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RESEARCH ARTICLES

AUTHOR GUIDELINES

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.

All articles will be discussed by experts in the field of scholarly concern (peer reviewer) and will be edited by the editor. The editor reserves the right to add or subtract sentences, both abstracts, and scripts without changing the meaning. Manuscripts that are accepted for publication will become the property of the publisher. It is not allowed to be published in other media. The needed revised manuscripts will be returned to the author. Research articles must be approved by the health research ethics committee or consider the ethical aspects of research accounted for.

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Table title is the typed center, font size 11 pt, bold, initial letter of each word written with a capital letter, except conjunctions. The titles are numbered and written on top of the table. Example: Table 3 *Neisseria gonorrhoeae* Resistance to 8 Types of Antimicrobials in 20 Specimens. Table, no vertical dividing line, and there are only three horizontal borderlines. Created tables in sequence two spaces from the text. Table descriptions and abbreviations are placed in the table description, not on the table title.

Typed center figure title with 11 pt font size, bold, numbered according to the appearance in the text and typed under the image. The source of the cited image and or table should be added to references if it is not the author's work.

Figures (graphs, diagrams, and photos) and tables besides being written in place, are also made separately on other text pages with sufficient sharpness and darkness. A maximum number of tables and or images are 6 (six) pieces. Figures are sent in black and white or colored format when required, uploaded to the Supplementary File(s) are in high-resolution jpeg, jpg, or png formats.

Write correspondence as to the footnote on the first page containing the full name of the author with degrees/academic degrees, institution, address, mobile phone, and e-mail.

Content and Format Articles

The article contains results of original research in the field of basic medical or applied, and health. The article format consists of Title, Introduction, Methods, Results, Discussion, Conclusion(s), Conflict of Interest, Acknowledgments, and References.

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Maximum article title consists of 12 words (choose words and terms that are dense meaning and able to characterize the entire contents of the script). Typed with bold fonts, size 12 pt, one space, the initial letter of each word is written in capital letters (except the conjunctive), and center. The ownership row consists of 2 elements, the author name and origin institution. The author's name written with the initial fonts is capital and bold, size 11 pt, one space, and center. Institution name written with the initial fonts is capital, size 10 pt, one space, and center.

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

Introduction

The introduction begins with the general background of the study in a brief maximum of one paragraph. Then, load the State of the Art (a brief review of literature or previous studies, 1–2 paragraphs) to justify/strengthen the statement of novelty or significance or scientific contribution or originality of this article and try to have references to articles from journals of the last 10 years that strengthen the justification for originality or contributions.

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

terms of the importance of whether or not the research was conducted.

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.

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

Chapter in Book
Miller LG. Community-associated methicillin resistant *Staphylococcus aureus*. In: Weber JT, editor. Antimicrobial resistance. Beyond the breakpoint. Basel: Karger; 2010. p. 1–20.

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

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

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RESEARCH ARTICLE

Relationship of Illness Perception and Asthma Symptoms Control in Adolescents

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Abstract

Asthma has a high prevalence in Indonesia. Good self-management is necessary for therapy and greatly affects the level of asthma control symptoms. The patient's perception plays an important role in the success of asthma therapy, especially among students, because education affects a person's mindset and perception of disease conditions. The purpose was to determine the relationship between illness perception and control of asthma symptoms in adolescents. The method was cross-sectional and was conducted from November 2019 to January 2020. The variables were asthma control and illness perception. This research was conducted on a campus in Surabaya city. Respondents were asked to fill out the Illness Perception Questionnaire (IPQ) and asthma control test (ACT) questionnaire and analyze by calculating each answer point. This study used a chi-square test to analyze the relationship between ACT and Illness perception. This study involved 75 respondents. Of most of the respondents, 58 people have their asthma partially controlled. Most respondents experienced shortness of breath and wheezing symptoms, and most understood that they were related to their asthma. There was a relationship between asthma control scores and illness perception ($p>0.05$) on the timeline ($p=0.03$), personal control ($p=0.03$), and causal representation ($p=0.01$). Illness perception can affect asthma symptoms. Asthma will be experienced for a long time, and respondents will better adjust their lifestyle and have confidence that it was controlled. Material factors were also considered. If their asthma was controlled, it was hoped not to affect their finances.

Keywords: Adolescents, asthma symptoms, illness perception

Introduction

Asthma is a globally significant non-communicable disease with major consequences on the health of children and adults, including high morbidity and death in severe cases.[1] Early recognition of the level of asthma control against self-disease is highly recommended and can self-detect if asthma is not controlled because it can prevent acute asthma attacks.[2] One of the tools that patients can use in detecting the level of asthma control is the asthma control test (ACT) questionnaire, which can detect the worsening of the disease.[3] Early recognition of the level of asthma control against self-disease is highly recommended and can self-detect if asthma is not controlled because it can prevent acute asthma attacks.[4]

This ACT questionnaire can help us identify individuals at risk for developing asthma or who may experience mild asthma symptoms. The type of screening often used is the asthma symptom score scale. The patient-completed asthma control assessment includes five domains: activity restriction, frequency of day and night symptoms (based on criteria for frequency of night awakenings), triggers, adherence, and the patient's perceived response to treatment.[5,6]

The goals of asthma treatment are to minimize future risks, namely to maintain lung function and lung development, achieve good symptom control, maintain normal activity levels, provide information and support to maximize compliance and provide information on how to avoid triggers that can lead to asthma attacks. and minimize drug side effects.[7,8] Although treatment has been effective in reducing morbidity due to asthma, the effectiveness of therapy will be achieved if the use of drugs is in accordance with their use. In addition, the patient's perception also plays an important role in therapy success because each individual's perception produces a different response from one individual to another.[9] Not a few previous studies from home and abroad have proven that illness perception plays a major role in the therapeutic outcome of a disease so that illness perception can reflect disease control in each patient.[10] The Illness Perception Questionnaire

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(IPQ) is the first attempt to systematically assess core cognitive aspects of disease representation, as developed across various disease groups. Perceived personal control is stronger than perceived control over treatment.[11,12] IPQ is a very easy and fast questionnaire to determine a person's illness perception.[11] This study aimed to determine the relationship between illness perception and control of asthma symptoms in adolescents.

Methods

The research method was cross-sectional. This study determined the relationship between illness perception and asthma symptom control in outpatient adolescent asthma patients. The data was collected from November 2019 to January 2020 in Surabaya city by filling out questionnaires. The ethics committee of the University of Surabaya approved the study protocols (No. 109A/KE/XI/2019).

The independent variable was asthma control, and the dependent variable was illness perception. The measuring instrument used to determine asthma control was the ACT questionnaire. In this questionnaire, there were five questions with a score range of 1–5. Of the five questions, the results summed and categorized into three categories, namely very controlled (score 20), well controlled (score 16–19), and uncontrolled (score 16).[7,8]

Illness perception is an individual's response to the disease through a person's perception of the disease response. Each individual has a different perception of the disease.[13,14] In this study, IPQ was the measuring instrument used to determine pain perception. In this questionnaire, there were nine questions that can be categorized into nine categories: consequences, timeline, personal control, treatment control, identity (related symptoms), disease coherence, emotional response, understanding, and concern.[10–12,14,15]

The target population of this research was active students from one of the campuses in the Rungkut subdistrict, Surabaya city, East Java, Indonesia. Respondents were part of the population who met the criteria obtained 75 people. The non-probability sampling technique was purposive sampling.

