cellular ROS detection assay kit (ab113851) reagent analyzed by flow cytometer. While the intracellular NO levels were analyzed using the Greiss method. IFN- γ levels were analyzed using the human IFN- γ ELISA kit reagent (Elabscience, E-EL-H0108). IL-10 levels were analyzed using the human IL-10 ELISA kit (430601). The univariate analysis consisted of a frequency distribution (mean, standard deviation) and the Shapiro-Wilk test (normally distributed sample data). The bivariate analysis conducted was paired t test to determine whether there were differences between groups. All statistical calculations were carried out using IBM SPSS Statistic software version 25. This study was approved by the Health Research Ethics Committee of the University of Padjadjaran with letter 1499/UN6.KEP/EC/2019.

Results

The research subjects came from six TB patients aged >18 years at Pindad Hospital Bandung, consisting of 3 male patients and 3 female patients based on inclusion criteria. The results of the comparison of NC and PC are shown in Table. There was a significant difference between NC and PC with $p < 0.05$. There was a decrease in the phagocytosis activity of macrophages, ROS, NO, and IFN- γ in PC compared to NC, as well as an increase in IL-10 levels in PC compared to NC.

Discussion

This study requires a large number of mononuclear cell samples from TB patients, considering that each well requires 5×10^5 cells, and analysis carried out as many as five tests. PBMC culture must produce mononuclear cells

Table Differences in the Mean Phagocytosis Activity of Macrophages, Intracellular ROS/NO, IFN- γ , and IL-10 in the NC and the PC Groups

PBMC Culture Sample	Phagocytosis Activity of Macrophage (Mean ^a ±SD)	Intracellular ROS (Mean ^a ±SD)	Intracellular NO (Mean ^b ±SD)	IFN- γ (Mean ^c ±SD)	IL-10 (Mean ^d ±SD)	T Test
NC	20.63±0.26	3.34±0.29	17.13±0.96	16.65±0.13	9.06±1.50	p<0.05*
PC	10.30±1.24	2.16±0.79	12.16±0.59	11.28±0.11	45.28±1.17	

Note: ^amean percentage; ^bmean concentration of NO ($\mu\text{mol}/\text{mL}$); ^cmean concentration of IFN- γ (pg/mL); ^dmean concentration of IL-10 (pg/mL); NC: negative control group without ESAT-6; PC: positive control group with ESAT-6; *paired t test, it means if p<0.05

according to research needs, then approximately six patients' blood samples are needed. TB, according to the inclusion criteria, is an in-vitro model. ESAT-6 was used as a model for the virulence and pathogenesis of MTB bacterial infection, based on previous studies. The dose of ESAT-6 was determined based on references and analysis results in the laboratory, where the optimal amount gave the highest proliferation index of PBMC cells.

Monocytes derived from PBMC cultured cells of TB patients were induced with PMA, so they differentiated into macrophages. The phagocytosis ability of macrophages was assessed using a fluorescence latex bead as a microorganism model to be phagocytosed by macrophages. The analysis of the phagocytosis activity of macrophages showed that the highest average percentage was in the NC group compared to the PC group. The most increased phagocytosis activity of macrophages in the NC group was due to the optimal phagocytosis ability of macrophages (innate immunity) because it came from peripheral blood, which was not directly infected by MTB. The phagocytosis activity of macrophages includes nonspecific cellular immunity. The phagocytosis activity of macrophages is stimulated by various stimuli such as microbes and their products, antigen-antibody complexes, inflammation, sensitized T lymphocytes, cytokines, and trauma. The most potent activating cytokine is IFN- γ . The activated macrophages have an increased number of lysosomes microscopically and produce and release chemical mediators (IL-1, IL-12) that are useful in activating lymphocytes and releasing other cytokines. The fluorescence latex bead binds to receptors on the surface of macrophages cells, stimulates, engulfs, and destroys them through respiratory burst killing. Antigen-

presenting cells (APC), together with MHC class I/II, stimulate macrophages to produce cytokines and chemokines to attract other cells to the site of infection.¹⁴

In the PC group in Table, there was a decrease in the average percentage of macrophages phagocytosis activity after ESAT-6 was induced. ESAT-6 is vital in phagosome rupture and MTB cytosolic translocation, which causes impaired phagocytosis activity. ESAT-6 secrets by MTB through Esx-1/Esx-A (type VII secretory system), which can inhibit phagosome maturation. They damage the phagosome membrane, so these bacteria escape the elimination process by phagolysosomes and can cause macrophages' death.¹² In a study by Houben et al.¹⁵ using cryo-electron microscopy, MTB, and *Mycobacterium leprae* could translocate from phagolysosomes into the myeloid cell's cytosol, as well as ESX-1-mediated entry of mycobacterial cytosol. It depends on the secretion of ESAT-6 and CFP-10 as mycobacterial virulence. Simeone et al.¹⁶ showed that *Mycobacterium marinum* and wild-type MTB strains could induce phagosome rupture and translocate to the cytosol. Whereas *Mycobacterium marinum* and MTB secreted low levels of ESAT-6 and BCG could not induce phagosome rupture and translocated to the cytosol. ESAT-6 is predicted to inhibit the acidification and maturation of phagolysosomes by lowering the pH and inhibiting the accumulation of ATP and GTP vacuolar enzymes in macrophages.¹³ Phagocytosis activity of macrophages (chemotaxis, adhesion, ingestion, degranulation), formation of lysosomal membranes, phagocytosis vacuoles, phagolysosomal fusion, phagolysosomal maturation, phagolysosomal acidification, and a mechanism of suppression burst killing (producing ROS and NO) requires the activation

of cytokines, especially IFN- γ which is produced mainly by CD4+ (Th1) T cells. Decreased phagocytosis activity of macrophages could also be caused by reduced levels of IFN γ and increased levels of IL-10 after ESAT-6 induction.¹¹

Levels of PMA induction on PBMC cells, besides stimulating monocyte differentiation into macrophages, also stimulated macrophages to produce ROS and RNI in the NC group. Due to innate immunity, intracellular ROS levels in NC were higher than in PC. NC macrophages cells are derived from the peripheral blood of TB patients and do not experience direct infection compared to pulmonary macrophages cells. NADPH-oxidase produces ROS in macrophages activated by cells undergoing inflammation, injury, and infection by bacteria or viruses, as well as IFN- γ and TLRs (in this study, induced by PMA as a control). ROS will reduce oxygen molecules to H₂O₂ (respiratory burst killing).¹⁷

In the PC group in Table, which ESAT-6 had induced, the intracellular ROS levels decreased. Therefore, ESAT-6 is predicted to inhibit intracellular ROS levels. Mahesh et al.¹⁸ found that cofilin is an actin-depolymerizing protein or actin filament, which plays an essential role in phagocytosis, phagosome acidification, and phagolysosomal fusion in macrophages cells, decreased levels due to ESAT-6 produced by MTB. Decreased cofilin levels due to ESAT-6 can reduce intracellular ROS levels in macrophages. The study of Seghatoleslam et al.¹⁹ in Th1 cells and human macrophages induced by ESAT-6 and the combination of ESAT-6/CFP-10 showed a decrease in intracellular NO and ROS levels. ROS produced by NADPH phagocyte oxidase also induces the iNOS pathway (producing NO).¹⁷ The reduction in ROS levels will affect a decrease in nuclear factor kappa-light-chain-enhancer of activated B cells (NF- κ B) transcription, which plays a role in the expression of iNOS levels, causing a decrease in intracellular NO levels. ESAT-6 is predicted to induce macrophages cell apoptosis which is seen in decreased phagocytosis activity and decreased levels of intracellular ROS in the PC group.¹⁹ The interruption in the acidification process of phagolysosomes and lysis of lysosomal membranes, decreased levels of IFN- γ , and increased levels of IL-10 after ESAT-6 induction, caused a decrease in ROS levels.

Levels the results of the analysis of NO levels showed in Table, in which the highest mean concentration was found in the NC group. The mean NO concentration in NC was higher than

in PC and the intervention group, due to innate immunity, according to the macrophage's phagocytosis activity test and previous intracellular ROS levels. NC macrophages cells are derived from the peripheral blood of TB patients and do not experience direct infection compared to pulmonary macrophages cells. iNOS produce NO in macrophages that are activated by increased levels of ROS. ROS activates NF- κ B. This protein complex regulates DNA gene transcription and plays an essential role in the immune response against bacteria by inducing proinflammatory cytokines such as TNF- α , IL-12, IFN- γ , and iNOS.¹⁹ The iNOS enzyme will convert NO into RNI with the help of the NADPH-oxidase enzyme in the form of peroxynitrite (ONOO⁻), which can damage lipids, proteins, and bacterial DNA.¹⁴

In the PC group in Table, which ESAT-6 had induced, the mean of NO concentration decreased, so ESAT-6 was predicted to inhibit NO levels. The study by Xie et al.²⁰ on rat alveolar macrophages cells induced by ESAT-6/CFP-10 fusion showed a decrease in intracellular NO levels, which was predicted to be due to inhibition of macrophages cells proliferation, inhibition of NO production, and inhibition of apoptosis. The study conducted by Seghatoleslam et al.¹⁹ in Th1 cells and human macrophages induced by ESAT-6 or the combination of ESAT-6/CFP-10 showed a decrease in intracellular NO and ROS levels. ROS produced by NADPH-oxidase can also be caused by the iNOS pathway (producing NO). Decreased levels of ROS will affect the decrease in transcription of NF- κ B, which plays a role in the expression of iNOS levels, causing a reduction of intracellular NO levels. NO production requires the iNOS pathway, which ROS activates. In comparison, ROS is produced by NADPH oxidase, which involves the excretion of IFN- γ as an activator produced by Th1 cells. Therefore, the decrease in intracellular NO levels was caused by decreased levels of ROS, decreased levels of IFN- γ , and increased levels of IL-10 after ESAT-6 induction.

The results of the analysis of IFN- γ levels showed in Table that the highest mean concentration was in the NC group compared to the PC group. IFN- γ levels in NC are higher than in PC due to the natural immune response (innate immunity). NC macrophages cells are derived from the peripheral blood of TB patients and do not experience direct infection compared

to pulmonary macrophages cells. Macrophage cells in the NC group were derived from PBMC cells from TB patients, which differentiated into macrophages cells with the help of PMA as a control. PMA is often used as a promoter in research to activate protein kinase and NF- κ B enzymes for cell proliferation. Macrophages and T cells were stimulated to produce IFN- γ as a control.

In the PC group in Table, ESAT-6 induced a decrease in IFN- γ levels. ESAT-6 is predicted to inhibit IFN- γ levels. ESAT-6 can induce IFN- γ but can hinder IFN- γ production. Wang et al.²¹ found that ESAT-6 can decrease transcription of IFN- γ and reduce the activating transcription factor-2 (ATF-2) and c-Jun expression, which usually binds to the proximal IFN- γ promoter that stimulates mRNA expression in human PBMC cells. ESAT-6 can inhibit the production of IL-17 and TNF- α and increase the production of IL-2. ESAT-6 can directly inhibit T cell response to Ag MTB by interfering with the T cell receptor (TCR) signaling pathway in ZAP-70. Higher concentrations of ESAT-6 can directly inhibit the production of IFN- γ as a T cell response to MTB infection or can inhibit TCR activation by reducing T cell activation without affecting TCR signaling.¹¹ Kumar et al.²² demonstrated that induction of ESAT-6 in human mononuclear cells could reduce IFN- γ levels by downregulating MHC class II and binding to TLR2. While Abebe et al.¹¹ reported decreased levels of IFN- γ , TNF- α , and IL-10 during TB infection or close contact. They also said increased IFN- γ , TNF- α , and IL-10 in clinical TB during therapy 6–9 months after PBMC cells induced by ESAT-6/CFP-10 fusion. Wibowo et al.,²³ Bastian et al.,²⁴ and Marpaung et al.²⁵ reported no difference in IFN- γ levels after stimulation with ESAT-6/CFP-10 fusion in patients with active pulmonary TB and latent TB. It differs from Setiawan and Nugraha,²⁶ Safutri et al.,²⁷ and Prihantika et al.,¹⁰ where the levels of IFN- γ in PBMC cells with active TB were higher than in latent TB PBMC cells after being stimulated by ESAT6/CFP-10 fusion. The differentiation in results may be due to the different types and doses of antigens, the status of TB patients who are primarily malnourished, and the possibility of recurrent pulmonary TB disease. It was predicted because the T-cell immune response to ESAT-6 was more persistent in the long term than acute CFP-10. ESAT-6 is thought to have virulence and pathogenic effects that last longer than CFP-10.⁹ Decreased levels

of IFN- can be caused by an increase in IL-10, which also acts as an anti-inflammatory.¹¹ The reduction levels of IFN- γ can lead to decreased macrophages phagocytosis activity, inhibition of phagolysosomal acidification, inhibition of phagolysosomal maturation, reduced ability of suppression burst killing (reduced production of ROS and NO), inhibition of apoptosis and autophagy, inhibition of leukocyte aggregation to the site of infection, causing MTB to translocate to the cytosol, multiply in macrophages cells (dormant), and can spread if macrophages cells die so that MTB infection becomes difficult to eradicate.

The results of the analysis of IL-10 levels showed in Table, that the highest mean concentration was in the PC control group compared to the NC. In the PC group that ESAT-6 had induced, there was an increase in the average concentration of IL-10 levels. Various studies have been carried out which prove that IL-10 levels have increased in patients with active pulmonary TB. Research by Abebe et al.,¹¹ Setiawan and Nugraha,²⁶ Fatima et al.,²⁸ and Prihantika et al.,¹⁰ found an increase in IL-10 levels in PBMC cells of patients with active pulmonary TB after ESAT-6/CFP-10 induction. The growth in IL-10 after being induced by ESAT-6 is predicted to be due to a shift from Th1 to Th2 due to decreased CD4+ T cell proliferation,^{10,26} and regulatory T cells (Tregs) which act as suppressor T cells are involved in increasing IL-10 production.^{10,11} IL-10 is produced mainly by Th2 cells, regulatory T cells (suppressor T cells/Tregs), macrophages, Th17 cells, B cells, neutrophils, and some dendritic subsets. The shift in the balance of Th1 cells to Th2 cells is predicted to be caused by increased levels of IL-10, mainly produced by Th2 cells. Macrophage cells also produce IL-10 through programmed cell death protein 1 (PD1) to reduce apoptosis and stimulate Tregs to secrete IL-10 due to decreased production of CD4+ cells.²⁹ Safutri et al.²⁷ showed an increase in IL-4 In PBMC cells of active TB patients after being induced by ESAT-6/CFP-10. IL-4 is a cytokine mainly produced by Th2 cells, which is also predicted to shift from Th1 cells to Th2 cells. Regulatory T cells (suppressor T cells/Tregs) are a type of T cell that can suppress the immune system, significantly inhibiting the proliferation of CD4+ and CD8+ (Th1) by producing anti-inflammatory cytokines such as IL-10. Stringari et al.³⁰ study in PBMC cells with active TB patients showed an increase in the population of Tregs cells compared to PBMC cells in healthy people.

The increase in IL-10 levels was thought to be due to a decrease in IFN- γ levels after ESAT-6 induction. IL-10 is an anti-inflammatory cytokine or human cytokine synthesis inhibitory factor (CSIF), mainly produced by Th2 cells, Tregs, macrophages, B cells, neutrophils, and some subsets of dendritic cells. IL-10 can inhibit MHC class II, inhibit the proliferation of CD4+ T cells that differentiate into Th1 cells, and inhibit IL-12 excretion so that IFN- γ production decreases.¹⁴ IL-10 can inhibit macrophages' phagocytosis activity and phagolysosomal maturation and reduce ROS/NO, facilitating MTB's survival, virulence, and pathogenicity.

The limitation of this study is conducting in-vitro research, which uses PBMC cells of patients with active pulmonary TB outside the patient's body, which may have a different effect from the actual situation. In addition, in this study, we did not use MTB bacteria directly but only used ESAT-6 as a model for the virulence and pathogenicity of MTB in PBMC cells of active pulmonary TB patients, so it might give different results if the study was carried out directly either in-vivo or directly on patients with active pulmonary TB.

Conclusions

Virulence and pathogenicity of the ESAT-6 antigen can cause a decrease in macrophages phagocytosis activity, a decrease in intracellular macrophages ROS/NO, a reduction in IFN- γ , and an increase in IL-10 levels in PBMC cells with active pulmonary TB in vitro. There were significant differences in macrophages phagocytosis activity, intracellular RO/NO levels, ROS levels, and IL-10 levels after ESAT-6 induction in PBMC cultures of adult active pulmonary TB patients. Therefore, ESAT-6 is the primary vaccine candidate that should be added to the BCG vaccine. However, further research is needed on the effects of ESAT-6 in vivo.

Conflict of Interest

There was not a conflict of interest in this article.

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RESEARCH ARTICLE

Relationship of Vitamin D Intake with Obesity in Adolescents

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Abstract

Vitamin D deficiency is a problem worldwide, with the primary source of it being sun exposure, which activates the skin's vitamin D substrate. A diet lacking in vitamin D can put people at risk for obesity. The study aimed to determine the relationship between the risk of vitamin D deficiency and obesity in adolescents in Surabaya. It is a case-control research design conducted from March 2018 to January 2019 in a private university in Surabaya, East Java. Respondents were 200 students divided into two groups. The data collection method used the Food Frequency Questionnaire with Spearman correlation analysis to determine the relationship between vitamin D intake and obesity. The results are that the relationship between intake of vitamin D in food and obesity was very strong (0.816). The comparison between the two groups of respondents was 0.666, indicating that the non-obese group had an increased risk of vitamin D deficiency by 0.6 times compared to the obese group. There was a significant relationship between vitamin D intake in food and obesity. It is necessary to investigate further the intake of other foods and the factors that influence obesity in students.

Keywords: Food Frequency Questionnaire, obesity, students, vitamin D

Introduction

Vitamin D deficiency is a problem of concern today. The primary source of vitamin D is sun exposure, which activates the skin's vitamin D substrate. Sub-tropical and tropical countries show a high prevalence of vitamin D deficiency.¹ Vitamin D deficiency occurs not only in areas with less sunlight intensity but also in sub-tropical and tropical areas.² The prevalence of vitamin deficiency in South Asia is estimated to be around 70%, and in Southeast Asia, this figure varies between 6–70% depending on skin color, age, and habits of avoiding sun exposure.^{1,2}

In tropical countries in Asia, such as Indonesia, the need for sunlight should be sufficient, but it is estimated that the prevalence of vitamin D deficiency reaches 63%.³ Data on the prevalence of vitamin D deficiency in various countries varies widely.² Modernization also brings changes in lifestyle and diet to be low in vitamin D. In addition, increased pollution prevents sunlight from reaching the earth, blocking sun exposure on human skin.⁴ Asian people's daily behavior can also be associated with vitamin D deficiency. The classic beauty standard causes white people to look more beautiful than dark-skinned people. So that most Asian people choose to protect their skin from sun exposure with sunscreen, which

can prevent sun exposure to the skin.¹

According to the Regulation of the Minister of Health of the Republic of Indonesia in 2019,⁵ vitamin D's nutritional adequacy rate (recommended dietary allowances, RDA) is 15 mcg. Vitamin D deficiency can be one of the causes of various chronic diseases.⁶ Vitamin D is associated with multiple diseases such as cancer, hypertension, diabetes mellitus, and the increasing incidence of obesity.⁷ Low levels of vitamin D in the body are generally suffered by adolescents who are obese.³ Obesity is one of the most common health problems in modern times. Obesity is an abnormal or excessive fat accumulation that can interfere with health.⁸

Adolescents, including students, are most at risk of unhealthy lifestyles.⁹ A student usually has a reasonably high level of education but tends to have limited physical activity,¹⁰ and low vitamin D levels.¹¹ An unhealthy lifestyle, including an unhealthy diet, also triggers obesity. Many students also experience obesity.¹²

Adolescents are vulnerable to malnutrition due to unhealthy eating patterns and require higher nutrients due to increased physical growth.¹³ Excessive eating habits in adolescents without paying attention to the intake of nutrients consumed, especially energy intake.¹² The study stated that 90% of people who are obese also

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experience vitamin D deficiency. Research also shows that subjects given additional vitamin D will experience decreased appetite and weight loss.¹⁰ Modern lifestyles such as excessive eating patterns and limited physical activity will trigger obesity, which also causes low levels of vitamin D in the blood. Excess body weight that causes obesity can cause a decrease in the bioavailability of vitamin D from the skin and food because it accumulates in body fat.¹⁴ Although a high intake of dietary nutrients can cause weight gain, proper and healthy nutritional intake can increase vitamin D levels in the blood. Calcium and vitamin D intake can affect body weight, but this still requires further research and will depend on a person's healthy lifestyle.¹⁴

Related to the problem of low vitamin D levels in obese people, they may not consume enough foods that contain vitamin D. Vitamin D intake was assessed through the Food Frequency Questionnaire (FFQ) form. The advantage of FFQ compared to other methods is that it can provide a qualitative description of the frequency of food consumption patterns within a certain period. FFQ can be used to assess the condition of vitamin D intake validly.^{15,16}

This study aimed to determine the relationship between the risk of deficiency in intake of foods containing vitamin D and obesity in adolescents in Surabaya.