The validated questionnaires were ACT and IPQ. Content validity is an explanation of a measuring instrument substantively, or called substantive validity, which focuses on conceptualization and the extent to which previous concepts were presented in a literature review. The first step was to validate the content, with a questionnaire compiled based on the journal, which will then be translated from English to Indonesian. Then proceed with the validity test, namely assessing the questionnaire based on the concept or theory of the variables studied, by conducting trials on respondents who meet the criteria, totaling 30 people, and these respondents were not research samples. The data obtained were tabulated and correlated between instrument item scores with the help of a computer program, namely in this study using SPSS version 25 for Windows. In addition to considering the validity, the research instrument also considers the reliability aspect.

Respondents were asked to fill out and answer the IPQ and ACT questionnaire and analyze the questionnaire by calculating each answer point. Then, the respondents were asked to fill out and answer the Illness perception questionnaire. After the respondents filled in, the data and questionnaires were collected, and the questionnaires were analyzed and calculated for each question answer point. Then, the points/scores were added up, and the respondents were categorized by looking at the total number/score. This study used the chi-square test to analyze the relationship between ACT and Illness perception, whose data scale includes ordinal scale data.

Results

Respondents in this study were grouped by gender, age, formal education, occupation, length of illness, history of previous illness, family history of illness, history of allergies, and medication history. Most of the respondents were female, with an age in the late teenager range. Most respondent's education levels were senior high school. Most of the respondent's family history was no family illness (Table 1). Most of the respondents received oral short-acting beta-2 agonist (SABA) therapy, which was included in step 1 according to the guidelines of the Global Initiative for Asthma[7] (Table 2).

Asthma symptom control was measured using the ACT questionnaire, which showed that most of the respondents sometimes experienced asthma, which was felt to interfere with their daily activities. Most of the respondents never

Table 1 Frequency Distribution of Respondent Characteristics

Characteristics	n=75	%
Gender		
Male	25	33
Female	50	67
Age (years)		
Late teenager (17–25)	69	92
Early adulthood (26–35)	6	8
Education		
Senior high school	54	72
Bachelor degree	18	24
Post bachelor degree	3	4
Family disease		
Asthma	27	36
Diabetes mellitus	8	11
Hypertension	10	13
No family illness	30	40

Table 2 Asthma Control Level

ACT Total Value	n=75	%
Fully controlled (total score: 25)	3	4
Partially controlled (total score: 20–24)	58	77
Uncontrolled (total score: ≤19)	14	19

experienced symptoms of shortness of breath. Most of the respondents had never woken up at night/early, experienced 1–2 times/day using spray/oral medication to relieve breathing, and fully controlled against the control level. Table 2 showed that most of the respondents were partially controlled, as many as 58 people.

Most respondents experienced symptoms of shortness of breath and wheezing, and most respondents understand that these symptoms are related to their asthma. The cyclical timeline showed that most respondents said that they experienced asthma symptoms suddenly, while at some high points such as on the timeline (respondents realized that asthma would be suffered for life, personal control, treatment control respondents said the treatment was very helpful to overcome asthma, illness, coherence identity, emotion, and causal (Table 3).

Based on Table 4, it was known that the five most respondents answered about the cause of asthma, namely that asthma was caused by stress. Heredity, environmental pollution, overwork, and emotional feelings. With the answer choices, environmental pollution is the main cause (Table 5).

Table 6 showed that there was a relationship between asthma control scores and Illness perception ($p>0.05$) on the timeline ($p=0.03$), personal control ($p=0.03$), and causal representation ($p=0.01$).

Discussion

Gender can influence the development of asthma. The prevalence of asthma in boys was almost double that of girls at the age of <14 years, but the prevalence in girls was greater than in boys after 14 years.[16] The relationship between sex and asthma was unknown, although men's lungs are smaller at birth but larger in adulthood than women's. This may be due to pubertal sex susceptibility to the development of asthma, including hormonal changes and sex-specific differences in environmental exposure.[17]

In addition to gender, age also affects the severity and type of asthma. Late-onset asthma was experienced in some adult patients, especially women, who develop asthma in adulthood. Patients with this type of asthma were less likely to have allergies (non-allergic) and often require higher doses of ICS to treat corticosteroids.[18]

Asthma in this type of allergic asthma is closely related to genetics and is generally influenced by heredity. Increased exposure to allergens in genetically susceptible individuals can lead to allergic sensitization.[19] Continuous exposure to allergens can increase the risk of asthma and other allergic diseases. Genes can influence the pathogenesis of asthma development in the production of allergen-specific (atopic) IgE antibodies, which cause airway hypersensitivity, and inflammatory mediators (such as cytokines, chemokines, growth factors, and the ratio of the immune response ratio between Th1 and Th2).[20]

Most of the respondents received SABA therapy (Table 2). SABA, which was commonly used, was salbutamol, which acts as a reliever. These drugs were given to patients as first aid during asthma exacerbations or exacerbations. The frequency of SABA use will affect the asthma symptom control assessment. The more frequent use of SABA as a reliever indicates that the control of asthma symptoms was low because one of the requirements for asthma symptoms to

Table 3 Respondent's Perceptions of Asthma

Illness Perception			Respondent's Perceptions of Asthma			
Code	**Domain**	**Question**	**No**	**Answer Category**	**n=75**	**%**
B1	Consequence	How much does asthma affect activity?	1	Doesn't affect me at all	0	0
			2	Slightly affect	10	13
			3	Doubtful	9	12
			4	Enough Influence	25	33
			5	Very influential	31	41
B2	Timeline	How long have you had asthma?	1	Just a few days	8	10
			2	Several months	4	5
			3	Doubtful	12	16
			4	Several years	23	30
			5	Forever	28	37
B3	Personal control	How much do you feel about asthma?	1	Totally out of control	0	0
			2	A little control	17	22
			3	Doubtful	6	8
			4	Controlled	35	46
			5	Perfectly controlled	17	22
B4	Treatment control	How much do you believe that the treatment that has been done so far can help asthma?	1	Not helpful	1	1
			2	A little help	6	8
			3	Doubtful	3	4
			4	Help	31	41
			5	Very helpful	34	45
B5	Timeline cyclical	How often do you experience asthma symptoms?	1	Never	15	20
			2	1–2× a month	0	0
			3	Don't know (suddenly	57	76
			4	appeared)	1	1
			5	1–2× a week	2	2
				Every day		
B6	Illness	How much do you experience anxiety about asthma?	1	Not worried at all	26	3
			2	A little worried	15	20
			3	Doubtful	9	12
			4	Worry	17	22
			5	Very worried	8	10
B7	Coherence identity	How much do you understand asthma?	1	Do not understand	0	0
			2	Understand a little	19	25
			3	Doubtful	6	8.
			4	Understand	39	52
			5	Really understand	11	14
B8	Emotion	How much does asthma affect your emotions?	1	Doesn't make me emotional	23	30
			2	A little emotion	20	26
			3	Doubtful	5	6
			4	Emotion	9	12
			5	Very emotional	18	24
B9	Causal representation	How much does asthma affects your financial condition?	1	Not affect	25	33
			2	Slightly affect	23	30
			3	Doubtful	4	5
			4	Influence	6	8
			5	Very influential	17	22

Table 4 Respondent's Perceptions Regarding the Causes of Asthma Experienced

No	Asthma Cause	Number of Respondents Who Answered					
		STS	TS	R	S	SS	Total
C1	Stress or anxiety	0	31	0	36	8	75
C2	Heredity/genetics	0	35	2	24	14	75
C3	Germs, viruses, infections	9	40	8	14	4	75
C4	Eating patterns or habits	0	40	6	20	9	75
C5	Bad luck	4	54	4	6	7	75
C6	Bad treatment in the past	6	52	4	8	0	75
C7	Environmental pollution	3	0	0	52	17	75
C8	My behavior	2	31	5	28	7	75
C9	Always think negative	4	32	11	28	0	75
C10	Problems in the family	4	36	7	27	1	75
C11	Too much work	0	5	7	55	8	75
C12	Emotional feeling	4	27	4	33	7	75
C13	Aging/getting older	1	61	6	7	0	75
C14	Alcohol consumption	10	58	7	0	0	75
C15	Smoke	9	48	0	9	11	75
C16	Due to injury/accident	10	58	7	0	0	75
C17	Decreased immunity	3	45	11	10	8	75

Note: STS: strongly disagree, SS: totally agree, R: hesitated, S: agree, TS: disagree

Table 5 Respondent's Perceptions Regarding the Three Highest Factors that Cause Asthma

No	Asthma Cause	Number of Respondents Who Answered		
		1st	2nd	3rd
C1	Stress or anxiety	5	4	0
C2	Heredity/genetics	6	0	2
C3	Germs, viruses, infections	2	6	2
C4	Eating patterns or habits	2	4	4
C5	Bad luck	2	0	0
C6	Bad treatment in the past	0	0	0
C7	Environmental pollution	25	26	8
C8	My own behavior	2	7	4
C9	Always think negative	0	0	2
C10	Problems in the family	0	0	0
C11	Too much work	18	12	6
C12	Emotional feelings (such as feeling sad, lonely, anxious)	7	6	0
C13	Aging/getting older	0	0	0
C14	Alcohol consumption	0	0	0
C15	Smoke	1	4	0
C16	Due to injury/accident	0	0	0
C17	Decreased immunity	0	0	2

be well controlled was using a reliever maximum of twice a week.[21] Salbutamol belonged to the beta-2 agonist class (adrenoceptor agonists), having a smooth muscle relaxing action by activating 2 (β2AR) receptors and inhibiting the release of several mast cell substances, inhibiting microvascular leakage and increasing mucociliary transport by increasing ciliary activation or

Table 6 Cross-tabulation of Pain Perception and Asthma Control

No	Aspect	p
1	Consequences	0.92
2	Timeline	0.03*
3	Personal control	0.03*
4	Treatment control	0.61
5	Timeline cyclical	0.49
6	Illness coherence	0.25
7	Identity	0.36
8	Emotional response	0.06
9	Causal representation	0.01*

Note: *p<0.05 significant

affecting the composition of mucus secretion.[22]

Assessment of asthma control will affect the therapy used. Asthma treatment/management based on asthma control includes three things that need to be evaluated continuously, namely: assessment, including diagnosis, symptom control and risk factors (including lung function), inhaler technique and adherence (adherence).[7] Then the dose adjustment (adjust treatment) was carried out based on the results of the previous assessment, and then the response review was based on the previous dose adjustment. If the results of the response assessment have yet to be maximized, it needs to be considered for a return assessment.[7,9]

Most of the respondents' asthma control level was partly controlled. Factors that affect asthma control include obesity, stress, cigarette, and physical activity. Obese people with asthma have lower lung function and more comorbidities than normal-weight people.[23]

Asthmatic patients who experience stress and anxiety can trigger an attack; stress can trigger aldosterone secretion and the release of catecholamines in response to low cardiac output, thereby accelerating the decline in serum potassium levels. Stress also reduces the body's immune system's ability to fight off pathogenic bacteria. So those asthmatics who experience stress have a greater chance of experiencing exacerbations. The basic theory is that psychological stress works by changing the magnitude of the airway inflammatory response that causes irritation, allergens, and infections in people with asthma. This suggests that stress alone cannot modify immune function in a way that leads to asthma symptoms.[24]

Tobacco smoke in cigarettes accelerates the decline in lung function in people with asthma, increases asthma severity, and makes patients less responsive to treatment with inhaled and systemic glucocorticosteroids, but smokers tend to achieve control and remain at risk of exacerbations.[25]

Asthma patients believed that physical activity can worsen asthma symptoms, to the risk of the disease in the long term. Patients with serious illnesses had the belief that physical activity was not good for asthma. Reluctance to do physical activity was not only due to worsening asthma symptoms but also caused by psychological factors. Exercise-induced asthma is a symptom in non-asthmatic patients due to excessive physical activity. This can happen when a person is doing strenuous physical activity, and they will breathe faster through the mouth.[7,12]

Most respondents experienced symptoms of shortness of breath and wheezing (Table 5). This was in line with many respondents saying asthma-related symptoms are shortness of breath and wheezing. This was in accordance with the symptoms of asthma that do occur. The whistling sound was caused by interference with the respiratory tract or excessive mucous production. If breathing is difficult, then the body's cells experience a lack of oxygen supply, which could cause difficulty sleeping or waking up at night, in addition to causing the body to become tired. While sore throat, nausea, abdominal pain, stiff joints, eye pain, headache, dizziness, and weight loss were symptoms unrelated to asthma. However, it was likely that these symptoms might be caused by the side effects of medications used by patients.[7,12]

Respondent's perception of asthma had a low point in consequence (asthma greatly affected daily activity at 41.33%). Asthmatics do have limitations in their activities. Therefore, if it was known what activities can cause asthma, patients should be counseled to take medication first to prevent asthma attacks.[7]

Illness perception will affect the way asthma patients cope and self-management of the disease. This data can inform healthcare providers about a patient's psychosocial response to their asthma, whether they were responsive to changes in clinical meetings or through self-management intervention training. Therefore, exploring the patient's perception of the disease was an important component of good clinical

care.[9] One factor affecting self-management is illness perception, the patient's cognitive picture of the disease. This image was identified through five dimensions: identity, consequences, disease causes, timeline, healing, or control.[11] Knowing a person's perception of the disease can be done by providing education and more information to patients. In addition, efforts can be made to develop good health approaches and promotion strategies to reduce the number of patients exposed to asthma attacks and participate in improving the quality of life of patients.