Methods

The design used a case-control research design conducted from March 2018 to January 2019. This research received an ethics certificate No. 034/KE/I/2018 from Universitas Surabaya.

The variable was the frequency of foods containing vitamin D. The frequency of foods containing vitamin D was the amount of vitamin D intake from food and beverages that were often consumed by respondents and measured using FFQ.^{15,16}

The population used in this study were students (18–25 years old) from a private university in Surabaya, East Java. The respondents in this study were obese (BMI=27.0 kg/m²),¹⁷ and non-obese (BMI<27.0 kg/m²) students. The criteria are willing to become research respondents and not on a special diet (diet for chronic diseases and a strict vegetarian diet, as well as in a program to gain or lose weight). The sampling technique used was purposive sampling. The sample size

was 100 people for each group.

The data collection process was first the preparation of the FFQ (containing: a list of foods, the frequency of food at a specific time, and the portion of food consumed). This questionnaire began with determining a list of foods containing vitamin D. The frequency of eating was calculated by how many times the food has been consumed per day, week, and month. Meanwhile, the food portion was calculated based on the household size of each food;¹⁸ Secondly, we conducted a preliminary study to determine the types of food available and commonly consumed by the community around the research location. This preliminary study conducted interviews with 20 respondents. Foodstuffs that had never been or were not widely consumed are excluded from the list; Third, finalizing the list of foods to be used in the FFQ. Then an interview was conducted by exploring the foods often consumed by the respondents, asking about the frequency and portion, and recording it on the FFQ.

The data were processed using a NutriSurvey and determining the difference in the frequency of foods containing vitamin D in obese and non-obese students. Statistical analysis was carried out using SPSS for windows version 24.0. Spearman correlation test was conducted to determine the relationship between vitamin D intake and the risk of obesity (ordinal data scale). The odds ratio was used to compare the risk of deficiency related to the intake of foods containing vitamin D in obese (BMI=27.0 kg/m²) and non-obese students (BMI<27.0 kg/m²).

Results

Data were collected by conducting interviews with research subjects of obese and non-obese student groups, with each group having 100 respondents.

Table 1 describes the distribution of the respondent's age, gender, and body mass index (BMI). Based on gender, in the non-obese group, there were 22% (22 people) male and 78% (78 people) female, while respondents in the obesity category were male 31% (31 people) and female 69% (69 people).

Foods that contain vitamin D most who consumed two groups of respondents are eggs (20 SI D3 and D2), milk (100 SI/240 mL D3), cheese (100 SI/85 gram), catfish, fish, and shrimp (100 SI D3, Table 2).

From Table 3, the correlation coefficient was

Table 1 Characteristics of Respondents

Characteristics	Groups			
	Non-obese		Obese	
	n=100	%	n=100	%
Gender				
Male	22	22	31	31
Female	78	78	69	69
BMI (kg/m ²)				
Thin (<18.50)	2	2		
Normal (≥18.5–<24.9)	86	86		
Overweight (≥25.0–<27.0)	12	12		
Obesity (≥27.0)			100	100

0.816. It means that the level of strength of the relationship (correlation) between intake of vitamin D in food and obesity was very strong (>0.01). Therefore, when vitamin D intake is increased, the risk of obesity decreases. In addition, the significant value was 0.000 (p value<0.05), which means that there was a significant relationship between vitamin D intake in food and the risk of obesity.

The results of the analysis of vitamin D adequacy in the non-obese and obese respondent groups can be seen in Table 4. The non-obese group with a vitamin D deficit was 83% (83 people) and 88% (88 people) in the obese group. The data was analyzed using the prevalence odds ratio test to calculate the risk of vitamin D deficiency among the non-obese and obese groups.

The risk comparison between the two groups of respondents can be observed from the prevalence odd ratio (POR) value. The odd ratio (OR) value was 0.666 with a significant 95% CI of 0.300–1.478, indicating that the non-obese group of respondents had an increased risk of vitamin D deficiency by 0.6 times compared to the obese respondent group. In other words, it can be interpreted that the non-obese group had 1.6 times less at risk than the obese group (Table 4).

Discussion

In this study, the respondents included in the study were students. Healthy adolescents are still at risk for vitamin D deficiency. Daily vitamin D intake in young adults was often below the recommended intake of 200 international units (IU) per day. In Indonesia, the daily vitamin

D requirement for ages 18–25 is 15 mcg.⁶ The increasing use of sunscreens to reduce skin damage or cancer reduces or eliminates skin vitamin D synthesis.¹⁹

The respondents involved in this study were 200 people. Gender factors affect nutritional needs. Generally, men need more nutrients than women.²⁰ This study used respondents in the age range of 18–25 years which was included in the category of late teens. Based on previous research, young adults or adolescents were known to be at risk for vitamin D deficiency which was influenced by habits such as consuming vitamin D below the recommended limit per day and lack of outdoor physical activity.²¹

Respondents involved in this study consisted of non-obese and obese groups. Obesity was a risk factor for vitamin D deficiency.^{7,10} Research has shown that an increase in BMI was associated with lower levels of 25-hydroxyvitamin D (25D), the active form of vitamin D in the body.^{19–21} The mechanism of vitamin D deficiency in obese patients included high-fat accumulation resulting in a decrease in the bioavailability of vitamin D in the body due to the fat-soluble nature of vitamin D, causing a reduction in the release of vitamin D from fat into the systemic circulation.^{22,23}

There are two pathways for vitamin D intake: the first comes from food and beverages consumed. The second is the biosynthetic pathway for provitamin D to become vitamin D with the help of sunlight on the skin. The two tracks had a relationship because the skin has a biosynthetic path with the sun's UV rays that will be able to take place if the body has provitamin D fundamental ingredients obtained from the food we eat. Likewise, the opposite effect will be observed if there is no source of food containing

Table 2 Frequency of Foods Containing Vitamin D that Most Consumed by Respondents

Type of Food	Frequency		Groups				Total	
			Non-obese		Obese		n=200	%
			n=100	%	n=100	%		
Egg	Daily	1×	7	7	7	7	14	7.0
	Weekly	1-3×	25	25	16	16	41	20.5
		4-6×	64	64	71	71	135	67.5
		Monthly	1×	2	2	2	2	4
	Never	>1×	1	1	2	2	3	1.5
		1	1	2	2	3	1.5	
Milk	Daily	1×	57	57	59	59	116	58.0
	Weekly	1-3×	21	21	22	22	43	21.5
		4-6×	10	10	13	13	23	11.5
		Monthly	1×	5	5	0	0	5
	Never	>1×	5	5	0	0	5	2.5
		2	2	6	6	8	4.0	
Cheese	Daily	1×	1	1	3	3	4	2.0
	Weekly	1-3×	12	12	13	13	25	12.5
		4-6×	4	4	7	7	11	5.5
		Monthly	1×	40	40	31	31	71
	Never	>1×	10	10	9	9	19	9.5
		33	33	37	37	70	35.0	
Catfish	Weekly	1-3×	46	46	63	63	109	54.5
		4-6×	8	8	2	2	10	5.0
		Monthly	1×	1	1	4	4	5
	Never	>1×	2	2	7	7	9	4.5
			43	43	24	24	67	33.5
Milkfish	Weekly	1-3×	10	10	23	23	33	16.5
		4-6×	1	1	0	0	1	0.5
		Monthly	1×	20	20	14	14	34
	Never	>1×	0	0	6	6	6	3.0
			69	69	57	57	126	63.0
Indonesian salted-boiled fish (<i>pindang</i>)	Weekly	1-3×	31	31	39	39	70	35.0
		4-6×	2	2	2	2	4	2.0
		Monthly	1×	13	13	13	13	26
	Never	>1×	9	9	12	12	21	10.5
			45	45	34	34	79	39.5
Shrimp	Weekly	1-3×	13	13	57	57	70	35.0
		4-6×	33	33	4	4	37	18.5
		Monthly	1×	11	11	4	4	15
	Never	>1×	3	3	8	8	11	5.5
			40	40	27	27	67	33.5

Table 3 Relationship of Vitamin D Deficiency Related to Vitamin D Consumption

Vitamin D Status	Groups				Total n=200	Spearman	
	Non-obese		Obese			Correlation Coefficient	Sig. (2-tailed)
	n=100	%	n=100	%			
Deficiency	83	41.5	88	44.0	171	0.816	0.000
Adequate	17	8.5	12	6.0	29		

Table 4 Risk of Vitamin D Deficiency Related to Vitamin D Consumption

Vitamin D Status	Groups				Total n=200	Odd Ratio	
	Non-obese		Obese			POR	Conclusion
	n=100	%	n=100	%			
Deficiency	83	41.5	88	44.0	171	0.666	The non-obese group had a 0.6-fold risk of vitamin D deficiency compared to the obese group
Adequate	17	8.5	12	6.0	29		

vitamin D. The body will still lack vitamin D because there are no ingredients that will be used as vitamin D. Vitamin D obtained from food before use needs to be metabolized to become the active form. At the same time, vitamin D obtained from sunlight needs to be synthesized first by the skin and then processed in the body to produce an active form of vitamin D. Both states require sunlight to convert it into provitamin cholecalciferol (D₃) and vitamin ergocalciferol (D₂). Vitamin D₃ forms in the skin by ultraviolet light from 7-dihydro cholesterol. The amount of provitamin D and the active ingredients developed depends on the intensity of ultraviolet radiation, skin pigmentation, use of sunscreen, and the length of time exposed to sunlight.^{22,23}

Vitamin D was absorbed in the small intestine along with lipids with the help of bile and transported by D-plasma binding protein (DBP) to storage sites in the liver, skin, brain, bones, and other tissues. The process of vitamin D metabolism first begins in the liver. Vitamin D precursors, with the help of vitamin D-25-hydroxylase (25-OHase), are converted into 25-hydroxyvitamin D₂ and D₃. It will then be converted in the kidneys to 1,25-dihydroxyvitamin D with the help of the 25-hydroxyvitamin D-1 α -hydroxylase (1-OHase);²⁴ where the addition of two hydroxyl groups at the position so that it becomes an active form and functions to absorb calcium in the intestine. Increasing the amount of 1,25-dihydroxy vitamin D will affect 25-hydroxyvitamin D-24-hydroxylase (24-OHase) to catabolize 1,25-dihydroxy vitamin D and 25-hydroxyvitamin D to calcitric acid, an inactive and water-soluble form so that can be excreted outside the body. Provitamin D comes from animals to form 1,25-dihydroxycholecalciferol, also known as calcitriol. If it is extracted from plants, it forms 1,25-dihydroxy ergocalciferol or ercalcitriol. Calcitriol in the small intestine increases the absorption of phosphorus and calcium.

Parathyroid hormone is needed to stimulate the production of 1,25-dihydroxycholecalciferol by the kidneys. This hormone is released when the amount of calcium in the blood is low, affecting the increase in calcitriol synthesis carried out by the kidneys.²⁵

In the liver, the vitamin D₃ molecule is converted to 25-hydroxyvitamin D₃ (25(OH)D₃), the serum's most stable and abundant vitamin D metabolite. It has traditionally been used as a biomarker for individual vitamin D status. Further hydroxylation at carbon one yields 1 α ,25-dihydroxy vitamin D₃ (1,25(OH)₂D₃), which acts as an endocrine hormone as a high-affinity ligand to the transcription factor vitamin D receptor (VDR). The primary source of endocrine production of 1,25(OH)₂D₃ is the proximal tubular cells of the kidney. In a paracrine or autocrine fashion, monocytes, macrophages, and dendritic cells of the innate immune system, osteoblasts in bone, and skin keratinocytes are also capable of producing the hormone.²⁶

Factors that influence obesity are nutritional factors, physical activity, and genetic factors. The role of nutrition begins in the womb. The mother's weight affects the body fat and the baby's growth. Obese people have a higher average energy intake than non-obese people. Adolescents with high energy intake are 4.69 times more likely to be obese than adolescents with sufficient energy intake. Likewise, the input of fat and carbohydrates shows that most obese adolescents have an average intake of more. Adolescents with more fat and carbohydrate intake have a two times greater risk of being obese than adolescents with sufficient fat and carbohydrate intake.²⁷

The physical activity level of obese adolescents is lower when compared to non-obese adolescents—people who are less active need fewer calories than highly engaged people. Someone whose life is less active (sedentary life) or does not do a balanced physical activity and consumes foods high in fat will tend to be

obese. A lifestyle that lacks physical activity will affect a person's body condition. Physical activity is needed to burn energy in the body. If the energy intake is excessive and not balanced with balanced physical activity, it will make it easier for someone to become fat.²⁸

The results showed that adolescents with fathers and mothers with obese status had a greater risk of becoming obese than those with fathers and mothers who were not obese. Families pass on dietary habits and lifestyles that can contribute to the incidence of obesity. Families share the same food and physical activity habits, so the relationship between genes and the environment is mutually supportive.^{28,29}

Food frequency is a method to obtain qualitative food consumption data and descriptive information about consumption patterns. However, the FFQ can also be used to assess food consumption quantitatively. In practice, the frequency of food is often met with questions for respondents in the form of two main components: the list of foods and the frequency of food use. In the food frequency approach, the principle is that the relationship between food intake and the onset of reactions results from the long-term average intake starting from weekly, monthly to yearly. Using this method, it is also possible to know the value of using a particular food or food group (for example, a source of fat, a source of nutrition, a source of vitamin D, etc.).³⁰ Suggestions for further research are on the measurement of BMI. It is ideal because the body weight measurement should be done when waking up and adding a parameter of a serum 25(OH)D examination to determine vitamin D levels.

Conclusions

There was a significant relationship between vitamin D intake in food and the risk of obesity. Non-obese had an increased risk of vitamin D deficiency compared to obese.

Conflict of Interest

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

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RESEARCH ARTICLE

Association between Chronic Inflammation of Basal Plate and Decidua Existences with Placenta Accreta Spectrum

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Abstract

The placenta accreta spectrum (PAS) is an abnormal placenta condition with a high level of morbidity and mortality in both the mother and fetus. The PAS has a multifactorial etiology, one of which is a chronic inflammation of the basal plate (CIBP) and the decidua existences (DE). The study aims to analyze the association between CIBP and DE with PAS. It was an analytical observational with a cross-sectional study design on 50 placentae (25 PAS paraffin block, 25 standard placenta samples) from Dr. Hasan Sadikin General Hospital and other health centers that meet the inclusion and exclusion criteria. The data are taken from PAS patients from January 2015–December 2020. All samples will be stained with hematoxylin-eosin (HE), then undergo histopathological examination. The result of the studies analyzed statistically using Fisher's exact. CIBP in PAS was found in 21/25 cases, while in the normal placenta was found in 16/21 patients. The DE is positive in 15/25 cases of PAS, whereas the normal placenta was found in all cases. The association between CIBP and PAS is insignificant statistically ($p=0.19$), while the DE showed a significant relationship with PAS ($p=0.00$). The presence of the decidua is related to the regulation of trophoblastic invasion into the myometrium in PAS cases. CIBP can occur due to the reaction of decidua tissue to trophoblastic invasion or an infectious agent. The pathogenesis of PAS needs further understanding so that the appropriate therapy can be found for its prevention and management.

Keywords: Decidua, inflammation, placenta accreta spectrum

Introduction

The placenta accreta spectrum is defined as an abnormal attachment of the placenta to the myometrium with the varying invasion of trophoblastic. It is divided into three categories: 1) the attachment of the trophoblastic into the surface of the myometrium (placenta accreta), 2) trophoblastic invasion into the myometrium (placenta increta), 3) trophoblastic invasion through the entire thickness of the myometrium from the serous layer to the surrounding intraabdominal organs (placenta percreta).^{1,2}

PAS has increased tenfold worldwide in the last 50 years,^{3–5} showing an incidence of 3 in 1,000 pregnancies in the previous ten years.³ The PAS causes significant morbidity and mortality associated with postpartum hemorrhage.^{4,5} Wu et al.⁶ reported an increase in the incidence of PAS from 1:2,150 in 1994 to 1:533 in 2005. However, this incidence has increased to three per 1000 births in the last decade and is in line with the increasing rate of cesarean sections.^{3,7–9}

Maternal morbidity on PAS is reported to reach 60%, including hysterectomy, the need for blood transfusion, and prolonged stay with mortality exceeding 7%. In addition, the incidence of perinatal complications is increasing due to premature birth, low birth weight, and inadequate gestational period, which increases the need for neonatal intensive care unit (NICU) and resuscitation.^{10–12}

The PAS is a multifactorial process. The underlying molecular mechanism is not widely known. Several hypotheses regarding the formation of PAS reveal that the disorder's pathogenesis is caused by a decidual defect and excessive invasion of trophoblast cells into the myometrium.¹³ The underlying etiology is not clearly understood. Still, interactions between decidua tissue on the basal lamina, inflammatory cells, and extravillous trophoblast cells (EVT) are thought to be involved in developing PAS. Several studies have reported the relationship between pathological conditions on the basal plate and PAS.¹⁴

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Prior studies have shown that PAS is formed due to the failure of normal decidua formation, an endometrial defect, or a failure that changes the endometrium to decidua. In the absence of the typical decidua plate and Nitabuch layer, the villous trophoblast has direct access to the myometrium. Trophoblast migration and infiltration during normal placental development are affected by autocrine or paracrine behavior by various types of molecules such as growth factors and their receptors, cytokines, hormones, adhesion molecules, and enzymes. The decidua existence is thought to prevent abnormal placental formation by providing autocrine or paracrine regulation.^{15,16}

This study is focused on examining the association between chronic inflammation of the basal plate and decidua existences with PAS.

Methods

This research was an analytical observational study with a cross-sectional study design. The subjects of this study consisted of 50 placental samples (25 samples in the form of PAS paraffin blocks, 25 samples from normal pregnancies) from Dr. Hasan Sadikin General Hospital and other health centers that meet the inclusion and exclusion criteria. The data are taken from PAS patients from January 2015–December 2020. Data collection was carried out after an ethical review was received. The characteristics of the research subjects were obtained from patient's medical records, using purposive sampling as its research sample method. Tracing was done to placental paraffin blocks of patients with PAS, then underwent histopathological preparations in Dr. Hasan Sadikin Hospital Bandung. Meanwhile, placentas obtained from normal pregnancies as controls were prepped into paraffin blocks and histopathological preparations in the Clinical Laboratory of Universitas Islam Bandung. All samples were stained with hematoxylin-eosin (HE) and were examined histologically to assess the presence of decidua and chronic inflammation on the basal plate using an Olympus CX 21 LED light microscope at 200× and 400× magnification. Histopathological assessment was performed double-blind by two anatomical pathologists. Data of this study will be analyzed statistically using Fisher's exact to determine the association between the two variables. This study received its ethical approval from the Research

Ethics Committee of Universitas Padjadjaran with the number 777/UN6.KEP/EC/2021.