There was a relationship between asthma control scores and illness perception on a timeline, personal control, and causal representation (Table 6). This was different from previous research by Lorensia et al.,[13] which states that there was a relationship between asthma control and illness perception (on control and identity). Other research showed that most of the highest illness perceptions were about asthma symptoms experienced by respondents on individual scores related to permanent symptoms. When the influence of illness perception on symptoms, the results obtained were significant, such as how long asthma had been suffered and illness perception about the cause, which was significant for changes in asthma symptoms.[13]

Conclusions

Most of the respondents have their asthma partially controlled. Most respondents experienced shortness of breath and wheezing symptoms, and most understand that these symptoms are related to their asthma. There was a relationship between asthma control and illness perception on the timeline dimensions, personal control, and causal representation.

Conflict of Interest

The authors declare no conflict of interest.

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References

1. Schröders J, Wall S, Hakimi M, Dewi FST, Weinehall L, Nichter M, et al. How is Indonesia coping with its epidemic of chronic noncommunicable diseases? A systematic review with meta-analysis. PLoS One. 2017;12(6):e0179186.
2. Nguyen VN, Huynh TTH, Chavannes NH. Knowledge on self-management and levels of asthma control among adult patients in Ho Chi Minh city, Vietnam. Int J Gen Med. 2018;11:81–9.
3. Soler X, Holbrook JT, Gerald LB, Berry CE, Saams J, Henderson RJ, et al. Validity of the asthma control test questionnaire among smoking asthmatics. J Allergy Clin Immunol Pract. 2018;6(1):151–8.
4. Gemicioğlu B, Mungan D, Bavbek S, Yıldız F, Polatlı M, Naycı S, et al. Validity and reliability of the assessment tool for asthma (ATA) questionnaire: the ATA study. Turk Thorac J. 2020;21(2):93–9.
5. Alzahrani YA, Becker EA. Asthma control assessment tools. Respir Care. 2016;61(1):106–16.
6. van Dijk BCP, Svedsater H, Heddini A, Nelsen L, Balradj JS, Alleman C. Relationship between the asthma control test (ACT) and other outcomes: a targeted literature review. BMC Pulm Med. 2020;20(1):79.
7. Global Initiative for Asthma. Global strategy for asthma management and prevention, 2021. Fontana: Global Initiative for Asthma; 2021 [cited 2022 February 16]. Available at: https://ginasthma.org/wp-content/uploads/2021/05/GINA-Main-Report-2021-V2-WMS.pdf.
8. Lorensia A, Wahyudi M, Mayzika NA. Effectiveness of fish oil containing omega-3 in improving symptoms and lung function in asthma outpatient in Surabaya, Indonesia. IJPQA. 2018;9(3):260–6.
9. Papi A, Blasi F, Canonica GW, Morandi L, Richeldi L, Rossi A. Treatment strategies for asthma: reshaping the concept of asthma management. Allergy Asthma Clin Immunol. 2020;16:75.
10. Wang J, Yang Z, Zheng Y, Peng Y, Wang Q, Xia H, et al. Effects of illness perceptions on health-related quality of life in patients with rheumatoid arthritis in China. Health Qual Life Outcomes. 2021;19(1):126.
11. Sawyer AT, Harris SL, Koenig HG. Illness perception and high readmission health outcomes. Health Psychol Open.

2019;6(1):2055102919844504.
12. Lorensia A, Suryadinata RV, Istiqomah NL, Diputra INY. Aktivitas fisik dan risiko PPOK pada pengemudi becak di Surabaya. JSK. 2021;3(5):706–14.
13. Lorensia A, Wahyudi M, Yudiarso A, Kurnia SED. Effect of illness perception on improving asthma symptoms with omega-3 fish oil therapy: pre-post design. JAPS. 2020;10(6):62–71.
14. Lorensia A, Suryadinata RV, Ratnasari R. Gambaran persepsi penyakit terhadap kesehatan fungsi paru pada pasien asma di Surabaya. IJPH. 2019;14(2):263–71.
15. Indrayana S, Fang SY. Validitas dan reliabilitas the brief illness perception questionnaire versi bahasa Indonesia pada pasien diabetes mellitus. Dinamika Kesehat. 2019;10(1):361–8.
16. Trivedi M, Denton E. Asthma in children and adults—what are the differences and what can they tell us about asthma? Front Pediatr. 2019;7:256.
17. LoMauro A, Aliverti A. Sex differences in respiratory function. Breathe (Sheff). 2018;14(2):131–40.
18. Quirce S, Heffler E, Nenasheva N, Demoly P, Menzies-Gow A, Moreira-Jorge A, et al. Revisiting late-onset asthma: clinical characteristics and association with allergy. J Asthma Allergy. 2020;13:743–52.
19. Schoettler N, Rodríguez E, Weidinger S, Ober C. Advances in asthma and allergic disease genetics: is bigger always better? J Allergy Clin Immunol. 2019;144(6):1495–506.
20. Murrison LB, Brandt EB, Myers JB, Hershey GKK. Environmental exposures and mechanisms in allergy and asthma development. J Clin Invest. 2019;129(4):1504–15.
21. Kaplan A, Mitchell PD, Cave AJ, Gagnon R, Foran V, Ellis AK. Effective asthma management: is it time to let the AIR out of SABA? J Clin Med. 2020;9(4):921.
22. Jahedi L, Downie SR, Saini B, Chan HK, Bosnic-Anticevich S. Inhaler technique in asthma: how does it relate to patients' preferences and attitudes toward their inhalers? J Aerosol Med Pulm Drug Deliv. 2017;30(1):42–52.
23. Tashiro H, Shore SA. Obesity and severe asthma. Allergol Int. 2019;68(2):135–42.
24. Landeo-Gutierrez J, Celedón JC. Chronic stress and asthma in adolescents. Ann Allergy Asthma Immunol. 2020;125(4):393–8.
25. Tiotiu A, Ioan I, Wirth N, Romero-Fernandez R, González-Barcala FJ. The impact of tobacco smoking on adult asthma outcomes. Int J Environ Res Public Health. 2021;18(3):992.

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RESEARCH ARTICLE

Community Perception in Preventing Cases of COVID-19 in Bogor City in 2020

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Abstract

The COVID-19 outbreak of a coronavirus that causes illness shocked the world. Health precautions must be implemented to limit the number of COVID-19 cases or prevent transmission. This study aims to ascertain the public's perception of the COVID-19 case in the community. This report is one of the findings of a survey of the association between comorbidities and preventative behavior in COVID-19 cases, specifically public perceptions of COVID-19 cases in Bogor city. This study took place from March through the end of September 2020. Data were obtained through in-depth interviews utilizing a guideline developed based on the parameters of a qualitative study. The prior recommendations were validated, and the data was represented using transcripts and a data matrix to aid in the descriptive data analysis. According to a study on public views of COVID-19, individuals realize the risks they face if they do not adhere to the government's health protocols. According to quantitative data, the proper use of masks when outside the home is only 18.0%, the correct use of hand sanitizers is 26.2%, the correct use of soap is 80.3%, the proper use of hand sanitizers is 90.2%, and the correct coughing and sneezing behavior is 60.7%. In general, research data findings have not been encouraging for COVID-19 prevention; therefore, you will be prone to COVID-19 infection if you disregard health regulations, particularly by correctly wearing masks. As a result, in general, the findings of public perception have not been able to diminish the number of COVID-19 instances.