Results

The numbers of patients were 25 patients who had been diagnosed histopathologically with placenta accreta, increta, and percreta. Placenta accreta is characterized by the attachment of chorionic villi to the myometrium without interference by the decidua or fibrinoid tissue. In contrast, placenta increta is diagnosed when the chorionic villi infiltrate the myometrium. Placenta percreta is defined as the presence of chorionic villi infiltration throughout the thickness of the myometrium or serous layer (Figure 1). In addition, the placentas from patients with uncomplicated pregnancies collected from 25 patients from various hospitals were used as controls.

In this study, observations under the microscope were made on all samples. The Table presents data from histopathological examination to assess the presence of decidua and chronic inflammation of the basal plate on hematoxylin-eosin stained PAS and normal placentas.

The Table shows that basal plate inflammation in PAS is found in 21/25 cases. Decidua basalis is found in 15 cases of PAS in this study. Sixteen cases had signs of inflammation of the basal plate in the normal placenta, while all cases with normal pregnancies show the presence of decidua. The table above shows an insignificant association between basal plate inflammation and PAS statistically, while the decidua existences had shown statistical significance with PAS. The ratio of the presence of decidua in the PAS group is significantly different, with $p=0.00$.

Discussion

In this study, CIBP in PAS (Figure 2) did not significantly differ from normal pregnancies. Chronic inflammation of the placenta can be caused by cytomegalovirus, *Toxoplasma gondii*, and *Treponema pallidum*, although most chronic inflammation lesions are proven caused by non-infectious factors.¹⁷ Chronic inflammation of decidua (deciduitis) is diagnosed by the presence of lymphocytes and plasma cells in the basal plate that has an incidence of 1–4% of unknown etiology. In this study, CIBP in PAS may represent an immune response at the fetal and maternal interface. It may be found as a basal plate reaction

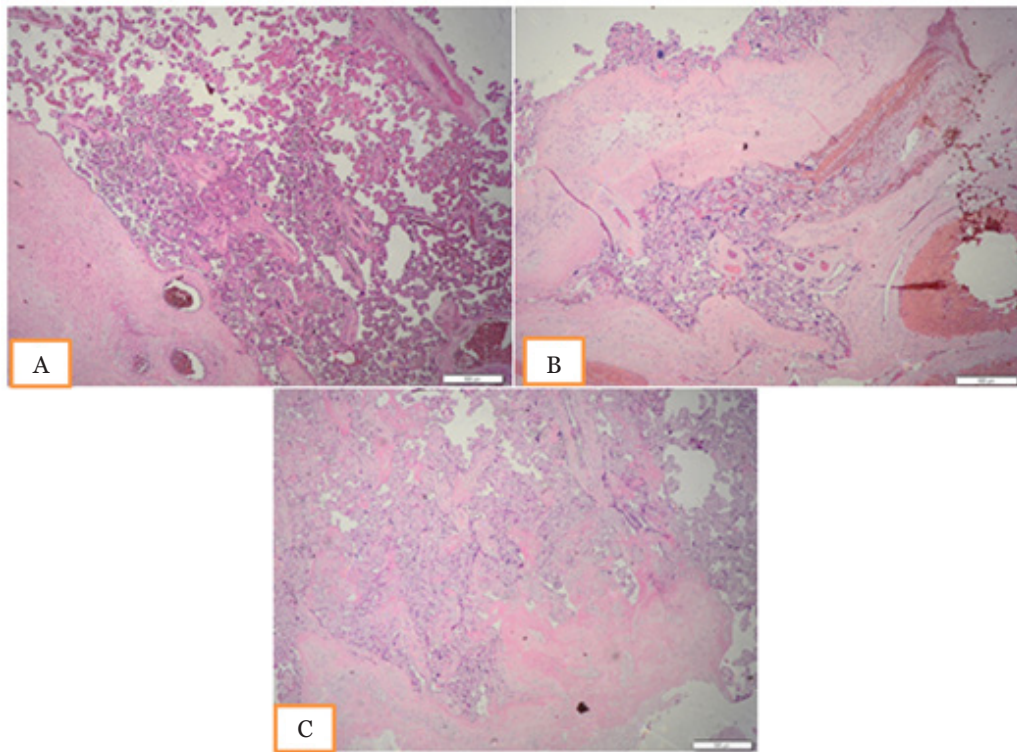


Figure 1 Histopathological Appearance of Placenta Accreta Spectrum
 Hematoxylin-eosin staining, 100× magnification. (A) Placenta accrete. (B) Placenta increta. (C) Placenta percreta

to trophoblastic tissue invasion that plays a role in controlling its invasion.^{18,19} Ernst et al.¹⁸ suggested when PAS is identified; the placenta is more often affected by chronic inflammation of the basal plate, altered maternal vascular malperfusion, and subchorionic/intervillous hemorrhage. Several research found a close relationship between the microenvironment of PAS and tumor behavior. Both conditions require

the ability of cells to defend local immunological systems, trophoblast invasion activity, and angiogenesis.¹⁹

Successful pregnancies depend on fetoplacental mediated suppression of the host immune response to prevent maternal rejection. Chronic inflammation of the basal plate is associated with PAS incidence. The significance of the leukocyte subpopulations and their

Table Association between Chronic Inflammation of Basal Plate and Decidual Existences with Placenta Accreta Spectrum

Criteria	Placenta		Total (n=50)	p*
	PAS (n=25)	Normal (n=25)		
Chronic inflammation basal plate				
Negative	4	9	13	0.190
Positive	21	16	37	
Decidual existences				
Negative	10	0	10	0.000
Positif	15	25	40	

Note: PAS: placenta accreta spectrum; *Fisher's exact

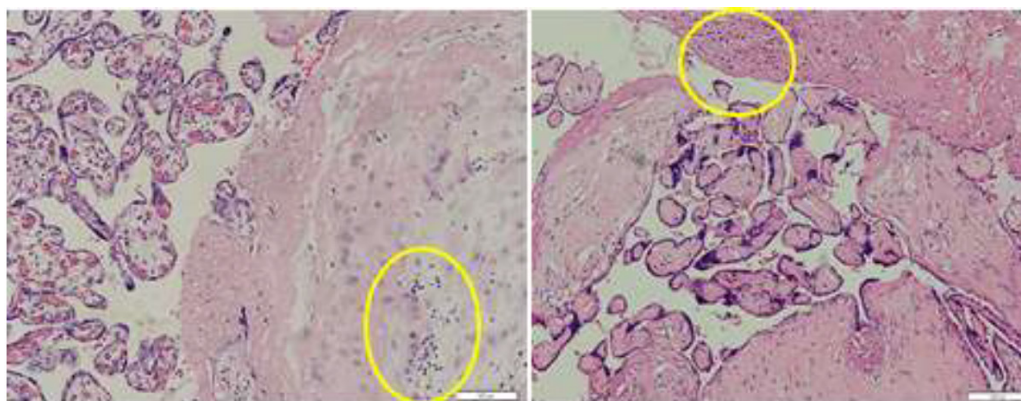


Figure 2 Chronic Inflammation of the Basal Plate

Hematoxylin-eosin staining, 200× magnification

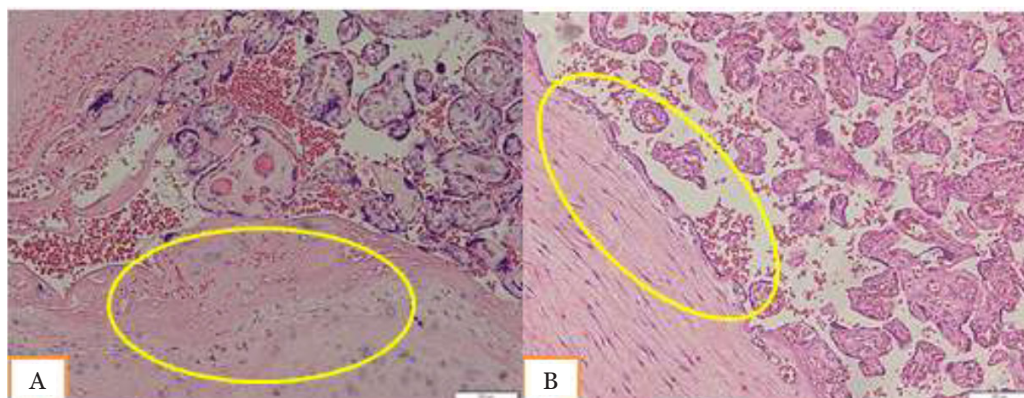


Figure 1 (A) Decidual Existences (Yellow Circle). (B) Chorionic Villi Attached Directly to the Myometrium without Decidua (Yellow Circle)

Hematoxylin-eosin staining, 200× magnification

contribution to EVT over-invasion in PAS requires further investigation. Ernst et al.¹⁸ demonstrated an increase in lymphocyte infiltration at the implantation site of PAS specimens compared with patients with placental malignancies without clinical suspicion of PAS.

Lymphocytes are known to participate in placental implantation and remodeling of the blood vessels. Decidual natural killers (NK) are inflammatory cells that regulate placenta implantation and the spiral arteries' remodeling process.^{16,20} Laban et al.¹⁶ report the role of NK cells in PAS development. The decrease in the NK cell population was closely related to PAS incidence. Nevertheless, increased NK cells may give protection effects against EVT invasion. Plasma cells are not a normal component of the

endometrial stroma, and the accumulation of these cells indicates the abnormal condition of the endometrium.

The local uterine injury (e.g., previous cesarean section) could result in impaired decidualization/local scarring and abnormal placental attachment in subsequent pregnancies that correlates with PAS cases. Although it is associated with the cesarean delivery history, even a minor disruption of the uterine lining can cause subsequent placenta accretion.^{21–23}

In this study, most cases of PAS showed the presence of decidua (Figure 3). It is characterized by direct contact between the chorionic villi and the underlying myometrial structure histopathologically.¹⁹ However, some studies reported that decidua is still found around the

trophoblast invasion in 44–69% of cases of PAS.²³ Microscopic examination of the placenta also confirms the presence of placental basal plate myometrial fibers, although these findings may be seen in a normal pregnancy. Their presence indicates an abnormal separation of the placenta from its place.²⁴ Hannon et al.¹⁴ reported the absence of local decidua was associated with a more significant number of interstitial EVT—rather than endovascular EVT involved in spiral artery remodeling—that invaded the myometrium with less multinucleated trophoblast giant cells (MTGC) formation. The capacity of MTGC is associated with the cessation of trophoblast invasion into the myometrial wall.

During normal pregnancy, EVT invades the myometrium's decidual and inner third layer. Invasion occurs through two pathways; interstitial EVT invades the decidua from anchoring villi and cytotrophoblasts, whereas endovascular EVT arises from an intravascular invasion of transmural migration of interstitial EVT into spiral arteries lumens to change the endothelial cells. Terminal differentiation of the EVT, with the formation of MTGC in the decidua and inner third of myometrium, will restrain trophoblast invasion of the myometrium. In PAS cases, abnormal EVT invasion is found, and the number MTGCs has been reported to be reduced. However, these findings are inconsistent in several studies.¹²

There was some weakness in this study, including the limited number of samples and not including several clinical data/patient characteristics that may contribute to the study results. In addition, this study still uses the assessment/evaluation of the existence of the decidua using the HE staining. Therefore, it is needed to conduct further research to evaluate the association between chronic inflammation of the basal plate and the decidua existences by using immunohistochemically staining with a more significant number of samples.

Conclusion

The decidua existences in placental preparation are relevant significantly with the PAS, whereas the signs of chronic inflammation of the basal plate did not provide a significant association.

Conflict of Interest

None declared.

Acknowledgments

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RESEARCH ARTICLE

Association between Serum Alpha-Synuclein Levels and Parkinson's Disease Stage

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Abstract

Parkinson's disease (PD) is the second most common neurodegenerative disease after Alzheimer's. It is chronically progressive with the main symptoms of resting tremor, rigidity, bradykinesia, and postural disturbances. Lewy's body and Lewy's neurite are the main findings in brain biopsies of patients with PD. The main component is alpha-synuclein, a misfolding protein that plays an essential role in the pathogenesis of PD. This study aims to determine the association between serum alpha-synuclein levels during the PD stage and compare the levels between PD patients and healthy populations of the same age. A case-control study was conducted on 62 people with PD and 20 normal subjects as controls in the outpatient Department of Neurology of Dr. M. Djamil General Hospital and Ibnu Sina Islamic Hospital, Padang, from March to September 2020. The ELISA method examined serum alpha-synuclein examination, and the PD stage was assessed according to Hoehn and Yahr stages. The differences in alpha-synuclein levels between cases and controls and between stages of PD were analyzed by the Mann-Whitney test. Alpha-synuclein levels in PD patients were higher than in controls, and this difference was statistically significant ($p < 0.05$). On the other hand, alpha-synuclein levels were higher in the severe stage than in the mild stage but not statistically significant ($p > 0.05$). In conclusion, there was no association between alpha-synuclein levels and the stage of Parkinson's disease. Still, serum alpha-synuclein levels in PD patients were significantly higher than in the healthy population.

Keywords: Alpha-synuclein, Hoehn and Yahr stage, Parkinson's disease

Introduction

Along with the increase in life expectancy, the incidence of neurodegenerative diseases also increases, one of which is currently in the spotlight of the medical world is Parkinson's disease (PD). The disease affects up to 2% of the population aged >65 years and >3% of the population 80 years. The symptoms are resting tremor, rigidity, and bradykinesia, responsive to the administration of levodopa.¹ In America, about 60,000 new cases are reported every year. Parkinson's disease (PD) occurs due to the degeneration of dopamine-producing neurons in the midbrain, precisely in the substantia nigra pars compacta.² PD can significantly affect a person's quality of life, especially motor symptoms such as stiffness and tremors, cognitive decline, and depression can also occur.³

Alpha-synuclein is a protein thought to be essential for the pathogenesis of PD, although the mechanism by which this protein causes neurotoxicity and degeneration is not fully understood.⁴ Alpha-synuclein is a protein that

forms energy in cells that makes our brains work. For each protein to function correctly, it must be folded into the correct shape. In healthy brain cells, normal alpha-synuclein is usually found right on the surface of the membranes surrounding the cell body and at the ends of branches extending from the cell (presynaptic terminals) that are important for relaying messages between neurons.⁵ However, in PD, some alpha-synuclein proteins were found to be folded in the wrong way. This incorrectly constructed version of alpha-synuclein then clumps together with other pathological proteins to form the aggregates we call Lewy's bodies. Lewy bodies are especially abundant in areas of the brain that have experienced cell loss, such as areas containing dopamine neurons.^{6,7}

The main pathological feature of PD is the finding of the pathological protein alpha-synuclein in the form of Lewy's bodies and Lewy's neurites in cells of the central nervous system. Until recently, especially in developing countries, most diagnoses of PD were made from clinical symptoms. However, we know that

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these symptoms will only appear when more than 60–80% of the dopamine-producing cells in the substantia nigra are damaged.⁸ It means that when a clinical diagnosis is made, the pathological conditions in the brains of people with PD are already severe. In this regard, we are interested in examining serum alpha-synuclein levels associated with the clinical stage of PD and comparing their levels with the normal population.

Methods

An observational study with a case-control design was carried out on PD patients treated at the outpatient Department of Neurology of Dr. M. Djamil General Hospital and Ibnu Sina Islamic Hospital, Padang, from March to September 2020. The research protocol has passed the ethical approval from the Research Ethics Committee of the Faculty of Medicine, Universitas Andalas, Padang, with registry number: 355/UN.16.2/KEP-FK/2021. The diagnosis of PD was made clinically according to the criteria of the United Kingdom Parkinson's Disease Society Brain Bank (UKPDSBB)⁹ by a neurologist. Patients with atypical symptoms, secondary Parkinson's, multiple systemic atrophy, corticobasal degeneration, post-stroke, and Parkinson's due to the use of neuroleptic drugs were excluded.

We got 62 patients with PD who met the requirements, and all of these patients were examined for serum alpha-synuclein levels and the clinical stage of PD.

According to Hoehn and Yahr stage, in this study, patients with PD were only grouped into two stages of the disease, namely mild stage (stages 1, 2, and 3) and severe stage (stages 4 and 5). Alpha-synuclein levels were checked by ELISA method using enzyme-linked immunoassay kits for humans from the Bioassay Technology Laboratory (BT Lab). SPSS version 22.0 was used for statistical analysis. The average difference in serum alpha-synuclein levels at mild and severe stages and between cases and controls was tested using a t-test if the data were normally distributed and a Mann-Whitney test if the data distribution was not normal. In addition, the effect of confounding factors on the disease stage was tested with the chi-square test.

Results

The data on the characteristics of the research subjects can be seen in Table 1. There were 82 study subjects consisting of 62 PD patients and 20 healthy adult controls of the same age and gender. The cases of PD consisted of 35 men and 27 women. From the stadium examination, it was found that stage 1 with 8 people, stage 2 with 15 people, stage 3 with 27 people, stage 4 with 9 people, and stage 5 with 3 people.

The basic data for age, gender, and level of education between the severe and mild stage groups with PD patients were relatively equal, which was indicated by a p value > 0.05, but for the length of illness, there was a significant difference

Table 1 Characteristics of Respondents

Variables	Healthy Adult Control (n=20)	Parkinson's Disease		p*	OR
		Severe Stage (n=12)	Mild Stage (n=50)		
Age (years old)					
≥65	11	9	37	0.944	1.05
<65	9	3	13		
Education (years)					
≤12	10	4	19	0.766	0.82
>12	10	8	31		
Gender					
Men	10	6	29	0.619	0.73
Women	10	6	21		
Duration of illness (years)					
≥5	NA	8	14	0.013	5.14
<5	NA	4	36		

Note: *chi-square test

with a p value=0.013, where the duration of illness in the severe stage group is longer than the mild stage group.

The bivariate analysis of differences in alpha-synuclein levels between the case and control groups (healthy population) can be seen in Table 2. Alpha-synuclein levels in the case group were higher than in the control group and this difference was statistically significant with a p value=0.034.

The difference in the average levels of groups with severe and mild stages can be seen in Table 3. Alpha-synuclein levels in the severe stage were higher than in the mild stage, but this difference was not statistically significant with a p value=0.323.

Discussion

The study aims to analyze the serum alpha-synuclein levels of PD patients and compare them with the normal population of the same age. It also analyses the association between serum alpha-synuclein levels and the stage of PD. The study involved 62 PD patients and 20 healthy adults as a control group. Out of the 62 PD patients, there were more males than females with a ratio of 1.48:1. It is similar to other studies that PD affects males 1.5–2 times more often than females.^{10–13} However, the mortality rate and speed of disease progression are higher in women than in men.

Most (80.6%) PD patients who participated in this study were in stages 1, 2, and 3 Hoehn and Yahr (mild stage), and the others were in stages

4 and 5 (severe stage). There is a significant association between length of illness and disease stage. Parkinson's disease patients in the severe stage group suffer longer (≥5 years) than those in the mild stage group. Parkinson's disease patients who have suffered from this disease for five years have a 5.14 times risk of being in a severe stage compared to PD patients who have suffered less than five years. Parkinson's disease is a chronic progressive disease that will continue to get worse over time. Moreover, many studies state that when PD symptoms appear, the damage to dopamine-producing cells in the substantia nigra pars compacta is more than 60%, where this damage continues. Thus with increasing time, the patient's clinical stage will be more severe.

Alpha-synuclein levels were found to be higher in PD patients than in the healthy population (control), and the difference was statistically significant (p<0.05). Also, serum alpha-synuclein levels were higher in the severe stage group than in the mild stage group, although this difference was not statistically significant (p>0.05). Alpha-synuclein is one of the pathological proteins that co-forms Lewy's bodies and Lewy's neurite (LB and LN) along with other pathological proteins. On autopsy examination of the brain of patients with PD, there were pigmented areas in the substantia nigra of the midbrain. It microscopically corresponds to the neuromelanin dopaminergic neurons of the substantia nigra pars compacta.^{15,16} Eosinophilic inclusions (5–30 in diameter) can also be found in the soma neurons that are still intact. Lewy's bodies

Table 2 Differences in Alpha-Synuclein Levels between Case and Control Groups

	Healthy Control (n=20)	Parkinson's Disease (n=62)	P
Alpha-synuclein level (ng/L)	199.5 (152.2–246.9)	396.2 (309.4–483.0)	0.034*

Note: *Mann-Whitney test

Table 3 Differences in Alpha-Synuclein Levels between Severe and Mild Parkinson's Disease Groups

	Parkinson's Disease		P
	Severe Stage (n=12)	Mild Stage (n=50)	
Alpha-synuclein level (ng/L)	275.76 (91.95–1,260.69)	226.73 (50.71–1,318.53)	0.323*

Note: *Mann-Whitney test

and Lewy's neurite were seen alive in routine histopathological staining.^{15–17}

Although alpha-synuclein is the dominant protein in LB and LN, other proteins such as ubiquitin, neurofilament protein, ubiquitin-binding protein p62, tubulin, and synphilin-1 are also present in the structure.^{15–18} The results of this study are similar to a study by Chang et al.,¹⁹ which reported increased peripheral circulating (plasma and serum) alpha-synuclein levels in PD compared to age-matched health and found an association between serum alpha-synuclein levels and clinical disease severity. Other studies have also observed increased alpha-synuclein levels in the plasma of PD patients compared to controls, but the associated parameters vary variably.^{20–23} However, several other studies found decreased alpha-synuclein levels in the plasma of PD patients compared to controls, and there was no significant difference in this parameter between the two groups.^{19,24} Thus, although peripheral alpha-synuclein (serum or plasma) is considered a promising candidate biomarker, the present study results are inconsistent. It is due to several things that are difficult to avoid, such as the various stages of disease and duration of illness of PD patients included in the study. In addition, most studies are still in the cross-sectional method, and the control group included in the study is almost always normal subjects.

Conclusions

There is no association between serum alpha-synuclein levels in Parkinson's disease patients with the stage of the disease. However, the alpha-synuclein levels were higher in patients with Parkinson's disease than in healthy individuals.

Conflict of Interest

There is no conflict of interest in this research.

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RESEARCH ARTICLE

Physical Environmental Conditions and Germ Number in Bedroom of Tuberculosis Patients in Kupang City, East Nusa Tenggara Province

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Abstract

The ability of *Mycobacterium tuberculosis* as the agent of tuberculosis (TB) to live in the air is generally very dependent on environmental factors, which can cause bacteria to last long in the air and increase the risk of transmission of TB. The research purpose was to analyze the relationship between the physical environment condition and the number of germs in the bedroom of TB patients. This cross-sectional research was conducted in Kupang city, East Nusa Tenggara province, in January–June 2022 with 77 TB patients as samples, whose TB patients' rooms would be observed based on research variables for physical environmental conditions. Data were collected directly by observing and measuring directly from the variables studied and then analyzed using a correlation test and linear regression test to see the relationship between variables and the effect of the physical environmental condition on germ number in the bedroom. The correlation test shows the variables related to the bedroom germ number ($p < 0.25$) were the number of people sleeping the TB patients, lighting, humidity, ventilation size, percentage of ventilation compared to room size, and room density. The model equation explains that 28.8% of the germ number variation in bedroom TB patients depends on the constant reduction (789,884) added to 19,217 times the bedroom humidity, then reduced by 9,518 times the percentage of room ventilation and also reduced by 31,185 times the density of the room occupancy. The most significant influence on the germ number in TB patients' bedrooms is the room humidity, which is 0.319.

Keywords: Bedroom, germ number, physical environmental, tuberculosis

Introduction

Tuberculosis (TB) is an infectious disease caused by the bacteria *Mycobacterium tuberculosis* that enters the body through the respiratory tract. This disease is still a public health problem worldwide, and Indonesia has the 2nd highest TB cases after India.¹ TB cases in Indonesia have reached 1,000,000, with some deaths yearly.² In Kupang city, the number of cases of pulmonary TB for the year 2018–2020 respectively was 670 cases, 667 cases, and 522 cases.³

Many factors trigger the occurrence of TB transmission in the community, including the presence of TB germs, individual characteristics, and environmental factors.^{4–7} House conditions such as humidity, temperature, lighting, and ventilation conditions, as well as residential density and house floors, are also associated with the incidence of TB transmission and determining factors for the presence of TB germs in people's homes.^{5–8–11} Behavior has also been related to the incidence of TB transmission in the community.^{12,13}

Environmental factors strongly influence the presence of TB germs.^{5,6,9,14} Therefore, it is also necessary to intervene in physical environment risk factors so that the risk of TB transmission in the community can be reduced, especially among family members of TB patients at home.¹⁴ The nature of germs in the air, in general, has similarities with the nature of TB germs, so this research aims to determine the relationship between the physical environmental conditions and the number of air germs in the bedroom of TB patients in Kupang city. Both the community and the government can use the research to prevent the transmission and incidence of TB in Kupang City.

Methods

This is a cross-sectional study conducted in Kupang city, East Nusa Tenggara province, from January to June 2022. The samples included 77 tuberculosis patients whose bedrooms were observed based on research variables spread over 11 health centers in the working area of the Health

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Office of Kupang City. They include bedroom size, temperature, number of family members sleeping with TB patients, room occupancy density, lighting, humidity, ventilation size, and airborne germ numbers in the bedroom. All research data except the airborne germs numbers were collected directly by observing and measuring the variables studied using roll Meter and environmental multimeter.

The airborne germ number is the number of pathogenic or non-pathogenic microorganisms floating in the air either together/attached to droplets (water) or particles (dust). We cultured them in the agar media to form colonies that can be observed visually or with magnifying glasses, then calculated based on the colony to be converted into colony-forming units per cubic meter (CFU/m³). First, air samples were taken with a microbial air sampler. Then the agar strip was put in an incubator of 30–35°C for 24 hours and repeated for another 24 hours if there was no growth of germs. Finally, the number of germ colonies grew was counted using the colony counter.

The data from the bedroom's TB patients were analyzed statistically using the bivariate test to see the relationship between the variables and the effect of the independent variables on the dependent variable using the multivariate linear regression test. This research has obtained ethical clearance from Politeknik Kesehatan Kemenkes Kupang with the number LB.02.03/1/0008/2022.

Results

TB patients' ages here range from 8 to 83 years, with varying physical environmental conditions in their bedroom, as shown in Table 1. The

number of germs in TB patients' rooms ranges from 1 to 2,010⁴ CFU/m³. It means that not all rooms meet the requirements, such as the germ number should be <700 CFU/m³. Table 1 also shows that most TB sufferers sleep with others, and some even share with up to 7 people. Kupang city's temperature is quite hot, with the average temperature of the bedroom being 32.5°C, the average humidity of the bedroom being 69.81% RH, and lighting 59.71 Lux. The average ventilation percentage of the bedroom meets the requirements (19.846% of the bedroom size).

Based on bivariate analysis using a correlation test, the variables related to the germs number in the bedroom (p<0.25) were the number of people sleeping in the same room, lighting, humidity, ventilation size, percentage of ventilation compared to bedroom size, and also bedroom occupancy density (Table 2).

Variables related to the number of bedroom germs (p<0.25) were analyzed using a multiple linear regression test with the backward method. The model summary generated in this analysis shows that the coefficient of determination (R²) was 0.288. It meant that the regression model obtained can explain 28.8% of the variation in the number of germs in a room with tuberculosis patients. Therefore, the model generated in the resulting equation is quite good. The results of the F test also show the p value (significance F) is 0.000. The resulting regression model fits the existing data, which means the variables of the bedroom's size per person, humidity, and percentage of ventilation can significantly predict the number of air germs in the bedroom (Table 3).

The regression equations generated in this research are:

$$\text{Total germ number} = -789,884 + 19.217^* \text{bedroom}$$

Table 1 Description of the Physical Environment Condition and Germ Number of a TB Patients Bedroom in Kupang City in 2022

Variable for Bedroom (n=77)	Min–Max	Mean	SD
Bedroom germ number (CFU/m ³)	1–2.104	194.62	417.053
Bedroom size (m ²)	3–28	8.977	5.4631
Bedroom temperature (°C)	29–35	32.55	1.259
Number of roommates (people)	1–7	2.12	1.235
Bedroom occupancy density (m ² /person)	1.3–24.0	5.391	4.0338
Bedroom lighting (Lux)	14–196	59.71	36.235
Bedroom humidity (% RH)	60–93	69.81	6.927
Ventilation size (m ²)	0.0–5.0	1.455	0.8672
Ventilation percentage (%)	0.0–48	19.846	11.8624

Table 2 Relation between the Physical Environmental Condition with the Germ Number in Bedroom's TB Patients

Variable for Bedroom (n=77)		Bedroom Germ Number (CFU)
Bedroom size (m ²)	Pearson correlation	0.025
	Sig. (2-tailed)	0.828
Bedroom temperature (°C)	Pearson correlation	-0.017
	Sig. (2-tailed)	0.886
Number of roommates (people)	Pearson correlation	0.298
	Sig. (2-tailed)	0.009
Bedroom occupancy density (m ² /person)	Pearson correlation	-0.287
	Sig. (2-tailed)	0.011
Bedroom lighting (Lux)	Pearson correlation	-0.298
	Sig. (2-tailed)	0.009
Bedroom humidity (% RH)	Pearson correlation	0.390
	Sig. (2-tailed)	0.000
Ventilation size (m ²)	Pearson correlation	-0.319
	Sig. (2-tailed)	0.005
Ventilation percentage (%)	Pearson correlation	-0.284
	Sig. (2-tailed)	0.012

Table 3 Prediction Model of the Bedroom Germ Number of the TB Patients in Kupang City in 2022

	Unstd. Coeff.		Std. Coeff.	t	Sig.
	β	Std. Error	β		
Constant	-789.889	455.251		-1.735	0.087
Bedroom humidity (% RH)	19.217	6.075	0.319	3.163	0.002
Ventilation percentage (%)	-9.518	3.574	-0.271	-2.663	0.010
Bedroom occupancy density (m ² /person)	-31.185	10.376	-0.302	-3.006	0.004

humidity - 9.518*bedroom ventilation percentage - 31.185*bedroom occupancy density.

This equation also shows that the variable with the greatest influence (β) in determining the number of germs in the air in the bedroom is bedroom humidity, which is 0.319.

Discussion

Tuberculosis, where Indonesia ranked 2nd after India,¹ was in the world's top 10 leading causes of death.¹⁵ TB cases are decreasing yearly, but the change is still not following the target of the End TB Strategy in 2020. It targeted a decrease in the 2015–2022 period by 20%; however, the reduction achieved is only around 9%.¹⁵

TB is a disease in which most of the risk factors for its occurrence are environmental and

behavioral factors, so these two factors need special attention in prevention and control so that transmission does not occur. No new cases can become a source of new transmission for people around them.¹⁶

This research found bedroom occupancy densities ranged from 1.3–24 m²/person, which was related to the number of germs in the bedroom. The correlation was negative, i.e., the higher the bedroom size per person, the lower the germ number. The number of people sleeping with TB patients ranged from 1 to 7 people, and it's positively correlated, namely, the more people who sleep in the same bedroom, the more germs number in the bedroom increases. On the other hand, if the number of germs in the room is high or 700 CFU/m³,¹⁶ it is also necessary to reduce the number of people sleeping in the room because it

will facilitate the transmission of disease if one of them has a respiratory infection, including TB sufferers.

Decree of the Minister of Health Republic of Indonesia Number 829/Menkes/SK/VII/1999 regarding Housing Health Requirements stated that the minimum bedroom size is 8 m² and cannot be more than two people in a bedroom or at least 4 m²/person.¹⁷ The average occupancy density of rooms in this research has met the requirements (5.3 m²/person), but many still do not meet the criteria. Some even have an occupancy density of only 1.3 m²/person, with up to 7 people sleeping in the same bedroom.

TB transmission mainly occurs due to close contact with patients through sputum sprinkling, which is estimated to produce 3,000 sputum sprinklings once a cough, while when clean, it can expel 4,500–1,000 TB germs in the droplets.¹⁸ The more people sleep together and are in close contact with TB patients daily, the transmission of *Mycobacterium tuberculosis* and the TB incidence increases. Previous research in Pontianak found a relationship between bedroom occupancy density and germ number.¹⁹ Based on the Ministry of Health Republic of Indonesia that close contacts are a risk group for TB transmission,²⁰ a study in Serang city concluded that household contact is associated with the incidence of TB with $p=0.011$.²¹ and TB patients have a risk of transmitting this disease to 2–3 people of their family members.²²

Based on these results, TB patients need to have their bedrooms until they are declared cured by the health workers responsible for the examination and treatment. The longer the close contact with the patient, the greater the number of inhaled germs, and the risk of TB transmission increases. If sleeping separately with a TB patient is not possible, other means must be found to prevent TB transmission, for example, wearing a mask or covering the mouth/nose when coughing/sneezing and washing hands with soap and running water.

The bedroom lighting, humidity, and the size of ventilation in this research showed a relationship with the germ number in the bedroom's TB patients. Transmission of TB disease mainly occurs in dark, humid places with less ventilation.²⁰

Mycobacterium tuberculosis germs will survive a long time in humid conditions and are not exposed to direct sunlight. In a poor

ventilation room, there is less air movement, and TB germs will last a long time in the room, increasing the risk of transmission, especially for close contacts, namely those who sleep in the same bedroom as the TB patient.²⁰

Mycobacterium tuberculosis germs will survive a long time in humid conditions and are not exposed to direct sunlight. In a poor ventilation room, there is less air movement, and TB germs will last a long time in the room, increasing the risk of transmission, especially for close contacts, namely those who sleep in the same bedroom as the TB patient.²⁰

Previous studies have found a relationship between lighting, ventilation, and humidity and TB incidence.^{19,23} This condition in Kupang city shows that there are still many housing conditions that do not meet the requirements for healthy housing following the standard of the Ministry of Health Republic of Indonesia, which are room temperature 18–28°C, humidity 40–60% RH, lighting ≥ 60 Lux, ventilation area 10% per size floor.^{16,17}

The condition of bedrooms in Kupang city allows the risk of transmission and incidence of TB, which is always high in Kupang city. For this reason, it is necessary to take fundamental measures to prevent and control TB from the community and the government, especially by building healthy houses.

Based on this research, TB patients should sleep separately in their bedrooms to decrease the transmission risk to close contact, always wear a mask, or cover the mouth/nose when coughing/sneezing, and wash hands with soap and running water.

The community should keep the sunlight entering the bedroom directly and lower the humidity by adding the ventilation size or placing the room position that allows direct sunlight to enter the room to reduce the risk of TB transmission in the room.

The Kupang City Health Office, the Public Works and Public Housing Office, and other related agencies need to carry out more stringent supervision on housing construction permits to follow the Ministry of Health's Decree for housing building or repairing.

The summary model and the results of the F test show that the higher the bedroom humidity and room density, the higher the germ number will be. Conversely, the greater the percentage of ventilation size, the less germ number.

TB germs are resistant to low temperatures and will survive for a long time at temperatures between 4°C and -70°C. TB germs are susceptible to heat, sunlight, and ultraviolet. Direct exposure to ultraviolet light will cause most TB germs to die within a few minutes, while in sputum at temperatures between 30–37°C, they will die in approximately one week and 5 minutes at 70°C.^{18,24} There is a temperature range favored by the *Mycobacterium tuberculosis*, which allows the bacteria to proliferate. *Mycobacterium tuberculosis* is a mesophilic bacterium that grows fast at 25°C–40°C. The bacteria will grow optimally at 31°C–37°C. Humidity plays a role in the growth of microorganisms, including pulmonary tuberculosis (TB) bacteria. High humidity in the house can increase the life of tuberculosis (TB) bacteria.²⁴

Based on the results of this research, it is necessary to take measures to ensure healthy home conditions that are not optimal for *Mycobacterium tuberculosis* to survive and grow to reduce the risk of transmission and incidence of TB. These actions include lowering room humidity and increasing natural lighting, namely sunlight entering the bedroom. The simple way to reduce the moisture that the community can take is by adding ventilation.¹⁶ The additional ventilation increases the space for airflow, which allows the release of some germs in the room and to be replaced by fresh air from outside to reduce the risk of TB transmission in the room.

A minimum room lighting needs around 60 Lux.¹⁶ The addition of ventilation can increase the sunlight that enters the bedroom. The morning sun, which contains ultraviolet light, will kill TB germ in minutes. On the other hand, poor air circulation and no sunlight will increase the risk of TB transmission.¹⁸ Ventilation will increase air circulation in the bedroom and reduce the risk of TB transmission for the room's occupants.

One way to control the number of germs in a room is to sterilize the room. Room sterilization with ultraviolet (UV) light is proven to be able to reduce the number of germs in the air.²⁵ The nature of germs in the air, in general, has similarities with the nature of TB germs, so if the germs in the room are successfully lowered by UV sterilization, the TB germs will also reduce. Sterilization of rooms with ultraviolet can be natural by using sunlight. It is necessary to increase the ventilation area of the room or the placement of the position of the room that allows

direct sunlight to enter. Sterilization of rooms also can be done artificially using UV lamps, so it is necessary to investigate further the effectiveness of UV lamps in reducing the number of germs in the room.

Conclusions

This study finds the equation model to determine the number of germs. The variation was the germ number in a TB patient's bedroom, the room humidity, room ventilation, and the density of the room occupancy. The most significant influence is the room humidity.

Conflict of Interest

There was no conflict of interest in this study.

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RESEARCH ARTICLE

Correlation of Knee Osteoarthritis Patients' Characteristics and the Results of 30-Second Sit-to-Stand Test with Quality of Life

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Abstract

Pain, joint stiffness, and difficulty performing activities like rising from sitting to standing are signs and symptoms of knee osteoarthritis (OA). These conditions are risk factors for limited mobility and lower quality of life. Knee OA is closely associated with age, women, obesity, and other characteristics. The study's objectives were to determine the correlation of knee OA patients' characteristics with functional mobility using the 30-second sit-to-stand test (30STS) and the correlation of functional mobility with quality of life using the Western Ontario and McMaster Universities Osteoarthritis (WOMAC) index. The research method was descriptive-analytic cross-sectional using medical records of 73 knee OA patients at the Medical Rehabilitation Clinic at Soreang Hospital, Muhammadiyah Hospital, Al Islam Hospital, Al-Ihsan Regional General Hospital West Java Province, Bandung, from March until August 2021. Patients' characteristics such as age ($p=0.02$), onset ($p=0.01$), OA grade ($p=0.03$), and knee deformity ($p=0.04$) have a negative correlation with functional mobility based on 30STS as well as functional mobility had a negative correlation with various aspects of quality of life, such as pain ($p=0.03$), stiffness ($p=0.02$), and functional limitation ($p=0.00$) subscales based on WOMAC index. Age, the onset of disease, OA grade, and knee deformity significantly correlate to functional immobility. Based on the WOMAC index, functional immobility correlates with the patient's quality of life.