Keywords: COVID-19, health protocols, prevention behavior, perception

Introduction

In late 2019, a new illness known as coronavirus disease 2019 (COVID-19) appeared in China. This deadly illness targets the respiratory system. COVID-19 has a rapid transmission rate and can infect multiple continents at once. Similar incubation periods (average 4–5 days) and symptoms (pneumonia) but distinct host reservoirs characterize this virus, which is related to severe acute respiratory syndrome (SARS) and Middle East respiratory disease (MERS) viruses. While civets transmit SARS to humans, humped camels are responsible for MERS transmission, and bats are responsible for transmitting COVID-19.[1,2]

Mild, moderate, or severe symptoms can induce COVID-19 infection. The main clinical symptoms are fever, cough, pain, and dizziness. In severe conditions, patients can experience severe shortness of breath. In connection with these non-specific signs, the focus of reducing the number of COVID-19 cases is the prevention of transmission by implementing the COVID-19 transmission prevention protocol. The responsibility for preventing transmission is shared between the government and the community.[3] In addition, the spread of this disease has a broad social and economic impact.[4]

To stop the spread of COVID-19 cases, the government issued policies, including restrictions on physical and social contact known as large-scale social restrictions (LSSR) and regulations to accelerate the spread of COVID-19 so that they could be implemented immediately in various regions through the Minister of Health of the Republic of Indonesia. Minister of Health Regulation Number 9 of 2020 contains the LSSR rules. The Minister of Health issued a Minister of Health Regulation about LSSR regulations involving DKI Jakarta on April 10, 2020. Furthermore, the Minister of Health of the Republic of Indonesia published a Ministerial Regulation on LSSR for West Java province. LSSR was issued for Bogor-Depok-Bekasi or Bodebek on April 15, 2020.[5] People must be active and work for their needs to be met and for the economy to continue functioning. In contrast, interacting with others increases the likelihood of COVID-19 transmission. Seeing

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this, the government has adopted a new normal, namely, an order to adjust new habits for people to continue living productively by changing their lifestyle so they do not develop COVID-19.[6]

The COVID-19 pandemic has also affected the world of education. The temporary suspension of educational institutions to prevent the global spread of the COVID-19 pandemic, which has prevented millions of students from attending school, is also in effect in Indonesia. Problems arise in the teaching and learning process between students and instructors due to learning at home or through distance education. Both educators and students must be able to adapt rapidly to existing changes. In this situation, Ningsih[7] conducted a study of 95 students from the Education Technology Study Program at Universitas Baturaja in South Sumatra, and the results showed that 93.3% of students preferred to study in class face-to-face (offline) because there were obstacles encountered when learning was done online at home. As many as 32.3% of respondents admitted to wasting their internet quota. Then, 24.2% of respondents indicated that the lecturer's content description needed to be revised. Then, 24.2% of students stated that the internet signal was limited, 16.1% stated that learning interaction was limited, and 3.2% said that online learning media was difficult to follow, knowledge of the topic was not optimal, and engagement was limited. This challenge arises due to the constraints of students who must constantly meet their internet quota during COVID-19.

The COVID-19 epidemic has also had an impact on economic conditions. According to Permatasari et al.'s[8] research, many people complained about financial concerns. People who run home-based enterprises and traders see a considerable drop in sales income/turnover compared to before the epidemic. On the other hand, it is difficult for people to find work; many who have worked have been laid off and have yet to be called back. The rising number of COVID-19 cases in the area highlights the need for research or studies focused on gauging public awareness of the pandemic.[9] Preliminary data According to the quantitative data from this study showed that 18.0% correctly used a mask outside the home, 80.3% washed their hands with soap, 26.2% used hand sanitizers, 90.2% maintained a physical distance, and 60.7% implemented good coughing and sneezing etiquette. The preventive behavior seen in this study was implemented in response to the suggestion, yet some continue to disregard it, affecting the addition of COVID-19 incidents.[10]

This study aims to ascertain the public's perception of the COVID-19 case in the community.

Methods

The research is being conducted in Bogor. The Ministry of Health Republic of Indonesia conducted a study on the association between comorbidities and COVID-19 preventative behavior in Bogor in 2020, which included all research participants. This study took place from March through the end of September 2020. The research design was qualitative, with the Rapid Assessment Procedures (RAP) approach used to gather detailed information about public attitudes and community behavior towards the COVID-19 pandemic, particularly COVID-19 preventative behavior. Which was compiled using a structured questionnaire with variables such as the patient's name, age, and eight open questions about health conditions, behavior for seeking health facilities, preventive behavior two weeks before treatment, during treatment, and after treatment, efforts to prevent illness experienced, and contact history with COVID-19 patients. RAP is a quick approach for researchers to confirm quantitative data quality by taking 5 to 10% of the complete quantitative sample. Purposive sampling was used to select informants from the research site. There were 12 research samples, six verified cases of COVID-19, and six non-COVID-19 responses. Qualitative data is collected through direct talks on mobile phones, including voice calls and video calls using the WhatsApp function, as well as standard voice calls; all calls are recorded after getting consent from the respondent.

Data processing and analysis were performed manually by compiling data from interviews, field notes, and other materials. In this study, content analysis techniques were employed to analyze the answer matrix from the informants. This study activity has gained ethical approval from the Health Research Ethics Committee, National Institute of Health Research and Development, Ministry of Health Republic of Indonesia, No. LB.02.01/2/KE.505/2020.

Results

According to the characteristics of the 12 informants interviewed in-depth, they ranged in

age from 29 to 82 years old, were predominantly male (9 men), and held occupations (5 male and two female). Data collected from in-depth interviews with participants about their health conditions indicates that the community enjoys generally good health, with little or no significant health complaints. However, one of the informants stated that a family member had died due to COVID-19. Some informants said that most participants frequently receive routine health assessments because they had several types of previous COVID-19 illnesses that required them to control their healthcare facilities, such as diabetes, herpes, cholesterol, and gout. Still, there were a small number of informants who rarely checked into health facilities.

Signs and symptoms of COVID-19 obtained from participants in the two weeks before hospitalization related to general health conditions revealed that the participants experienced fever, not feeling well, feeling weak, and decreased appetite, even though they felt before the informant was sick (in-patient), still doing activities as usual, such as going to the market, going to the office, and traveling out of town. However, some still claim they only do activities at home

In light of the COVID-19 incidents causing public concern, hospital in-patients must receive improved care and treatment. It is consistent with most informants' statements that treatment can be adequately performed, such as IV administration, the availability of oral medications, injections, and the friendly services provided by health personnel by handing masks to patients. However, one source continued to react as follows:

"Not all medical services are performed, such as laboratory examinations, x-rays, physiotherapy, and others, which the administration should monitor based on the patient's health condition."

In-depth interviews revealed that nurses generally wear personal protective equipment (PPE) appropriately and correctly, are very professional, and are responsible when the community is asked about the quality of service at the hospital when the informants are being treated. However, there are still differing viewpoints among the informants, who state;

"Because the informant rarely visited the hospital, he could not provide information or assess the hospital's service quality because informants only do their treatment by purchasing medicine from a stall or drug store and consuming traditional medicine by drinking herbal medicine, etc."