Keywords: 30-second sit-to-stand test, functional mobility, knee osteoarthritis, quality of life, WOMAC index

Introduction

Osteoarthritis (OA) is the most common form of arthritis in the community, and knee OA is one of the most common forms of OA. In 2020, approximately 654.1 million people (40 years and older) have knee OA. The prevalence was 19.2% in Asia, 13.4% in Europe, 15.8% in North America, 4.1% in South America, 3.1% in Oceania, and 21.0% in Africa.¹ Indonesia does not have data on knee OA yet, but according to Indonesia's Basic Health Research (*Riskesmas*) 2018, the prevalence of joint disease based on doctor's diagnosis in 15 years and above population age in Indonesia was 7.3%, West Java province was 8.86%, and Bandung city 9.35%.^{2,3}

Knee OA patients often have difficulty performing daily activities, such as walking, climbing stairs, and getting up from sitting to standing.⁴ Study of knee osteoarthritis patients show limited function in daily living after having

knee osteoarthritis. In Indonesia, where most people have a squatting culture to defecate or urinate, it is difficult for knee OA patients to perform these activities.⁴

To avoid pain and overcome limitations of motion, knee OA patients compensate in their daily activities, resulting in changes in walking patterns, climbing stairs, and sitting to standing. Knee OA patients exhibit increased weight-bearing asymmetry, limited flexion on the affected knee, increased trunk inclination toward the healthy side, more trunk flexion during sitting to standing movements, and lower moment of knee extension due to decreased quadriceps strengths. These conditions cause the sitting to standing movement to become longer. On the other hand, slow sitting to standing may also be a deliberate strategy to reduce acceleration, joint force, and pain. Due to asymmetric loading, the contralateral joint tends to become OA. Knee osteoarthritis patients with obesity experience

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a decrease in the hip and knee range of motion, decreasing peak hip and knee moments.⁵

Functional mobility of knee OA patients is performed by checking the sit-to-stand ability using the 30-second sit-to-stand test (30STS), which assesses the number of repetitions sitting to standing that can be done for 30 seconds. There are several variations of the sit-to-stand (STS) test, apart from the 30STS. The five-repetition sit-to-stand test (FRSTST) assesses the time to perform five times sit-to-stand and 10 times repeated sit-to-stand (10STS), which rates the time to complete ten times sit-to-stand. The 10STS or 30STS test describes more endurance than the FRSTST test.⁶

The Western Ontario dan McMaster Universities Osteoarthritis (WOMAC) index is one of the questionnaires to assess the quality of life. According to the World Health Organization, "quality of life" is an individual's perception of their position in life in the context of the culture and value systems in which he lives and concerning his goals, expectations, standards, and concerns.⁷ Higher WOMAC indexes indicate worse pain, stiffness, and functional limitations.

The prevalence of knee OA increases with age and obesity, two of OA patients' various characteristics. Then the ability to rise from sitting to standing effectively is essential to achieve independence and participation in the community. The study analyzes the correlation of knee OA patients' characteristics with functional mobility using the 30-second sit-to-stand test (30STS) and the correlation of functional mobility with quality of life using the Western Ontario and McMaster Universities Osteoarthritis (WOMAC) Index.

Methods

This study is a descriptive-analytic with a cross-sectional method. The data was taken from the medical records of 73 knee OA patients at the Outpatient Medical Rehabilitation Clinic at Soreang Hospital, Muhammadiyah Hospital, Al Islam Hospital, and Al-Ihsan Regional General Hospital West Java Province, Bandung, from March until August 2021. All patients recruited for the study, either new or follow-up with a diagnosis of knee OA, went to the physical medicine and rehabilitation outpatients during the time of study in the respective hospitals and were accepted to be tested for 30STS and filled

out the WOMAC index questionnaire.

Patients' characteristics such as age, gender, height, weight, body mass index, waist circumference, hip circumference, waist-hip ratio, onset (duration of experiencing knee OA symptoms), pain intensity (numeric rating scale, NRS), varus/valgus deformity.

Patients' BMI based on the WHO Asian-BMI classification as follows, BMI < 18.5 kg/m² (lean or underweight), 18.5–22.9 kg/m² (normal), 23–27.49 kg/m² (overweight) and 27.5 kg/m² or above as (obese).⁸ The patient's waist circumference cut-off point based on the International Diabetes Federation classification for Asians is >90 cm in men and >80 cm in women, and the waist-hip ratio cut-off point based on the WHO classification for Asians is >0.90 in men and >0.80 in women.⁹

Patients need to meet outpatient inclusion criteria and have primary knee OA. They were excluded if they had one of the following limb contracture, OA hip, OA ankle, balance disorders, vertigo, and low back pain/lumbar radiculopathy.

The STS test is an assessment tool that investigates the ability to stand up from a sitting position. Using a standardized chair, the subject needs to change status from sitting to standing repetitively in 30 seconds.⁴

WOMAC index is a self-administered measure of health status that assesses dimensions of pain, stiffness, and function (either separately or as an overall index) in patients with hip or knee OA. Three subscales (pain, stiffness, and physical function) and a total (WOMAC index) reflect overall disability.¹⁰

The frequency distribution was analyzed by assessing the mean-median difference, standard deviation, minimum to maximum values, skewness, kurtosis, and the Shapiro-Wilk test for all variables. Variables that meet the assumption of a normal distribution are analyzed for their correlation using Pearson correlation. In contrast, Spearman correlation is used to analyze the correlation of variables that do not meet the assumption of a normal distribution. The correlation will be accepted if the p-value < 0.05 and also analyze the r value to know which correlation meets the negative or positive criteria.¹¹ Statistics analysis using Stata version 15.0 (Stata Corp., Texas, USA).

This study has been approved by the Health Research Ethics Committee of Al Islam Hospital Bandung number 019/KEPPIN-RSAI/09/2021.

Results

Of 74, unfortunately, a participant was deceased, so a total of 73 participants took part in this study. The subjects were 54 women (74%) and 19 men (26%).

The variables of age, weight, height, body mass index (BMI), waist circumference, hip circumference, waist-hip ratio, and 30STS meet the assumption of a normal distribution. Set and numeric rating scale (NRS) do not meet this assumption. In this study, participants were, on

Table 1 Knee OA Subject Characteristics

Characteristics	Median	Range	Mean±SD
Age (year)	67	44–92	65.53±9.76
Weight (kg)	63.1	40–92.4	63.43±12.45
Height (cm)	150.5	136–169	151.95±7.27
Body mass index (kg/m ²)	26.95	15.8–48.7	27.93±6.21
Waist circumference (cm)	94	58–110	90.74±12.43
Hip circumference (cm)	104	72–133	102.14±11.85
Waist-hip ratio	0.9	0.74–0.98	0.89±0.06
Onset (years)	2	1 week–20 years	4.61±6.31
Numeric rating scale	6	0–8	5.67±1.62
30STS (times/30 second)	8	0–16	8.41±3.24

Table 2 Correlation of 30STS with Knee OA Characteristics

Characteristics	r	p
Age (year)	-0.28	0.02
Weight (kg)	0.09	0.43
Height (cm)	0.09	0.41
Body mass index (kg/m ²)	0.06	0.60
Waist circumference (cm)	-0.09	0.47
Hip circumference (cm)	0.04	0.76
Waist-hip ratio	-0.24	0.07
Onset (years)	-0.29	0.01
Numeric rating scale	-0.14	0.23

Note: p<0.05 significant

average, 65.53±9.76 years, which was included in the older adult category (Table 1). The mean value of BMI is 27.93±6.21 kg/m² (category obese 1), waist circumference is 90.74±12.43 cm (abdominal obesity), waist-hip ratio is 0.89±0.06 (abdominal obesity), and numeric rating scale is 5.67±1.62 (moderate pain intensity). The median for the numeric rating scale was 6, with the highest pain score of 8. Overall the result for the functional immobility test using 30STS has a mean of 8.41 with a standard deviation of 3.24. It means that in 30 seconds, subjects can do eight times sit-to-standing activities.

Table 2 shows a negative correlation between

Table 3 Distribution of 30 STS in Gender, Deformity, and OA Grade

	Median	Mean±SD	p
Female	8	8.37±3.06	0.85
Male	8	8.52±3.79	
Non-deformity	9	9.12±2.74	0.04
Deformity	8	7.54±3.61	
Valgus	6	4.02±5.86	0.06
Varus	8	8±3.44	
OA grade 1	7.5	9±3.37	0.03
OA grade 2	9	9.05±2.53	
OA grade 3	8	8.25±3.12	
OA grade 4	5	4.75±3.61	

Note: p<0.05 significant

Table 4 Frequency Distribution and Correlation of WOMAC Index

	WOMAC Index	
	Median	Mean±SD
Pain	9	9±9.08
Stiffness	2	2.66±31.72
Activity difficulties	33.5	31.72±16.09

Table 5 Correlation of 30STS and WOMAC Index

	r	p
Pain	-0.25	0.03
Stiffness	-0.28	0.02
Activity difficulties	-0.33	0.00

Note: p<0.05 significant

age (p=0.02) and onset (duration) of knee OA (p=0.01) with 30STS results. Each increase in age and onset (time) of OA symptoms separately will be accompanied by a decrease in the 30STS score. From the r value, it can be seen that the onset of the disease has a higher r value than age.

Table 3 shows no significant difference in the mean of 30STS between the men and women groups. Both deformity and OA grading significantly differ in the result of 30STS. Females have a lesser amount of sit-to-stand in 30 seconds, and grade 4 osteoarthritis also has the least amount of sit-to-stand. There are no differences between valgus or varus in this study.

Table 4 shows that the highest score of the sub-component WOMAC index was in activity difficulties 31.72±16.09. The lowest mean was in the score of stiffness.

Pearson correlation was used to see the correlation between 30STS and the WOMAC index. Table 5 shows a significant correlation in each component of the WOMAC index.

Discussion

Participants in this study were included in the category of abdominal obesity based on the waist circumference cut-off point and the waist-hip ratio cut-off point for Asians,⁹ in the category of obesity based on the mean BMI,⁸ and in the category of moderate pain intensity. This study did not separate the characteristics by gender, including anthropometric traits.

The participants had experienced symptoms related to knee OA for an average of 4.61±6.31 years. It is not the same as the study by McCarthy et al.,¹² the average duration of experiencing symptoms is 0.5–2 years. The systematic review and meta-analysis by Blagojevic et al.¹³ indicate increased BMI, history of a knee injury, presence of hand OA/Heberden's nodes, female gender, older age, intensive physical activity, certain physical, occupational activities (e.g., kneeling, squatting) and increased bone mineral density to be risk factors for the onset of knee OA in older adults. In this study, the abovementioned factors were not investigated.

In a community, the proportion of people with knee OA tends to increase due to aging and rates of obesity or overweight. Women, especially those 55 years old, tend to have more severe OA in the knee but not elsewhere. The prevalence of knee OA in men is lower than in women.¹⁴ Osteoarthritis is an inevitable result of aging and the wear and tear of joints. The aging process of articular cartilage increases the risk of degeneration, including articular surface fibrillation, decreased size and aggregation of proteoglycan aggrecans, increased collagen cross-linking, and the loss of tensile strength and stiffness. These changes are most likely due to the aging process of chondrocyte function, which reduces the ability of cells to maintain tissue.¹⁵ Knee osteoarthritis is not only a result of aging but the disease itself.¹⁶ Excessive load on the joints due to obesity can affect the biomechanical pathways. Increased central fat affects gait and balance, which are associated with radiographic knee osteoarthritis. However, the increased mechanical load is not the only pathophysiology of OA. Metabolic factors, such as elevated blood glucose were associated with radiographic knee osteoarthritis regardless of age and BMI. Inflammatory mediators also play a role in the pathophysiology of knee OA. Interleukin-6 and other inflammatory mediators are produced in central obesity or abdominal fat accumulation conditions.¹⁷

The 30STS results from Table 1 and Table 3 show that participants in this study have an average risk of falling according to the Centers for Disease Control and Prevention (CDC) scores.¹⁸ STS performance is associated with disability, falls, hip fractures, and death among older adults. The STS performance is correlated with muscle strength and power of the lower limbs. It does not represent an estimate of muscle strength or

power.¹⁹

Sitting to standing consists of two phases; phase 1: from the beginning of the movement to the lift of the buttocks (buttock off/seat off) and phase 2: from the buttock off until motion termination. Sitting to standing activity is a series of movements which include: (1) Movement of the mass center of the body (MCB) forward and then upwards, and the upper body segment leans forward and shifts the MCB. It is on the broad base of support (BOS) formed by the buttocks, thighs, and legs, toward the narrower BOS formed by both legs, without losing balance. The position association between MCB and BOS is used as a postural stability index. (2) Sitting to standing shifts the MCB forward and upward, which requires joint movement and a high hip and knee extension moment to lift the MCB against gravity. Thus, anthropometric factors, which are weight and height, need to be considered. (3) Leg extension from sitting to standing is produced by some monoarticular leg muscles and the articular hamstring muscles.²⁰ The rectus femoris muscle is active isometrically, transferring the moment from the hip joint to the knee joint, directing the ground reaction force backward, and controlling balance after the seat.²¹

This study shows a negative correlation between age, onset (duration) of knee OA, waist-hip ratio (WHR) and the 30STS results. Each increase in age, onset (duration) of OA symptoms, and WHR will be accompanied by a decrease in the 30STS score. It is considered that increasing age changes fat distribution; waist circumference increases with age. Waist circumference is greater in older than younger adults up to age 70 in both sexes.²² The combination of obesity and knee OA causes the joint range of motion of the affected knee and hip to decrease, resulting in biomechanical changes during sitting and standing movements.⁵ In this study, although the average BMI indicates obese one and waist circumference indicates abdominal obesity, the WHR is the one that correlates with 30STS, even though the correlation is weak.

In contrast to this study, Verlaan et al.'s⁵ study on healthy people, obese and non-obese knee OA patients, found that in the sitting to the standing motion of three groups, the extension phase was the longest, followed by the leaning phase and the momentum phase. The time from sitting to standing was not significantly different between the three groups. In the obese knee OA

group, a decrease in knee and hip joint range of motion was associated with lower maximal knee moment and hip extension moment compared to the control group. In obese knee OA, the vertical Ground reaction force (GRF) is reduced, and the medial GRF is increased, indicating the use of compensatory mechanisms to reduce the load on the knee in obese knee OA patients.

Different test methods were performed by Bohannon et al.⁶ on subjects ranging from adolescents to older adults (those who are 14 until 85 years). They were able to walk without the use of assistive devices. They had no heart or blood vessel problems, blood, lung, or bone/joint resistance to standing up from a chair or climbing stairs) indicating that the time to perform FRSTST was lower in stronger, younger, shorter, and lighter subjects. It means the stronger, younger, shorter, and lighter a person, the faster they can do five repetitions of STS.

In Table 2, the onset/duration of experiencing OA has a negative (significant) correlation with 30STS, in which the more prolonged the onset, the smaller the 30STS, but it is found that the degree of pain, indicated by a numeric rating scale did not correlate with the 30STS outcome. In contrast, Turcot et al.'s²² study shows a weak correlation between knee pain and the average time to complete the STS task.

Table 3 shows no significant difference in the median of 30STS between the men and women groups. Perhaps because the number of samples of male participants was less than women. Although women's knees are retrained smaller and have less cartilage than men's tend to cause joint problems.²⁴

Table 3 shows a negative correlation between deformity ($p=0.04$) and OA grade (severity) ($p=0.03$) with the 30STS results. Each increase in OA severity (grade) and the presence of deformity will be accompanied by a decrease in the 30STS score. The median value of 30STS was significantly different between the deformity and non-deformity groups. The non-deformity group had a median value of 30STS which was greater than the deformity group ($p=0.04$). Valgus deformity had a median 30STS lower than the varus. There is a significant difference in the median value of 30STS between OA grades 1 to 4, and the lowest median is OA grades 4. While the median value of 30STS between OA grades 1 to 3 is not so different. Like this study, Kocak et al.'s²⁵ research found knee function scores measured by

the sit-to-stand test were lower in osteoarthritis patients than in healthy controls. The scores in grades 1 and 2 knee patients were similar, although they were higher than in grades 3 and 4. In the sit-to-stand test, osteoarthritis patients showed lower independent status than healthy controls. Kocak et al.'s²⁵ research findings suggest that radiographic severity does not correlate with functional disability, which may be due to population heterogeneity, radiographic data, and clinical criteria for evaluation.

Thicker articular cartilage is considered healthier cartilage. Cartilage thinning is associated with the development of knee osteoarthritis.²⁵ As OA progresses, the cartilage diminishes and breaks down. Full-thickness cartilage loss (FTCL) is typical in the medial and patellofemoral knees. According to the Kellgren-Lawrence system, the OA grade has the highest correlation with confirmed cartilage loss in patients after total knee arthroplasty.²⁴ In this study, the OA grade was based on the Kellgren-Lawrence system. The OA of the patellofemoral joint is very common and is a significant source of pain and impaired function. The prevalence of OA of the patellofemoral joint (PFJ) is as high/higher than OA of the tibiofemoral joint (TFJ).²⁶ Peak knee flexion moment and flexion moment impulse during the second half of standing are associated with the development of PFJ OA. Reduced flexion moment and vastus muscle force indicate reduced quadriceps performance in individuals showing the progression of PFJ OA.¹⁹ This may cause a decrease in 30STS results, as well as knee OA with varus and valgus deformities, respectively, increasing the risk of progression of biomechanical stress in the compressed compartment and reducing the risk of progression in the non-load-bearing compartment.²⁷

In this study, all categories of WOMAC Index had a significant correlation with 30STS, although the correlation was weak (Table 5). The results of the 30STS showed a reasonably reliable and valid indicator of lower body strength in older adults living in a generally active society.²⁷ Turcot et al.'s²³ study showed a correlation between the pain sub-scores of the WOMAC index questionnaire and the average time to complete the STS task. Between the total score of the WOMAC index questionnaire and the average time to complete the STS, a positive but not significant correlation was observed between

the WOMAC index function and time to perform the STS task. Furthermore, another result of Katia Turcot's study showed that decreased functional capacity was associated with reduced knee flexor moment and was closely associated with quadriceps weakness recognized in knee OA.

It has been mentioned above that in this study, the lower the 30STS result, the higher the WOMAC value, meaning that the pain, stiffness, and functional limitations were higher. The results of 30STS were representative of the patient's condition, such as the increasing age associated with cartilage aging and joint wear and tear. WHR (abdominal/central/visceral obesity) causes excessive load on joints and decreased range of motion of the knee and hip joints, resulting in impaired sitting to standing patterns. The reduced extension moments and the release of inflammatory mediators by fat cells affect the pathogenesis of OA. In addition, various risk factors influence the onset of OA; an increase in OA grade and deformity is associated with progressive cartilage depletion and suggests a decrease in quadriceps performance. These biomechanical and metabolic changes affect sitting to standing performance, which correlates with the WOMAC domains, i.e., pain, stiffness, and activity difficulties.

In the physical function domain, there are questions about the difficulty of descending and ascending stairs. Some participants admitted that they were afraid when descending and climbing stairs and even reported that they had not done ascending and descending stairs for a long time. Some participants who experienced mild pain showed low sitting to standing performance. There are psychological factors that must also be investigated. In this study, knee OA patients aged >75 years were 18%. It is also necessary to consider sensorimotor, balance, and psychological factors, which will affect the performance of sitting-standing.²⁹

The WOMAC Indonesia questionnaire has been validated and reliable for use on the Indonesian population. The pain and stiffness subscales are very well-received, but there are some problems with the function subscales. Some patients experience some ambiguous terms, such as the term "toilet". Indonesian habit of using a toilet is by squatting rather than sitting. "Rising from bed" in Indonesian has the perception of waking up (opening their eyes) instead of getting out of the bed. "Lying in bed" has a biased meaning

to sleeping. "Lying" or sleeping for Indonesians has almost the same meaning. Similarly, "getting in/off the bath, wherein Indonesia, it is rare to find a bathtub, so additional information is needed. Getting out/into the bath (stepping as high as +50 cm)". For some Indonesians, the term "sit" means sitting on the floor rather than on a chair.³⁰ So that in giving the questionnaire, it is necessary to provide additional information.