Furthermore, maintaining personal hygiene and following healthy living habits are critical to retaining cleanliness. The informant stated that he improved his hygiene by washing his hands frequently, eating nutritious food, engaging in modest exercise activities such as walking, running, and taking vitamins or herbal medicines to boost his immunity. Some informants stated that when they leave the house, even in their private automobiles, they still follow health measures such as donning masks to avoid infection with the COVID-19 virus.

Regarding seeking treatment before being admitted to the hospital, most informants said they treat and buy medicine for themselves and rarely go to the health service or general practitioner's clinic for a health assessment. If necessary, the informants go to the doctor. According to one source:

"When I am sick, I am too lazy to go to the hospital; instead, I rely on antibodies and eat a lot." I was consuming sanmol from stalls and herbal medications sent by the office manager at the time."

Concerning the COVID-19 infection in the community, most informants stated that they had never come into contact with COVID-19 patients. However, there was information from a few informants exposed to the virus at work. According to the informant, COVID-19 can infect persons of all ages, from children to adults. Furthermore, patients with COVID-19 who have comorbidities are more likely to develop the condition. However, among the informants, there are still many who are unconcerned about the environment, as evidenced by their indifferent responses to the COVID-19 outbreak, as mentioned below:

“I don't care about people who don't wear masks or just ignore them.”

Concerning the public health hazards linked with the current COVID-19 pandemic, a few informants still perform health checks such as blood or rapid/swab tests. One source explained

it this way:

"I still go to the doctor regularly because I have other diseases, such as diabetes."

Discussion

According to the findings of the research paper by Senewe et al.,[10] the behavior of preventing COVID-19. However, some public views still need to be addressed, such as using masks and coughing behavior. Those are apparent in the responses of respondents on COVID-19 prevention. Looking at the percentages, 90.2% of informants maintain physical distance, 60.7% cough and sneeze correctly, and 80.3% wash their hands with soap. Just 18% of informants who used masks outside the house were at an increased risk of contracting COVID-19. This lack of awareness has resulted in coronavirus transmission from one person to another. Furthermore, many people take this infection casually by passing regulatory rules. Again, just 26.2% of respondents prefer to use hand sanitizer properly.

This reflects that COVID-19 prevention has yet to be a primary priority for some district officials. Because informants do their treatment by purchasing pharmaceuticals at stalls or drug stores and taking traditional treatments by drinking herbal medicine, research by visiting health institutions such as hospitals is rarely conducted. The informant stated they must be more active in the hospital or other health facilities if sick. As a result, they attempt to treat themselves and purchase medication.

All humans, particularly those in Indonesia, value their health significantly. However, maintaining a consistently healthy and fit life requires effort because numerous circumstances might influence it. According to multiple social media accounts, bodily immunity is crucial in preventing the spread of the COVID-19 virus. If the immune system drops, the virus can easily infiltrate the body and create significant health problems. As a result, if the stress and anxiety caused by the COVID-19 infection persist, it will cause a decline in immunological levels. As a result, the spread of COVID-19 disease will skyrocket.[11]

Because the COVID-19 pandemic is becoming increasingly severe, the government has declared a public health emergency and issued three regulations as a form of public health protection, namely: 1) financial policy and financial stability for dealing with the COVID-19 pandemic; 2) declaration of a public health emergency, and 3) LSSR. At the same time, LSSR restricts some activities of residents in an area suspected of being infected with a disease or contaminated to prevent the disease or contamination from spreading. On the one hand, some people advocate installing the LSSR since it can disrupt the transmission chain. This strategy is consistent with WHO recommendations for physical and social distance.[12,13] Finally, the government elected not to impose a regional quarantine policy, instead opting for the large-scale social restriction (LSSR) strategy, as stated in Government Regulation 21 of 2020.[14]

Regarding the issues above, which are tied to people's behavior, people are still unaware of their daily actions related to COVID-19 transmission. COVID-19 could still be in our surroundings. According to Kalangie,[15] the characteristics of human conduct that affect health can be divided into two categories: 1) behavior that helps the health of individuals or social groups and 2) behavior that affects health. Based on the findings of this investigation, the general population explained behavioral practices that were not recognized as COVID-19 transmission routes, such as sipping coffee with colleagues at work. This virus begins to show symptoms in five to seven days, after which an assessment with the same friends who have already been infected with COVID-19 is performed. This could be interpreted as purposeful behavior.

According to our research, 18.0% of people use masks appropriately before leaving home. This tiny statistic suggests that health behavior in the current case reduction technique needs to be revised. A mask is required for all activities, including grocery shopping, meeting loved ones, participating in events, and attending religious services. Data on the efficacy of health protocol monitoring in ensuring mask-wearing compliance show that the 1.4 million people under observation exhibit high adherence. While 1.4 million may appear tiny compared to Indonesia's total population, it is critical to improve this amount to strengthen public health protocol adherence and ensure the safe continuation of community activities during COVID-19 transmission.[16]

Since the COVID-19 case, there have been restrictions on educational activities that are particularly harmful to the development of our generation of students and a loss of government

revenue owing to the denial of retribution and income tax. This is unquestionably risky because your safety is not guaranteed, and your health and capacity to operate in society are jeopardized. The next difficulty is a house condition that could be more conducive to school circumstances, particularly if parents need to facilitate the situation at home so that children do not have a comfortable learning environment. As a result, many respondents confessed that it was difficult to concentrate while studying at home, not only because of the improper setting but also because they were frequently disturbed by other family members while studying and performing assignments. Furthermore, children may believe their parents should be more patient when accompanying them to school. Even though parents are the most essential part of the learning process at home.[17]

This can be accomplished by enlisting volunteers, TNI, POLRI, and other community organizations to monitor and enforce health protocol compliance. Then, for all regions in Indonesia, the reduction in the LSSR level has several effects on expanding population movement. To increase community mobility, greater adherence to health procedures, such as wearing masks, adopting social distancing, and constantly practicing excellent hand cleanliness, must be balanced.

Geldsetzer[18] believes public health officials and the media should prioritize COVID-19 communication activities in 2020. This information could provide valuable insights, such as the low case fatality rate, recommended treatment-seeking behavior, the low risk of individuals of East Asian ethnicity living in the United States and the United Kingdom, and the perception that children are less susceptible to fatal diseases than adults. Furthermore, to ensure that individuals focus on the most effective preventive measures, this study suggests that it is essential to inform the public about the comparative effectiveness of general versus frequent surgical masks, wash hands thoroughly, and avoid close contact with sick people. As a result, the generalizability of these findings may be enhanced. Furthermore, sure participants' statements may be chosen randomly to lessen their time investment in receiving the $1.50 incentive. Participating in the survey is required, and earning $1.50 as a monetary prize is a reasonable incentive. Third, users can search for answers to several questions online before replying. To summarize, people in the United States and the United Kingdom appear to have significant misconceptions about COVID-19. Correcting these beliefs should prioritize government awareness campaigns, doctor-patient communication, and media coverage.