Based on this study's results, an exercise program is needed to increase the quadriceps muscle's maximum concentric and eccentric strength, co-activation of the lower knee muscles, and better joint coordination, which may be beneficial in improving functional ability in OA patients. It is also essential that obesity needs to be an important target for restoring healthy sit-to-stand biomechanics. In addition, OA patients need to develop adaptive activities and self-care tools to protect their joints (joint protection). Finally, to improve the functional ability of knee OA patients, it is necessary to have an examination and treatment related to decreased psychological and neurological function.

Conclusion

Age, the onset of disease, OA grade, and knee deformity have a significant correlation to functional immobility and also a correlation of functional immobility with the patient's quality of life based on the WOMAC index.

Conflict of Interest

There is no conflict of interest in this study.

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RESEARCH ARTICLE

Factor Affected Stunting Prevention in North Bengkulu District: a Qualitative Study

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Abstract

Stunting has been a considerable problem that indicates the poor level of public health in Indonesia. There are various efforts made to reduce stunting rates. The North Bengkulu regency has significantly successfully reduced the stunting rate over three years. This study aims to determine the measures to accelerate stunting reduction in the North Bengkulu regency. This is a qualitative descriptive study with data collected through focus group discussions and in-depth interviews. The study was implemented at the North Bengkulu regency in October 2021. There were five participants in the focus group discussion, and two participants were in-depth interviewed. The data were then transcribed verbatim and analyzed using the narrative analysis technique. The result of this study shows that the Head of the North Bengkulu Regency has been an outstanding leader with a strong commitment and vision to prevent stunting. The head of villages in North Bengkulu regency collaborates with public health centers in using village funds and determining the priority scale for stunting prevention. The involvement of cadres to empower the community is essential. The implementation of cross-program cooperation has been implemented. However, the cross-sectoral collaboration was not optimal. There is a difference in determining to stunt between cadres and nutrition workers. The training for stunting cadres and nutrition officers was carried out in stages. The cross-sectoral collaboration needs to increase to improve the program's effectiveness. The cadres and nutritionists need to train to determine stunting rates.

Keywords: Collaboration, cross-sectoral, prevention, stunting

Introduction

Stunting is a condition of failure to grow and develop in children under five years of age due to malnutrition, so the child is too short for his age. The incidence of stunting is measured after the child is two years old, even though malnutrition occurs since the baby is in the womb and in the early days after the baby is born.¹⁻³ Stunting was a condition of a child who was short or very short and not by his age, which was a factor of malnutrition and repeated diseases for a long time in the fetal period until the first two years of a child's life.^{4,5}

The prevalence of stunting in developing countries is in the high category.⁵⁻⁷ It is at 30.8% in Indonesia, still above the world's 22.2%. Stunting in sub-Saharan Africa is 34.5%, in Ethiopia, 52.4%, and its prevalence in Congo at 40%. The prevalence of stunting in Indonesia is higher than in other countries in Southeast Asia, such as Myanmar (35%), Vietnam (23%),

and Thailand (16%), and ranks fifth in the world. The World Health Organization has determined that nutritional problems in a country should be less than 20%.⁷ The percentage of children under five who are very short and aged 0–59 months in Indonesia in 2018 is 11.5% and 19.3%, respectively. This condition increased from the previous year, namely 9.8% and 19.8%.⁸

The Basic Health Research (*Riskesmas*) Bengkulu Province in 2018 illustrates the prevalence of nutritional status (height/age) in children aged 0–23 months, showing the percentage of concise children at 10.4% and 18.6% short children, which is below the national average on a tiny scale.⁹ Data for monitoring the movement's implementation for measuring the growth and development of toddlers at the local integrated healthcare center (*posyandu*), Bengkulu province, in 2021 shows the most significant number of toddlers in North Bengkulu regency spread over 19 sub-districts with the percentage of stunting toddlers of 8.79%. North

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Bengkulu regency was one of the regencies in 160 stunting locus regencies/cities in Indonesia. The stunting rate was at 35.8% and 25.9%, which fell drastically to 10.53% in 2017, 2018, and 2019 respectively.¹⁰

In 2020, the stunting rate in the North Bengkulu regency fell to 9.5%. For this remarkable achievement, North Bengkulu regency has won an award from the Bengkulu Provincial Government as the most innovative, inspiring, replicative, and best performing district in the implementation of convergence actions to reduce stunting rates and was appointed as the district representing Bengkulu province to participate in the national level competition of stunting prevention.¹⁰

The decline in the stunting rate in the North Bengkulu regency is an intelligent work of the North Bengkulu Government in the stunting prevention program. Therefore, knowing what activities have been carried out by the North Bengkulu regency related to reducing the stunting rate is necessary. Therefore, this study aims to analyze the program activities implemented by the North Bengkulu Regency associated with the acceleration of stunting reduction.

Methods

The research was a qualitative approach with a policy study design in the North Bengkulu regency. Informants came from stakeholders who were North Bengkulu Regency Stunting Team members. Informants were recruited through the purposive sampling technique.¹¹ This research was conducted in October 2021 at North Bengkulu regency. The data were collected through in-depth interviews with two stakeholders of North Bengkulu regency (Head of Health Department and Manager of Nutritional Program). The focus group discussions (FGD) were conducted with five participants. They are Head of Early Childhood Education Division of the Education Office, Head of Horticultural and Plantation Food Crops Office, Head of Marine and Fishery Office, Head of Livestock Office, and Head of Social Office.

The FGD and in-depth interviews aimed to obtain information on the acceleration of stunting reduction in the North Bengkulu regency based on the five pillars of the stunting reduction acceleration program. An in-depth interview was carried out based on the interview guide that was adapted from the

five pillars of stunting prevention. In addition, the FGD is also carried out based on topics as a guide to ensure the discussion stays focused on the issue of stunting prevention.

The author maintains the study's trustworthiness using several steps. The interview and FGD were recorded with an audio recorder, transcribed verbatim, and the researcher also applied the triangulation technique. The data was then analyzed with the narrative analysis technique to understand what action the stakeholders in North Bengkulu have taken that contributed to the success of the acceleration of the reduction rate of stunting. This analysis also fits to know what is the stakeholder's view of the five pillars of stunting prevention in the North Bengkulu regency.

This research passed the ethical clearance test based on ethical clearance certificate number 283/UN9.FKM/TU.KKE/2021 from the Health Research Ethics Committee, Faculty of Public Health, Universitas Sriwijaya.

Results

The factors that influence the success of stunting reduction programs include support for cross-program, cross-sector activities, and strengthening operational strategies to improve the quality and scope of interventions. Further, increasing human resource capacity, improving service quality, strengthening nutrition education, strengthening management of nutrition interventions at the public health center and *posyandu*, and supportive policy.¹²

The results of the research on factors that influence the success of reducing the incidence of stunting in the North Bengkulu regency are based on five pillars: (1) leadership commitment and vision; (2) national campaign and behavior change communication; (3) convergence, coordination, and consolidation of central, regional, and village programs; (4) food security and nutrition; and (5) monitoring and evaluation (Figure).

Based on FGD observations, the leadership's commitment and vision have gone very well. The regent's regulations indicate the commitment to stunting prevention and the formation of a stunting cluster team. The North Bengkulu Regency Government has a policy of Regent Regulation Number 23 of 2019 and a Regent's Decree of 2019. It favors the use of village funds to implement



Figure Five Pillars of Stunting Prevention

stunting program convergence. The village Government also runs the village fund program in stunting implementation. Together with the public health centers, The village government made a stunting management program, including family latrines, supplementary food provision, etc. Solid and consistent commitment to all relevant stakeholders, making nutrition and health programs work in synergy because there is support from the non-health sector and the support of other stakeholders. The following is an excerpt from the results of an in-depth interview with the Head of the Health Office:

"At the time of 2018/2019, the central (government) conveyed to North Bengkulu regarding stunting. Initially, it was the same as other districts. We conveyed to the team that stunting is not only a matter for the Health Service. We must make the team by the regent or the governor's representative and so on."

"We formed a regulation for the working group (pokja) consisting of 17 regional apparatus organizations (organisasi perangkat daerah, OPD) by the direction of the national

stunting management strategy. We make the regulations. The decree was signed by the regent and consisted of 17 OPD. After that, we formed a regent regulation related to the convergence of stunting in North Bengkulu. Each pokja and the regulations have several job descriptions that each OPD must carry out concerning their respective job description. Coordination of the implementation is that we draft regional action plans for each OPDs."

The national campaign to change community behavior has implemented the behavior of clean and healthy life activities, socialization of stunting, prospective brides, and maximum reproductive counseling. However, there are still some obstacles, such as a lack of advocacy, campaigns, and dissemination related to stunting and efforts to prevent it, especially for adolescents and eligible women. The following is an excerpt from the results of in-depth interviews with the Head of the Health Office and nutrition program managers:

"Pregnancy care for pregnant women is not good in some villages. Exclusive breastfeeding and

family habits should be given more attention. Starting from pregnant women because stunting doesn't only happen or develop after the baby is born. The average husband's attention is good. However, in some areas, it is not. Pregnant women should be kept from inhaling cigarette smoke when their husband smokes. If you want to smoke, you can, but smoking is outside the house. Then there is also an additional source of clean water that is not optimal because the number of clean water sources is low, the result of our health evaluation. The regional work unit takes care of public works or settlements. If the health recap of sanitation data is only, the drinking water or clean water supply in North Bengkulu is still below 60% while the national target is 90%."

Convergence, coordination, and consolidation of central, regional, and village programs. The stunting prevention program has been running simultaneously in all ministries. In addition, cross-sectoral and cross-program collaboration has been running based on ministry programs. The program is aimed at priority targets for the first 1,000 days and uses the provided intervention package. Based on the results of the FGD with stakeholders, one of which was the Head of Early Childhood Education (PAUD), the following information was obtained:

"In our PAUD, we carry out activities such as measuring children's weight and height in collaboration with the Health Service, in this case, the public health center in their respective regions. Implement to provide additional food to socialize stunting. What is stunting, and how can we act in synergy with parents? In PAUD, there is parenting to explain how to provide balanced nutrition."

Social assistance and nutritional non-cash food assistance have been carried out by the duties of the relevant ministry functions. Department of Horticultural and Plantation Food Crops with the assistance program of plant seed, sustainable food garden, preparation of seed houses, demonstration plots, and member's yards. Department of Marine and Fisheries with the fish breeding program, and the Department of Social with the family hope program. Efforts have been made to develop food diversification based on local food resources. The Health Office has trained nutrition workers, and the village

government has undertaken and funded village cadre activities. Village cadres have measured stunting children. The following is an excerpt from the results of the FGD with the Head of the Horticultural and Plantation Food Crops service:

"The Horticultural and Plantation Food Crops service assists agricultural seeds, such as rice, corn, and large livestock such as cows and goats. We do this and, of course, indirectly reduces stunting and has an economic impact on the community in the near term, meaning that if we have rice or corn seed assistance in 3–4 months, we can already enjoy the results, of course, this will have an economic impact. There are also cows and goats; if the goats are also six months or one year old, you can enjoy the results. We have been handling this activity for a long time. We already know that all activities that assist the community without ongoing assistance have such an impact, but because field extension workers are involved, all of them are involved. The program we worked on together turned out to be able to bear fruit."

Stunting data were obtained from the electronic-community-based nutrition recording and reporting conducted by the Health Service through the public health center. Still, the stunting reduction rate from the public health centers varied. Based on information from the Head of the Health Office and the Head Department of Nutrition, it was stated that there was a decline in the stunting rate in the last three years reaching 8.9% in 2020:

"Specifically for stunting, what was shown earlier was not the results of 2018, 2019, and 2020 surveys. Instead, it was electronic-community-based nutrition recording and reporting data, carried out twice a year, weighing and measuring with the target of all toddlers in North Bengkulu. Therefore the results of community-based measurements show the numbers have decreased from the first 35% in 2018, 25% in 2019, and 2020. The electronic-community-based nutrition recording and reporting measurement was carried out because there was no special survey related to nutrition and stunting, only in 2020 the data was only 8.9%."

Based on the results of FGD information related to the training of nutrition workers,

the informant stated that it was not possible to equalize stunting data:

"Our survey for basic health research is conducted every five years. However, because the nutrition sector has not submitted the stunting data to the Development Planning Conference (Musrenbang), we have initiated a mini basic health research study program every year to monitor the overall nutritional status in Indonesia. I don't think I can equalize it. First, the Indonesian nutritional status survey uses sampling data. It uses the Statistics Indonesia data, in which one can use ten samples. We only sample 300 children under five each year from 22,398 children under five from North Bengkulu regency. As for the electronic-community-based nutrition recording and reporting, the central guidelines are obligated to measure all targets in the working area. At least we enter the report at 90%, which means logically, in our research, the larger the sample, the smaller the data. If they do it in stunting spots, that number will be high while we measure it for all targets. The measurement technique is the same, the tools used are the same as the education, and the sample size affects the numbers."

Discussion

This study's results indicate a strong political commitment from stakeholders in the North Bengkulu regency regarding stunting prevention. Various strategic plans have been prepared and implemented by the North Bengkulu regency. The leadership's commitment and vision are outstanding; there is a regent regulation related to stunting prevention and forming a stunting cluster team. In utilizing village funds, the village head is above the attention of the public health centers in determining the priority scale for stunting prevention and the involvement of human development cadres to empower the community.

The problem of stunting can be overcome with a strong political commitment from a leader to mobilize all sectors that will handle stunting. Stunting is a priority problem in the regions that can be resolved through the commitment of regional leaders and cooperation between regional apparatus organizations. In addition, political commitment is needed in the government's agenda to improve nutrition to reduce the incidence of stunting.

Commitment is a will, desire, or step that aims to fulfill the goal of achieving an effort or endeavor. Political commitment is significant because fulfilling a nation's goals must be supported by a politician or leader of the nation itself. Without political commitment, what is expected and planned will not be achieved with good results.¹⁴

The interviews with policymakers in the North Bengkulu regency show that verbal, institutional, and commitment have gone very well. The attention from leaders to the problem of stunting, coordination of multi-sectoral nutrition programs, implementation of stunting policies, and the existence of a particular budget for stunting in regional and institutional budgets shows a strong political commitment from the North Bengkulu regency to stunting prevention.

The community behavior change campaign has been implemented in the North Bengkulu regency, but there are still various obstacles related to behavior change in preventing stunting. For example, attention to pregnant women, exclusive breastfeeding that has not been maximized, smoking habits in the house, and little clean water are different obstacles in preventing stunting in the North Bengkulu regency.

Many things affect people's behavior. Behavior is formed due to environmental adaptation. The lack of knowledge and unsupportive attitudes cause difficulty in changing people's behavior in implementing healthy living. The behavior also causes a slow decline in stunting rates in the regions.¹⁵

Healthy conditions can be achieved by changing behavior from unhealthy to healthy behavior and creating a healthy environment in the household. Therefore, various strategies have been developed to change people's behavior towards healthy behaviors that can help accelerate stunting reduction, namely (a) National campaigns and outreach using various forms of media and various community activities; (b) Interpersonal communication to promote behavior change at the household level; (c) Ongoing advocacy to decision-makers at various levels of government; and (d) Capacity building for program managers. The achievement strategy is implemented through a behavior change communication approach outlined in the communication strategy at the center and the local level.¹³

The convergence, coordination, and consolidation of central, regional, and village

programs in the North Bengkulu regency have been going well. Convergence is an approach to delivering coordinated, integrated, and joint interventions to prevent stunting to priority targets. Convergence efforts to accelerate stunting prevention are carried out by planning, implementing, monitoring, and evaluating programs/activities. Convergent implementation of interventions by aligning planning, budgeting, implementation, monitoring, and controlling activities across sectors and between levels of government and society.

Efforts to accelerate stunting prevention will be more effective if specific and sensitive nutrition interventions are combined. Therefore, a convergence of service delivery requires an integrated process of planning, budgeting, and monitoring of government programs/activities across sectors to ensure each specific nutrition intervention service's availability to prioritize target families and sensitive nutrition interventions for all community groups, especially the poor.

Implementing total convergence does promise a change in the number and management of stunting cases. For this reason, converging is one of the main pillars in the national strategy to accelerate the prevention and reduction of stunting. In implementing this convergence, the role of the Regional Development Planning Agency (*Bappeda*) is crucial because the organization functions in planning aspects of development activities in the area.¹³

Based on the results of this study, it was found that to improve food and nutrition security in the North Bengkulu regency, cross-program collaboration has been carried out well, but cross-sectoral collaboration has not been optimal. Each institution has implemented all programs related to the accelerated improvement of under-five nutrition, but each seems to be running separately. The National Team for the Acceleration of Poverty Reduction states that the five pillar aims to increase access to nutritious food and promote food security. A good cross-program and sector collaboration are needed because the programs that have been prepared can be implemented correctly and on target.¹³

Development of food security is carried out to meet basic human needs that provide benefits fairly and equitably. It is based on independence and does not conflict with community beliefs so that quality, independent, and prosperous Indonesian people are formed by realizing

sufficient, safe, quality, nutritious, and affordable food availability. Diverse and evenly distributed throughout Indonesia and affordable by the community.^{16,17}

Many factors that affect food security, such as family income, education, and ownership of productive assets, affect food insecurity.¹⁸ The number of family members, education level, food prices, and family income also affect household food security.¹⁹ Households in the insecure food category have family members who have access to food in quantity and quality. It will impact meeting the nutritional needs of children under two to achieve optimal dietary status.^{20,21} Children in food-secure household conditions have good energy and protein adequacy. In contrast to children from food-insecure families who experience growth delays because they lack access to food, the portion of food is reduced to share with other family members.²²⁻²⁴

Cross-sectoral and cross-program cooperation is needed to avoid food insecurity. Therefore, the five pillars are coordinated by the Ministry of Agriculture and the Ministry of Health, involving the relevant technical ministries and the regional and village governments. In addition, the Ministry of Social Affairs, through the provision of cash assistance, such as the family hope program and the food social Assistance, including non-cash food assistance, and the Ministry of Health guarantees the availability of exceptional supplementary food for pregnant women and children suffering from malnutrition.

Monitoring and evaluation are essential in implementing stunting prevention and reduction programs. One of the strategies in the five pillars is to improve the data collection system, which can monitor stunting data accurately and periodically at the national and district/city levels. The intervention data management system is an effort to manage data at the district/city level to the village level, which will be used to support the implementation of other integrated actions and assist the management of integrated stunting reduction programs/activities. The data management system includes data from each indicator, from stunting data to the coverage of specific and sensitive nutrition interventions. The data management system generally aims to help provide and facilitate data access to manage integrated stunting reduction programs.²⁴

This study indicates that there are still differences in stunting measurement data between community cadres and health center

nutrition officers. Given the importance of this data, the Health Office regularly conducts stunting measurement training for nutrition officers and cadres. Today's stunting data is derived from electronic-community-based nutrition recording and reporting. In addition, monitoring and evaluation activities related to stunting prevention programs are always carried out by the public health center and the North Bengkulu Regency Health Office.