Faasse and Newby[19] indicated in 2020 that significant and continuing involvement with health-protective behaviors (i.e., hygiene and social distancing) is necessary to control the COVID-19 pandemic successfully. The online survey, which included 2,174 Australians, was done between March 2 and 9, 2020, during the early phases of the COVID-19 outbreak in Australia. The findings revealed that two-thirds of respondents were at least moderately concerned about the widespread COVID-19 epidemic. Concern about attacks and subsequent media coverage were consistent predictors of increased engagement in health-protective behaviors and higher vaccination intentions. Uncertainty and misconceptions concerning COVID-19, including whether people have natural or pre-existing immunity to the virus, are frequent. There is debate whether specific home remedies (such as vitamins and saline solution) will provide protection and whether the virus is artificial and purposely distributed. Such misunderstandings often generate alarm among members of the public. The findings also emphasize psychological and demographic characteristics associated with reduced involvement in health-protective behaviors, such as male gender, younger age, and lower degrees of concern about the outbreak. These findings suggest possible intervention pathways and targets for promoting health-protective behaviors.

According to Tejamaya et al.,[20] societal perceptions of an early-stage pandemic may have substantial ramifications for disease control and management in the future. This survey has a total of 1,043 participants. Respondent's primary sources of information are social media (85.2%) and Internet news (82.2%). Almost all respondents know that COVID-19 is a viral disease that spreads primarily through saliva droplets (97.1%) and contaminated surfaces (86.5%). COVID-19 is regarded as serious or extremely serious by more than 95% of respondents. However, the respondent's anxiety level is mild, showing that risk tolerance exists in the community. Gender, educational background, and occupation were shown to have statistically significant correlations with perceived risk and patience, while volunteer

participation in control measures was high and comparable. This suggests that the COVID-19 health campaign in Indonesia at the start of the pandemic was successful. The study also identifies areas where health promotion, education, and awareness might be enhanced.

Jaber et al.[21] discovered good responses to various questionnaire items among participants. About 55.0% of Jordanian and 56.0% of Iraqi participants self-reported being aware of COVID-19. In comparison, only 72.3% of Jordanian and 73.3% of Iraqi participants self-reported being aware of COVID-19 protective and precautionary measures. Total awareness is calculated as the sum of the consciousness as mentioned above subscales. Regarding developing signs of COVID-19 infection, practically all Jordanian and Iraqi subjects experienced fever (98.0% and 96.3%, respectively). More than 90% of Jordanian and Iraqi participants recognized dyspnea as a typical symptom. Approximately 90% of both groups believe COVID-19 can be transmitted through shaking hands and contact with contaminated surfaces. Furthermore, over 80% of both groups' participants reported that the virus could be transmitted through droplet inhalation. Over 96% of Jordanian and Iraqi participants indicated avoiding crowded locations to reduce the risk of infection. Furthermore, almost 90% of both groups reported significant reductions in shaking hands and kissing. Furthermore, approximately 90% of Jordanian and Iraqi participants reported regularly washing their hands with soap and water. There is currently no cure for COVID-19, according to three-quarters of Jordanian and Iraqi participants. In contrast, 34.8% of Jordanian and 47.3% of Iraqi participants thought vitamin supplementation was a feasible therapy option. Furthermore, nearly 30% of both groups thought paracetamol might be used to treat COVID-19. Geriatric patients were identified as being the most vulnerable to COVID-19-related mortality by around 30% of both groups. Furthermore, more than half of both groups believe the COVID-19 mortality rate is less than 5%. Our findings revealed a statistically significant difference in the Iraqi cohort's mean precautionary score between the two sexes (p=0.01). Women were more likely than men to have higher mean conscientiousness assessment scores (mean difference=0.1903; confidence interval=0.07–0.3). Furthermore, statistically significant relationships were found among Jordanian and Iraqi participants between different age groups and transmission, preventative measures, and treatment ratings (all $p<0.05$). Post-hoc analyses failed to reveal consistent trends across age groups and consciousness subscales. In conclusion, the population level of consciousness was competent but deficient in crucial dimensions such as transmission and treatment awareness. Both populations appear to have comparable attitudes and perception tendencies about the COVID-19 epidemic, resulting in an equivalent culture. To assist the people in dealing with the challenges of the growing pandemic, relevant authorities should devote time and money to raising awareness through official forums and significant social media efforts.

According to Shelat et al.,[22] the susceptibility of family and friends had the most significant impact—nearly twice the own health risk. Respondents who traveled more considerable distances by train were deemed four times more dangerous than those who traveled fewer. When the two models are combined, we will pay for mitigating factors such as reduced overcrowding, enforced mask use, and improved sanitation. As a result, we may utilize forecast models to anticipate behavior under complex pandemic scenarios after evaluating the impact of many variables on route choice behavior.

Alkhaldi et al.[23] noted that most respondents (74%) were worried about the COVID-19 epidemic, and 27% of them reported that it was likely that they would be infected with COVID-19; 16% believed it would be life-threatening or severe. However, just 11% of respondents reported high levels of anxiety. Adoption of hygiene practices and social distancing is lower among older (>65 years) compared to younger (18–24 years) respondents (95% CI=0.01–0.28, OR=0.06; and 95% CI=0.01–0.27, OR=0.06, respectively). Those with the lowest gross household incomes and at least one flu symptom were less able and willing to separate themselves. Significant increases in anxiety levels, perceived effectiveness of social distance, and cleanliness habits were observed in the post-lockdown compared to the lockdown.

Conclusions

The residents of Bogor city have a negative opinion of the practice of preventing COVID-19 by following the required health regulations. When treated with COVID-19, patients tend to

believe that not all patients undergo medical examinations, that medicating themselves is better than having to go to the hospital or seek treatment, and that does not be fooled or ignorant about the adherence to wearing masks properly, but for sufferers with chronic or comorbid diseases such as DM, etc., routinely carry out periodic controls/examinations at health care facilities. It is vital to enhance socialization by applying 5M, meaning keeping distance, using masks, avoiding crowds, washing hands, and decreasing mobility, to break the cycle of the spread of the pandemic and return to everyday life as quickly as possible. Next, if there is a suspicion of a perceived complaint about the health of the body, go to a health care center.

Conflict of Interest

None declared.