Monitoring and evaluation are essential things in the context of accelerating stunting prevention. In general, the purpose of monitoring is to monitor program progress, increase accountability, and learn. Specifically, monitoring is aimed at obtaining: regular reports on program progress and target achievement prepared for the steering committee, program implementing partners, and beneficiaries; a data management system that is reliable, easy to use, and useful for monitoring program progress, identifying problems in implementation, to take corrective action promptly and make decisions and policies; utilization of learning outcomes from monitoring data analysis which will be presented in the form of recommendations, good practice documentation for replication, as well as policy papers. The evaluation aim is to see the achievement and implementation of the national strategy related to stunting. They included the how, to what extent, under what conditions, and the contribution to the acceleration of stunting prevention. This evaluation also includes the effectiveness of independent intervention (single intervention), interventions carried out simultaneously/convergently, including input, process, output, and impact.²⁵

Conclusions

The stunting prevention program in the North Bengkulu regency has been implemented well. However, increasing cross-sectoral collaboration to coordinate stunting prevention efforts is still necessary. In addition, training for nutritionists and cadres needs to be carried out continuously so that there are no differences in determining stunting rates.

Conflict of Interest

Researchers say that there is no conflict of interest in implementing the research and following the

basic research principles.

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RESEARCH ARTICLE

Perception of Health Workers on Preventing COVID-19 Transmission Behavior based on Work Area and Exposure

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Abstract

Coronavirus disease 2019 (COVID-19) emerged at the end of 2019 and spread worldwide, becoming a pandemic on March 11, 2020. Agents, hosts, and the environment influence disease transmission. Perception influences healthy behavior in preventing disease transmission. This study aims to determine differences in the perception of health care workers (HCWs) on COVID-19 prevention behavior based on the area of work and exposure. This study is a cross-sectional study with a survey method using the health belief model questionnaire with research subjects who were HCWs on duty during the COVID-19 pandemic from May to July 2021 in Dr. Hasan Sadikin General Hospital. Statistical tests used were chi-square and Kruskal-Wallis tests. From 346 subjects, it was found that the perception of susceptibility and self-efficacy of HCW in the yellow and red zones was higher than in the green zone ($p=0.002$). In comparison, the perception of barriers in the yellow zone was higher than in the red area ($p=0.014$). Health care workers had relatively similar mean scores in terms of knowledge (median 7 of 9), perceived benefits (median 27 of 30), cues to action (median 20 of 20), and perceived severity (median 19 of 30). Based on the history of exposure, the parameter of cues to the action of HCWs exposed to COVID-19 was better than those never exposed ($p=0.009$). HCW of Dr. Hasan Sadikin General Hospital has good knowledge and perception of the prevention of COVID-19. Differences in the perception of HCW between the work area and exposure history require more targeted and specific educational interventions and actions.

Keywords: COVID-19, exposure, perception, work area

Introduction

At the end of 2019, a mysterious case of pneumonia appeared, which was first reported in Wuhan, Hubei province of China.¹ This disease is called coronavirus disease 2019 (COVID-19) and has become a pandemic since March 11, 2020.² As of April 14, 2022, the total number of confirmed cases was 500,186,525 cases with 6,190,349 deaths.³ The proportion of health workers affected by COVID-19 reached almost 10%. This proportion varies between countries, ranging from 4.2% in China and 17.8% in the United States.⁴ These conditions can create depression, anxiety, and fear and distracts health workers' focus because they are at risk of infection and transmitting it to family.⁵

COVID-19 is a positive single-strain RNA virus encapsulated and unsegmented.⁶ Epidemiologically, the transmission factor of the disease is influenced by agent, host, and environmental factors.⁷ Previous studies on

severe acute respiratory syndrome (SARS), ebola, and H1N1 stated that the host factor of perception and healthy behavior is essential in overcoming a pandemic.⁸

Knowledge is vital for health workers to have confidence in their attitude and behavior. The higher the knowledge, the higher the confidence to be able to fight COVID-19.⁹ Good perception encourages people to implement healthy behavior, which is the behavior of a person with awareness to achieve the expected health condition.¹⁰ Behavior tends to persist for up to 3 months from the presence of behavioral intervention.¹¹ Healthy behavior habits, such as hand hygiene and wearing masks, are influenced by the risk of exposure to COVID-19. If the risk of exposure is high, healthy behavior tends to be better.¹²

Dr. Hasan Sadikin General Hospital Bandung, the main referral hospital in West Java, has mobilized massive resources to handle the COVID-19 pandemic. Health workers are

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vulnerable to being exposed to COVID-19 due to workplace risks, length of working hours, and hand hygiene that is not optimal after contact with patients.^{8,13} In Dr. Hasan Sadikin General Hospital, HCWs infected with COVID-19 was 59% in the yellow zone than red zone (9%).¹⁴ Health workers are assigned to several work areas in the red zone directly dealing with COVID-19 patients, such as the isolation ward and emergency room. The yellow zone does not deal directly with COVID-19 patients, such as non-isolation wards and outpatient departments, and the green zone does not deal with patients, such as the pharmacy and administration. As a result, more and more health workers are exposed to COVID-19 disease, which can disrupt health services and programs to handle the pandemic. As mentioned above, perception and healthy behavior are essential factors in preventing the transmission of COVID-19, especially among health workers, and overcoming a pandemic. Research is needed to see the differences in the perception of health workers on preventing COVID-19 transmission behavior based on work area and exposure.

Methods

This study is a cross-sectional study with a survey method using the health belief model questionnaire. The questionnaire was adapted and obtained permission from research conducted in Taiwan by Tsai et al.,¹⁵ then translated by an official and certified translator. The results of the translated questionnaire were tested for validity and reliability to the respondents, and Cronbach's alpha score was calculated with a value >0.7 (acceptable).

The population of this study is all health workers who work in hospitals and health facilities that handle COVID-19. The affordable population is the health care workers of Dr. Hasan Sadikin General Hospital, who are on duty during the COVID-19 pandemic period from May to July 2021. The sample size is calculated based on the Slovin formula. The distribution of the number of samples was carried out by stratified proportional simple random sampling by dividing into three groups for each work area (red, yellow, and green) and exposure status according to the proportion of health workers on duty in the red, yellow and green of the population. The inclusion criteria are health care workers at Dr. Hasan Sadikin General Hospital who were on duty

during the COVID-19 pandemic between May and July 2021. Exclusion criteria include unwilling participation in research, not returning the questionnaire form, and incomplete researched data. This study is part of joint research between the Division of Tropical Medicine and Infectious Diseases, the Department of Internal Medicine of Dr. Hasan Sadikin General Hospital and the Infection Prevention and Control Committee, and the New Emerging and Re-emerging Infectious Diseases (*PINERE*) Team of Dr. Hasan Sadikin General Hospital. This research has received ethical approval from the Health Research Ethics Committee of Dr. Hasan Sadikin General Hospital with the number LB.02.01/X.6.5/329/2020.

Variables in this study: demographics (age, gender, education, profession, work area, exposure status, vaccination history, health conditions, and comorbidities) and perceptions (knowledge, susceptibility, severity, benefits, barriers, self-efficacy, and cues to action). The work area is divided into three areas that are: green zone (no patient contact like administration, pharmacy, and nutrition department), yellow zone (contact with non-COVID-19 patients like in outpatient department, non-isolation ward), and red zone (COVID-19 patient contacts like in an emergency room, isolation ward). Exposure status is divided into three levels that are: exposed (confirmed positive for COVID-19 in the last three months), have been exposed (not verified positive for COVID-19 in the previous three months, but confirmed positive previously), never exposed (never confirmed positive).

The knowledge and perception variables were tested for normality and the nonparametric Kruskal-Wallis test was performed using the median value. Finally, the Pearson chi-square test analyzed the demographic data to see the significance value (p) and displayed it in the form of numbers and percentages. Analysis using SPSS version 26.0 software.

Results

A total of 346 subjects, with the distribution of health workers in the green zone of 31 people (8.96%), the yellow zone of 160 people (46.24%), and the red zone of 155 people (44.80%). Subject characteristics can be seen in Table 1 and Table 2.

The results of the statistical test in Table 1 show that the basic characteristic factors that were significantly different ($p < 0.05$) in health

Table 1 Respondents' Characteristics based on Work Area

Characteristics	Green Zone (n=31)	Yellow Zone (n=160)	Red Zone (n=155)	P
Age (year)				
Median (min–max)	39 (30–59)	35 (25–65)	32 (27–58)	0.000*
Gender				
Male	9 (29.0%)	41 (25.6%)	81 (52.3%)	0.000*
Female	22 (71.0%)	119 (74.4)	74 (47.7%)	
Education				
Bachelor and above	17 (54.8%)	116 (72.5%)	133 (85.2%)	0.000*
Associate's degree	14 (45.2%)	44 (27.5%)	22 (14.8%)	
Profession				
Specialist/subspecialist	1 (3.2%)	19 (5.6%)	5 (3.2%)	0.000*
Resident doctor	6 (19.4%)	72 (45.0%)	106 (68.4%)	
Nurse	2 (6.5%)	49 (30.6%)	36 (23.2%)	
Other (pharmacist, nutritionist)	22 (70.9%)	30 (18.8%)	8 (5.2%)	
Vaccination history				
Never	3 (9.7%)	18 (11.3%)	7 (4.5%)	0.070
Have been	18 (90.3%)	142 (88.7%)	148 (95.5%)	
Patient contact history				
Nothing	16 (51.6%)	62 (38.8%)	43 (27.7%)	0.015*
Contact	15 (48.4%)	98 (61.2%)	112 (72.3%)	
Comorbid conditions				
Nothing	19 (61.3%)	113 (70.6%)	129 (83.2%)	0.005*
Having comorbid	12 (38.7%)	47 (29.4%)	26 (16.8%)	
Exposure history				
Never	21 (67.7%)	102 (63.8%)	96 (61.9%)	0.040*
Been exposed	2 (6.5%)	19 (11.9%)	34 (21.9%)	
Exposed	8 (25.8%)	39 (24.3%)	25 (16.1%)	
Health condition				
Good	30 (96.8%)	159 (99.4%)	152 (96.8%)	0.042*
Not good	1 (3.2%)	1 (0.6%)	5 (3.2%)	

Note: *p<0.05 significant

care workers based on the area of work were age, gender, education, profession, patient contact history, presence of comorbidities, exposure status, and health conditions.

In general, health care workers from the three groups have relatively similar characteristics. The only significant difference was from vaccination status, where health workers who were not exposed to COVID-19 were more dominant, having received three doses of vaccine, and from the work area where the most exposed health workers were those who served in the yellow zone.

Data from the questionnaire can be seen in Table 3 and Table 4. From Table 3, the parameters of perception of susceptibility, barriers, and self-efficacy have significant differences (p<0.05).

Health care workers in the red zone tend to have a better perception of susceptibility and self-efficacy than in the green and yellow zones, but have a poor perception of barriers. From Table 4, that is a significant difference in cues to action (p<0.05).

Discussion

Dr. Hasan Sadikin General Hospital HCW characteristics in the green zone which does not contact patients have a median age of 39 years. Most are women with a bachelor's education level, as supporting health workers (laboratorian, nutritionist, pharmacist), have no contact with COVID-19 patients, have no comorbidities, never suffered COVID-19, and are in good health

Table 2 Respondents' Characteristics based on Exposure Status

Characteristics	Exposed (n=72)	Been Exposed (n=55)	Never Exposed (n=219)	P
Age (year)				
Median (min-max)	34 (26-58)	32 (27-56)	34 (25-65)	0.243
Gender				
Male	26 (36.1%)	26 (47.3%)	79 (36.1%)	0.170
Female	46 (63.9%)	29 (52.7%)	140 (63.9%)	
Education				
Bachelor and above	52 (72.2%)	46 (84.6%)	168 (76.7%)	0.600
Associate's degree	20 (27.8%)	9 (16.4%)	51 (23.3%)	
Profession				
Specialist/subspecialist	3 (4.2%)	1 (1.8%)	11 (5.1%)	0.439
Resident doctor	34 (47.2%)	38 (69.1%)	112 (51.1%)	
Nurse	22 (30.6%)	12 (21.8%)	53 (24.2%)	
Other (pharmacist, nutritionist)	13 (18.0%)	4 (7.3%)	43 (19.6%)	
Vaccination history				
Never	9 (12.5%)	7 (12.7%)	12 (5.5%)	0.000*
Have been	63 (87.5%)	48 (87.3%)	207 (94.5%)	
Patient contact history				
Nothing	26 (36.1%)	17 (30.9%)	78 (35.6%)	0.935
Contact	46 (63.9%)	38 (69.1%)	141 (64.4%)	
Comorbid conditions				
Nothing	56 (77.8%)	43 (78.2%)	162 (74.0%)	0.304
Having comorbid	16 (22.2%)	12 (21.8%)	57 (26.0%)	
Work area				
Green zone	8 (11.1%)	2 (3.6%)	21(9.6%)	0.040*
Yellow zone	39 (54.2%)	19 (34.5%)	102 (46.6%)	
Red zone	25 (34.7%)	34 (61.9%)	96 (43.8%)	
Health condition				
Good	70 (97.2%)	54 (98.2%)	215 (98.2%)	0.201
Not good	2 (2.8%)	1 (1.8%)	4 (1.8%)	

Note: *p<0.05 significant

condition. Meanwhile, in the yellow zone, those who come into contact with non-COVID-19 patients have similar characteristics to the green zone, but the median age is younger (35 years) and sometimes contact with COVID-19 patients. The red zone HCW, which directly handles COVID-19 patients, has a younger median age (32 years), and males dominate (52.26%). Although the dominant percentage of education level, profession, and comorbid HCW in the red zone and other zones is similar, the percentage is higher.

Placement of health workers with proportions as above, following the workload and risks. Valiathan et al.¹⁶ stated that being older will lower your immune system and make you more susceptible to disease exposure. Physiological

aging is followed by decreased function and damage to the immune system, including the role of lymphocytes, CD4 helper T cells, CD8 cytotoxic T cells, B cells, and natural killer cells, where which will increase the susceptibility to the disease.

The exciting thing from the data shown in Table 1, although overall, most of them have never been exposed to COVID-19 (green zone 67.74%, yellow zone 63.75%, and red zone 61.94%), the percentage of HCW exposed to COVID-19 was more significant in the green zone (25.81%) and yellow zone (24.38%) than the red zone (16.13%). It is interesting because the red zone should have a higher risk of being exposed to COVID-19 than the yellow zone or green zone. This result is almost similar to the research conducted by Wang

Table 3 Knowledge and Perception Analysis based on Work Area

Perception Parameter	Question Item	Score Range Reference	Green Zone (n=31) Median (Min–Max)	Yellow Zone (n=160) Median (Min–Max)	Red Zone (n=155) Median (Min–Max)	p
Knowledge	9	0–9	7 (6–9)	7 (5–9)	7 (5–9)	0.948
Susceptibility	5	5–25	20 (11–25)	22 (14–25)	23 (16–25)	0.002*
Severity	6	6–30	19 (10–27)	19 (6–30)	19 (8–30)	0.962
Benefit	6	6–30	27 (20–30)	26 (14–30)	26 (14–30)	0.567
Barrier	6	6–30	24 (14–30)	24 (6–30)	22 (6–30)	0.014*
Self-efficacy	4	4–20	18 (13–20)	20 (8–20)	20 (12–20)	0.003*
Cues to action	4	4–20	20 (12–20)	20 (8–20)	20 (12–20)	0.081

Note: Kruskal-Wallis test, *p<0.05, barrier value is a reverse value

Table 4 Knowledge and Perception Analysis based on Exposure Status

Perception Parameter	Question Item	Score Range Reference	Exposed (n=72) Median (Min–Max)	Been Exposed (n=55) Median (Min–Max)	Never Exposed (n=219) Median (Min–Max)	p
Knowledge	9	0–9	7 (5–9)	7 (5–9)	7 (5–9)	0.617
Susceptibility	5	5–25	22 (11–25)	22 (16–25)	22 (14–25)	0.967
Severity	6	6–30	20 (8–28)	20 (9–30)	19 (6–30)	0.398
Benefit	6	6–30	26 (19–30)	27 (14–30)	26 (14–30)	0.486
Barrier	6	6–30	24 (6–30)	22 (6–30)	24 (6–30)	0.718
Self-efficacy	4	4–20	20 (13–20)	20 (16–20)	20 (8–20)	0.534
Cues to action	4	4–20	20 (12–20)	20 (16–20)	20 (8–20)	0.009*

Note: Kruskal-Wallis test, *p<0.05, barrier value is a reverse value

et al.,¹⁷ which stated that more health workers exposed to COVID-19 were not in the red zone, which dealt directly with COVID-19 patients, but in the general care department (yellow area).

Another thing that can cause HCWs in yellow and green zones to be more exposed than in red zone is the possibility of transmission outside the workplace. When exposure occurs at the place of duty, health workers in the red area are more susceptible to exposure and have the highest number of people exposed to COVID-19. The result was similar to research by Lepak et al.¹⁸ It concluded that health workers who are exposed to COVID-19 are those who are in contact with family and communities. Therefore, their exposure often comes from outside the place of work. Moreover, data on the perception of barriers appears that avoiding eating out together, having large gatherings or activities, and keeping the distance, seems complicated to do so it becomes

a risk factor for transmission.

Suitable knowledge parameters based on the work area and exposure status, there were no significant differences (p=0.948 and p=0.617). Furthermore, knowledge between the green, yellow and red zones and between the exposed, been exposed, and unexposed groups have the same score of 7 with a range of 5–9. It shows that the knowledge of HCW about COVID-19 is relatively evenly equal in the green, yellow, and red zones and among been exposed, exposed, and never exposed groups.

According to Table 3, the susceptibility perception parameter statistical test based on the work area showed a significant difference (p=0.002) between HCW in the green, yellow, and red zones. In addition, HCW in the red and yellow zones had a higher median score than in the green zone (median: 23 vs 22 vs 20). Table 4 shows the perception of susceptibility based

on exposure status is not significantly different. Hameed¹⁰ states that the susceptibility parameter assesses a person's perception of the belief in the susceptibility to contracting a disease which is usually associated with the idea that there will be a severe impact (severity) due to being infected. A person with a firm belief in this perception will lead to an understanding of dangerous and life-threatening conditions. It will lead to self-motivation to save his life by changing his behavior even to the point of being radical. Conversely, suppose a person believes he is not susceptible to being infected by a disease and does not feel it would be dangerous to suffer it. In that case, he will have a behavior that does not try to avoid being exposed to a disease.

The analysis results of perceived barriers based on the work area (Table 3) showed that health workers in the green zone and yellow zone had a higher median score than the red zone (median: 24 vs 24 vs 22) with $p=0.014$ which indicated there was a significant difference. A significant difference was found in the subjects' yellow and red zone groups. Meanwhile, based on exposure status (Table 4), there was no significant difference ($p=0.718$), with a median value between the been exposed group of 22, 24 exposed, and not exposed 24 with a scale range of up to 30. This result is a reverse value of the original answer value to the questionnaire to make the answers to the questionnaire unidirectional so that a good response is higher the value, which means lower the barriers to healthy behavior. The results of this study align with the results of Tsai et al.'s¹⁵ research, which states that the average value of perceived barriers is 15.17 on a scale of 30, indicating that the barriers to healthy behavior are insignificant. Hameed¹⁰ says that perceived barriers are beliefs about barriers that can prevent healthy behavior and disease transmission. For example, suppose someone believes there is no difficulty in carrying out a healthy behavior such as washing hands. In that case, it will be implemented and prevent someone from being exposed to the disease.

Conversely, if someone feels a lot of difficulty in carrying out a healthy behavior, such as if someone is going to apply hand hygiene but is constrained by the absence of adequate hand washing facilities, the unavailability of hand sanitizer at the location of exposure to the disease, it will prevent someone from having healthy behavior and will increase the risk of exposure

to disease. The barrier perception parameter average value shows that health workers in the red zone have relatively low average scores on several activities. For example, they avoid eating together, gathering at the outside workplace, then too much-measuring body temperature, and keeping their distance compared to other zones. What can be evaluated is that health workers find it difficult to avoid eating together outside or avoiding meetings, so facilities to facilitate this, such as the availability of safe dining areas and meeting areas and establishing health protocols, need to be considered.

Parameter of self-efficacy, Hameed¹⁰ states that this perception is a belief in oneself to be able to take action or healthy behavior to avoid exposure to a disease. After believing in the susceptibility and severity of exposure to the disease, the advantages and barriers to healthy behavior, and encouragement to perform healthy behaviors, self-efficacy is needed to carry out these healthy behaviors. The better the self-efficacy in the ability to perform a healthy behavior, the better a person's behavior in carrying out the healthy behavior will be.

The analysis of the cues to action based on the work areas listed in Table 3 does not show any significant differences, with the median value equivalent to the maximum upper limit of 20. Meanwhile, based on exposure status, $p=0.009$ indicates a substantial difference between the group that had been exposed to the group not exposed. Hameed¹⁰ states that the principle of cues to action is a sign or encouragement to perform a specific behavior manifested through socialization. They could be through mass media, invitations or encouragement from colleagues or people around, education or personal doctor advice, and the occurrence of illness that afflicts family or friends who provide a lesson about unpleasant conditions if it happened to him. If you look at the theory of behavior formation presented by Khanal¹⁹ and Bakanauskas et al.,²⁰ one of the factors that shape behavior is the cognitive component. The mental part can be influenced by factors of information, memory, and experience, causing positive and negative reactions to shape behavior. The exposed group whose experience is exposure to COVID-19 gives better information than those who have never been exposed and have no experience. This information and knowledge can lead to a better will to act.

Conclusions

Health care workers (HCWs) who work in the green, yellow and red zones have relatively equal knowledge, perception of severity, benefits, and cues to action. HCWs who work in the yellow and red zones have a better perception of susceptibility and self-efficacy than HCWs in the green zones. At the same time, HCWs who work in the yellow zone have a better perception of barriers than HCWs in the red zone. HCWs who have been exposed to COVID-19 have better cues to action than those who have never been exposed to COVID-19. Periodic education is needed and considering the differences in HCWs based on work areas and exposure history to be more specific and on target. Also, it is essential to facilitate gathering places for worship activities, meetings, praying, or breaks for HCWs, especially HCWs in the red zone, following the health protocol requirements.

Conflict of Interest

There is not any conflict of interest in this research.

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RESEARCH ARTICLE

Effects of *Binahong* Leaf Decoction on Perineal Laceration Healing in Postpartum Women

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Abstract

A perineal laceration is a wound of the skin and muscular area between the vaginal and anal introitus caused by a labor tear. Perineal lacerations might occur in sudden and rapid removal of the fetus' head, excessive fetus size, and the inability of the pelvic muscles and soft tissues to accommodate the fetus's birth. One of the empirical non-pharmacology approaches to this study sought to understand the effect of *binahong* (*Anredera cordifolia* (Tenore) Steenis) leaf decoction on peritoneal wound healing in postpartum women. This is a quasi-experimental post-test-only control group study on 30 postpartum women treated in 15 private midwife practices in Bengkulu city from 10 November to 10 December 2022 who met the inclusion criteria. Subjects were sampled using the accidental sampling technique and were randomly divided into two groups. Wound healing was assessed using the REEDA scale, and the results were analyzed statistically using the Mann-Whitney or Wilcoxon test and the chi-square test. The study's results showed that Hb, age, and the number of children's influenced perineal wound healing. The average number of days for wound healing in the treatment group was six days. For a control group that used povidone-iodine 10% was eight days. It is concluded that there is an effect of decoction of the leaves of *binahong* (*Anredera cordifolia* (Tenore) Steenis) on the healing of peritoneal wounds in postpartum women.

Keywords: *Binahong*, perineal wound, postpartum

Introduction

Postpartum infection is the second leading cause of maternal death after bleeding if not treated immediately.¹ In Indonesia, the incidence of infection during the postpartum period reaches 2.7%, with 0.7% developing into an acute infection.² One of the infections frequently seen among postpartum women is birth canal laceration/injury, and a perineal laceration is experienced by 79% of women who underwent vaginal delivery.³ In spontaneous vaginal delivery, the most postpartum woman received perineal sutures caused by an episiotomy due to a spontaneous tear.⁴ Complications of perineal lacerations are delayed wound healing and infection, leading to pain and fear of moving that can cause uterine sub-involution, disrupted lochia discharge, and postpartum hemorrhage, which ranks first as the cause of maternal death in Indonesia.^{2,5}

Birth canal laceration care in postpartum women aims to reduce discomfort, maintain hygiene, prevent infection, and accelerate perineal wound healing. The quality of the perineal suture is considered good if there are no signs of

infection, such as redness, swelling, hot feeling, pain, and less function. Efforts to prevent perineal laceration infections include pharmacological therapy and non-pharmacological therapy. Povidone-iodine 10% is the substance that is often used for pharmacological treatment in preventing perineal laceration infection. This substance is a polyvinylpyrrolidone chemical with an iodine element that is useful for perineal wound care. However, it also has the potential for triggering allergic reactions and hampering collagen production, which is necessary for wound healing.⁶

A previous study has scientifically demonstrated that the leaves of *binahong* (*Anredera cordifolia* (Tenore) Steenis) are effective for wound healing due to their active contents of flavonoids, alkaloids, terpenoids, and saponin.⁷ The active flavonoid compound directly works as an antimicrobial agent by disturbing the activities of microorganisms such as bacteria and viruses and playing a role as an anti-inflammatory agent, analgesic, and antioxidant.⁸ Several studies stated that the *binahong* leaf is significantly more effective in perineal suture wound healing in a postpartum woman compared to povidone-

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iodine 10%.^{9,10} A study showed a significant effect of *binahong* leaf decoction water on perineal wound healing in a postpartum women.¹¹

The author assessed the postpartum perineal trauma in this study using the REEDA scale. This scale includes five items in the healing process: redness, edema, ecchymosis, discharge, and approximation (REEDA). In this scale, the timing and wound density is measured and observed one day after treatment.¹²

This study aimed to explore a non-pharmacological approach to understand the effect of *binahong* (*Anredera cordifolia* (Tenore) Steenis) leaf decoction on peritoeal wound healing in postpartum women. It is expected that a product, such as *binahong* extract or cream, can eventually be produced as non-pharmacological midwifery care to improve the quality of midwife care in the community.

Methods

This study was a quasi-experiment study using a posttest-only control group design. Two groups were established in this study. The first group was a treatment group, and the second was a control group. The treatment group consumed *binahong* decoction, while the control group used povidone-iodine 10%. Subjects' characteristics of Hb level, age, education, number of children, and antenatal care (ANC) visits were also collected to assess their relationship with perineal wound healing.

To assess the postpartum perineal trauma in this study, the REEDA scale was used. REEDA scale is a tool to assess perineal wound healing developed by Davidson and further refined by Carey.¹² This scale includes five items in the healing process: redness, edema, ecchymosis, discharge, and approximation (REEDA). In this scale, the timing and wound density is measured and observed one day after treatment.¹² Data were analyzed using the chi-square test and Mann-Whitney test. The results of the analysis were then tabulated as shown below. Interpretation of the level of Hb measurement: normal ≥ 11 g/dL, mild 8–10 g/dL, moderate < 8 g/dL. The duration of healing: rapid < 6 days; moderate 6–7 days; slow > 7 days.

The population in this study was 30 postpartum women who delivered their babies in 15 private midwife practices in Bengkulu city from 10 November to 10 December 2022 with sutured

or unsutured perineal lacerations and on their second-day postpartum. The sample consisted of all postpartum women with perineal tears who delivered their babies in a private midwife practice in Bengkulu city. They met the inclusion criteria: spontaneous postpartum mothers on day 2 to day 7 experienced a maximum degree of 3rd degree perineal laceration. Physically and mentally healthy, has no history of birth canal disease, and is willing to fill out informed consent.

The *binahong* leaves used in this study were mature leaves, which were apparent from their dark green color. The decoction used 320 grams of leaves already rinsed under running water and then boiled for 15 minutes in 2 glasses (400 mL) of boiling water using the infusion technique. The boiling was done in a covered clay pot to avoid damage to the active contents of *binahong* leaves until the remaining water was only half of the glass (100 mL).

The decoction was cooled at room temperature until around 35–40°C (lukewarm) and then strained to separate the water from the leaves. The decoction was then given to the postpartum women who experienced perineal laceration and perineal sutures from the 2nd day postpartum to the 7th day. The women consumed 100 mL of this *binahong* water only once a day in the morning.

This study has been approved by the Health Research Ethics Committee of Universitas Bengkulu under the ethical clearance number: 310/UN30.14.9/LT/2020. Declared to be ethically appropriate following 7 (seven) the 2016 Council for International Organizations of Medical Sciences Guidelines, 1) social values, 2) scientific values, 3) equitable assessment and benefits, 4) risks, 5) persuasion/exploitation, 6) confidentiality and privacy, and 7) informed consent.¹³

Results

Table 1 demonstrates that more than one-third of subjects (11 of 30) with normal Hb levels experienced rapid perineal wound healing, and Hb level influenced perineal wound healing in postpartum women ($p=0.002$). Most subjects in the age group of 20–36 years old seemed to experience rapid perineal wound healing (17 of 30), and age-affected perineal wound healing in postpartum women ($p=0.000$). Postpartum women who graduated from senior high school experienced normal perineal wound healing (8 of

Table 1 Effect of Social Demographic Characteristics on Perineal Wound Healing

Characteristics	Wound Healing			Total (n=30)	P*
	Rapid (n=12)	Normal (n=10)	Slow (n=8)		
Hb level (g/dL)					
Normal (≥ 11)	11	4	1	16	0.243
Mild (8–10)	1	6	5	12	
Moderate (≤ 8)	0	0	2	2	
Age (years)					
11–19	0	8	5	13	0.000
20–36	12	2	3	17	
Education					
Elementary school	1	0	0	1	0.759
Junior high school	2	1	1	4	
Senior high school	6	8	6	20	
Undergraduate	3	1	1	5	
Number of children					
1	12	2	1	15	0.001
2	0	6	4	10	
3	0	2	2	4	
4	0	0	0	0	
5	0	0	1	1	
Occupation					
Housewife	7	9	7	23	0.437
Employee	1	0	1	2	
Teacher	3	1	0	4	
Civil servant	1	0	0	1	

Note: *chi-square test, $p < 0.05$ significant

30) compared with other groups, but educational background did not influence perineal wound healing in postpartum women ($p=0.759$). Women who had one child experienced rapid perineal wound healing, and the number of children affected the perineal wound healing in postpartum women ($p=0.001$). Nine out of 30 postpartum women who work as housewives experience normal perineal wound healing when compared to women with other occupations. The result of the analysis showed that occupation did

not affect perineal wound healing in postpartum women with $p=0.437$.

Table 2 presents the results of the Mann-Whitney test to see the difference and effect of *binahong* leaf decoction on perineal wound healing in postpartum women visiting private midwife practices in Bengkulu city. It was evident that there was a difference between the consumption of *binahong* leaf decoction and the use of povidone-iodine 10% in perineal wound healing. Thus, it can be stated that the provision

Table 2 Effect of *Binahong* Leaf Decoction on Perineal Wound Healing

Groups	Wound Healing			Total (n=30)	Mann-Whitney Test*	
	Rapid (n=12)	Normal (n=10)	Slow (n=8)		Statistics Test	p (Sig.)
Control	1	6	8	15	21,500	0.000
Treatment	11	4	0	15		

Note: * $p < 0.05$ significant

of *binahong* decoction affected perineal wound healing in postpartum women with a p value of 0.000.

Discussion

Low hemoglobin levels mean a decrease in the capacity of the blood to carry oxygen, so tissue hypoxia often occurs. In addition, oxygen plays an essential role in collagen formation, epithelial repair, and infection control.¹⁴ The analysis results in this study showed that the highest percentage with normal Hb levels could accelerate perineal wound healing. Furthermore, there was an influence between Hb levels and perineal wound healing in postpartum women with a p value=0.002.

It is similar to the study by Tarsikah et al.,¹⁵ that the OR value of 51.3 means that the hemoglobin level in the normal category has a perineal wound healing time of 51.3 times faster than the hemoglobin level in the anemia category. Normally, hemoglobin levels have a time of healing perineum wound by 51.3 times shorter than hemoglobin levels of anemia categories.¹⁶

In this study, most subjects in the age group of 20–60 years old seemed to experience rapid perineal wound healing. Also, the subject's age affected the perineal wound healing in postpartum women with a p value=0.000, in which perineal wounds healed faster at a young age than older age. It is because the fusion of skin tissue of postpartum women who are not of productive age has decreased due to age factors.¹⁷ Another study supports a significant relationship between maternal age and the duration of perineal wound healing in postpartum women. The analysis obtained OR=4.9, indicating that mothers not at risk tend to have five times faster perineal wound healing time.¹⁸

This study showed that postpartum women who graduated from senior high school experienced normal perineal wound healing. The analysis results with a p value=0.759 indicated that educational background did not influence perineal wound healing in postpartum women. It is supported by other study results that there is no relationship between education and the duration of perineal wound healing, with a p value=0.221.¹⁹ The results of this study differ from the theory stated by Notoatmodjo²⁰ that the level of education has an exponential relationship with the level of health. It means the higher the

level of education, the easier it is to digest the information received.

The results of the analysis show a relationship between maternal and parent's knowledge of perineal wound healing with a p value=0.001, the high expertise possessed by the respondents will support them to be able to treat the perineal wound properly. The result showed a correlation between maternal and parent knowledge of perineal wound healing with a p value=0.001. The high knowledge possessed by the respondent will support them in treating the perineal wound properly so as not to cause infection. Other studies have a relationship between the knowledge of mothers and parents about healing perineal wounds. They must know how to do it and what is not. For example, how to maintain cleanliness, color in the wound area, and how to prevent infection.²¹

Based on the results of this study, it is known that women who had one child experienced rapid perineal wound healing. The chi-square test results with a p value of 0.001 were the number of children affected by perineal wound healing in postpartum women. The results of other studies support a significant relationship between maternal parity and the duration of perineal wound healing in postpartum women. The OR value was 6.25, indicating that mothers with children less than 2 tend to experience six times better perineal wound healing.¹⁸ Mothers with high parity (often get pregnant and give birth) can make mothers experience problems with nutritional needs and nutritional status, which usually affects wound healing.²²

Table 1 showed that most postpartum women who were housewives experienced normal perineal wound healing. That occupation did not affect perineal wound healing in postpartum women, with a p value of 0.437. Analysis of four ANC visits on perineal wound healing respondents from both groups was made so that they had a percentage of 100%. Antenatal care is an antenatal service provided to pregnant women. Services are given to prepare for labor and birth to prevent, overcome, and detect problems that may arise during pregnancy. The government makes policies for antenatal care programs with a frequency of visits at least four times during pregnancy and applies a minimum service standard in its implementation.²³

The study aimed to determine the efficacy of *binahong* leaves on forming granulation

tissue and re-epithelializing open wound healing macroscopically and microscopically. Macroscopically, the wounds treated with *binahong* leaves looked smaller and dry, while those not given *binahong* leaves looked deep and red. Microscopically, the wound was given *binahong* leaves, more granulation tissue was formed, and re-epithelialization was faster than those not treated with *binahong* leaves. Giving *binahong* leaves to wounds helps wound healing by developing more granulation tissue and quicker re-epithelialization than wounds not given *binahong* leaves.²⁴

A perineal suture wound healing is characterized by the absence of infections such as color (heat), rubor (redness), tumor (swelling), dolor (pain), and functional (impaired function). Suture wound healing usually occurs from the fifth to the seventh day. It can also be faster than five days, characterized by dry wounds, no redness, swelling, fused tissue, and no pain when sitting and walking. The wound healing process divides into five stages, including the stages of homeostasis, inflammation, migration, proliferation, and maturation.⁶

Binahong (*Anredera cordifolia*) was proven empirically by the locals in assisting speedy recovery from an injury. Clinical research with lab animals receiving blunt trauma injury based on macroscopically shown signs of 1) redness, 2) heat, 3) swelling and 4) lack of activity. There is also a microscopic indication of Infiltration of inflamed cells (migration of cells to the trauma area), cell necrosis, congestion (as a result of dead red blood cells), and edema.

On administration of *binahong* for three days, there is a significant drop of 5% in cell inflammation 2% increase in fibroblast (cell membrane) count. *Binahong* does assist in reducing cell inflammation and increasing counts of cells fibroblast.⁷

Table 1 shows that the treatment group had the most rapid wound healing; 11 of 30 subjects had differences in perineal wound healing between the two research groups. Besides, there was a significant effect of *binahong* leaf decoction on perineal wound healing in postpartum women who delivered their babies in a private midwife practice in Bengkulu city with a p value of 0.000.

Another study assessing *binahong* leaf extract as an alternative treatment for perineal wound healing in postpartum women found that the average number of days for wound healing in

the treatment group was six days. In contrast, the average days for a control group that used povidone-iodine 10% was eight days. *Binahong* leaf extract showed a faster healing process than povidone-iodine 10% (the control group). It is observed that there is a significant difference in the duration of wound healing between the treatment group and the control group.²⁵

Imron and Risneni²¹ showed that the longest healing time experienced by postpartum women who were given laceration treatment with povidone-iodine is ≥ 7 days, namely 38 respondents (95%) with an average healing time of 8 days. Meanwhile, 20 respondents (50%) who used *binahong* leaf decoction showed the average healing time is five days. The t test p value was 0.000 ($p < 0.05$), meaning there was a significant difference between perineal wound healing using povidone-iodine and *binahong* leaf decoction.¹⁰ In line with a study conducted by Narsih et al.,²⁶ the sample of this study was postpartum women with grade 2 perineal wounds for 1–7 days. The results showed a significant effect of giving *binahong* leaf decoction to a perineal wound.

The results of the intervention group showed that 52.71% healed after receiving treatment for perineal wounds using a decoction of *Anredera cordifolia* that sat and soaked. On the other hand, in the control group, only using clean water showed a 27.90% recovery. Analysis of effect data using *Anredera cordifolia* decoction 25% containing perineal wound healing showed the effect of sitting and soaked *Anredera cordifolia* decoction on perineal wound healing for postpartum mothers.²⁷

Results of the ANOVA test indicated that these differences were significant ($p = 0.000$). The ethanolic extract of *binahong* leaves was effective in wound healing. Post-hoc ANOVA showed that differences in wound healing expression were significant differences ($p = 0.000$) between *binahong* leaf extract 40% with povidone-iodine and *binahong* leaf 10%.²⁸

Kaur and Mondal²⁹ stated that the topical application of *binahong* leaf paste showed better-wound healing results than 0.9% NaCl and povidone-iodine on rat skin so that it can be used as an alternative to traditional home wound treatment. The results showed that the ethanol extract of *binahong* leaves contained total flavonoids of 11.263 mg/kg (fresh) and 7.81 mg/kg (dry). The flavonoids in the dry and fresh extracts belong to the flavonol group. The ethanol

extract of *binahong* leaves has total antioxidants of 4.25 mmol/100 g (fresh) and 3.68 mmol/100 g (dry). *Binahong* leaf ethanol extract also has the capacity of an antioxidant.³⁰ The results of the bivariate analysis test obtained the Asymp value. Sig. (2-tailed) 0.013 (<0.05), which means spray gel *binahong* (with basic CMC-Na) is effective in healing perineal wounds in postpartum mothers.³¹

Based on this study's results, *binahong* leaves are recommended as a non-pharmacological treatment for mothers. It is expected that a product, such as *binahong* extract or cream, can eventually be produced as non-pharmacological midwifery care to improve the quality of midwife care in the community. Further study is needed to explore *binahong* leaves' effects on mothers with severe perineal wounds.

Conclusions

There is an effect of decoction of the leaves of *binahong* (*Anredera cordifolia* (Tenore) Steenis) on the healing of peritoneal wounds in postpartum women.

Conflict of Interest

The authors declare there is no conflict of interest.

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