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References

1. Direktorat Jenderal Pencegahan dan Pengendalian Penyakit, Kementerian Kesehatan Republik Indonesia. Pedoman kesiapsiagaan menghadapi infeksi novel coronavirus (2019-nCoV) [Internet]. Jakarta: Kementerian Kesehatan Republik Indonesia; 2020 [cited 2022 May 16]. Available from: https://infeksiemerging.kemkes.go.id/download/DOKUMEN_RESMI_Pedoman_Kesiapsiagaan_nCoV_Indonesia_28_Jan_2020.pdf.
2. Wu C, Chen X, Cai Y, Xia J, Zhou X, Xu S, et al. Risk factors associated with acute respiratory distress syndrome and death in patients with coronavirus disease 2019 pneumonia in Wuhan, China. JAMA Intern Med. 2020;180(7):934–43.
3. Quyumi RE, Alimansur M. Upaya pencegahan dengan kepatuhan dalam pencegahan penularan COVID-19 pada relawan COVID. J Public Health Res Commun Health Dev. 2020;4(1):81–7.
4. Susilo A, Rumende CM, Pitoyo CW, Santoso WD, Yulianti M, Herikurniawan, et al. Coronavirus disease 2019: tinjauan literatur terkini. J Penyakit Dalam Indones. 2020;7(1):45–67.
5. Letelay AM, Senewe FP, Tobing KL, Sitorus N, Pracoyo NE, Manalu HSP, et al. Clinical characteristics and severity of COVID-19 at COVID-19 referral hospital in Bogor, West Java, Indonesia. Univers J Public Health. 2023;11(2):242–50.
6. Kementerian Kesehatan Republik Indonesia. Pencegahan, pedoman, dan pengendalian coronavirus disease (COVID-19) [Internet]. Jakarta: Kementerian Kesehatan Republik Indonesia; 2020 [cited 2022 May 20]. Available from: https://covid19.go.id/storage/app/media/Protokol/2020/Juli/REV-05_Pedoman_P2_COVID-19_13_Juli_2020.pdf.
7. Ningsih S. Persepsi mahasiswa terhadap pembelajaran daring pada masa pandemi COVID-19. JINOTEP. 2020;7(2):124–32.
8. Permatasari NEF, Wardhani UC, Agusthia M. Studi fenomenologi: persepsi masyarakat kota batam tentang pencegahan dan perawatan COVID-19 tahun 2020. JIK. 2021;5(1):161–70.
9. Sarwono SW, Meinarno EA. Pengantar psikologi umum. 9th Printing. Jakarta: Rajawali Pers; 2018.
10. Senewe FP, Pracoyo NE, Marina R, Letelay AM, Sulistiyowati N. Pengaruh penyakit penyerta/komorbid dan karakteristik individu dengan kejadian COVID-19 di Kota Bogor Tahun 2020. J Ekol Kesehat. 2021;20(2):69–79.
11. Amalia L, Irwan, Hiola F. Analisis gejala klinis dan peningkatan kekebalan tubuh untuk mencegah penyakit COVID-19. JJHSR. 2020;2(2):71–6.
12. Harista RA, Lisiswanti R. Depresi pada penderita diabetes mellitus tipe 2. Majority. 2015;4(9):73–7.
13. Kresna A, Ahyar J. Pengaruh physical distancing dan social distancing terhadap kesehatan dalam pendekatan linguistik. JST. 2020;1(4):14–9.
14. Permadhi PLO, Sudirga IM. Problematika penerapan sistem karantina wilayah dan

PSBB dalam penanggulangan COVID-19. Kertha Semaya. 2020;8(9):1355–65.
15. Kalangie NS. Kebudayaan dan kesehatan: pengembangan pelayanan kesehatan primer melalui pendekatan sosiobudaya. Jakarta: Kesaint Blanc; 1994.
16. Kurniawan D. Masyarakat patuh pakai masker, kini kasus positif Covid-19 kian turun. Jawa Pos [Internet]. 2022 April 9 [cited 2022 June 10]. Available from: https://www.jawapos.com/nasional/01379769/masyarakat-patuh-pakai-masker-kini-kasus-positif-covid19-kian-turun.
17. Yunisya P, Sopandi AA. Penyelenggaraan pembelajaraan Penjas adaptif bagi tunanetra di rumah pada masa pandemi Covid-19 (SMK N 7 Padang). Ranah Res. 2020;3(1):20–4.
18. Geldsetzer P. Knowledge and perceptions of COVID-19 among the general public in the United States and the United Kingdom: a cross-sectional online survey. Ann Intern Med. 2020;173(2):157–60.
19. Faasse K, Newby J. Public perceptions of COVID-19 in Australia: perceived risk, knowledge, health-protective behaviors, and vaccine intentions. Front Psychol. 2020;11:551004.
20. Tejamaya M, Widanarko B, Erwandi D, Putri AA, Sunarno SDAM, Wirawan IMA, et al. Risk perception of COVID-19 in Indonesia during the first stage of the pandemic. Front Public Health. 2021;9:731459.
21. Jaber RM, Mafrachi B, Al-Ani A, Shkara M. Awareness and perception of COVID-19 among the general population: a Middle Eastern survey. PloS One. 2021;16(4):e0250461.
22. Shelat S, van de Wiel T, Molin E, van Lint JWC, Cats O. Analysing the impact of COVID-19 risk perceptions on route choice behavior in train networks. 2022;1–19.
23. Alkhaldi G, Aljuraiban GS, Alhurishi S, De Souza R, Lamahewa K, Lau R, et al. Perceptions towards COVID-19 and adoption of preventive measures among the public in Saudi Arabia: a cross-sectional study. BMC Public Health. 2021;21(1):1251.

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RESEARCH ARTICLE

Effect of Gratitude, Forgiveness, and Social Support on Retiree Well-being with Self-efficacy as a Mediator Variable

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Abstract

Many psychological problems arise when facing retirement due to unpreparedness during this period. Unpreparedness is commonly triggered by their fears of being unable to meet primary and secondary needs. Physical issues such as retirement health are essential, but paying attention to psychological problems is also necessary. Research on the well-being of retirees needs to be done to see what factors influence both internally and externally. This study aims to test the retirement well-being model in terms of such aspects as gratitude, forgiveness, and social support mediated by self-efficacy. This study used the structure equation model (SEM) approach with a sample of 220 retirees aged at least 55 through a convenience sampling technique. The data was collected in Bandung and its surroundings for six months, from August 2019 to March 2020, through well-being, gratitude, forgiveness, social support, and self-efficacy scales. The results of the research model tested have a good fit with empirical data and meet the goodness of fit requirements. There is a direct influence of gratitude, social support, and self-efficacy on well-being. There is an indirect effect of social support on well-being through self-efficacy. The value of the indirect effect is smaller than the direct effect, meaning that self-efficacy is not a good mediator variable for social support for well-being. In conclusion, most retirees experience well-being due to social support from their environment and their gratitude and self-efficacy. The well-being of retirees can be increased by appreciation, having social support from the environment, and having confidence in one's ability to deal with problems.

Keywords: Forgiveness, gratitude, self-efficacy, social support, well-being

Introduction

Retirement comes to everyone who works, either in the state or in private institutions.[1] The increasing number of retirees can also lead to a complexity of problems. Despite the different reactions to retirement, most retirees have the same response of worrying about income inflation and the inability to make ends meet with retirement benefits. Many retirees have to deal with stress and serious problems related to physical and mental health rather than enjoying their old age.[2] Retirees should have well-being as they must face a new phase in life. However, this issue has yet to be widely discussed; even if it has, it has mainly focused on the physical and financial domains, and only a few have investigated the psychological domain. It is essential to understand the factors that can improve retirees' well-being. In this study, the variables examined are gratitude, forgiveness, social support, and self-efficacy. These variables were chosen because there are still few studies that integrate these variables into one model, and there are still few studies that use Seligman's constructs. Based on this explanation, this study develops and constructs a theoretical model of retiree well-being regarding the influence of gratitude, forgiveness, and social support mediated by self-efficacy.

Many studies on retiree well-being are conducted in Western countries, but rarely in Eastern countries, including Indonesia, due to several factors, such as culture. Therefore, cultural differences need to be considered in this context. In the individualistic cultures of Western countries, positive self-evaluation plays an essential role in global well-being values. In collectivistic cultures reflected in Eastern countries, well-being depends on the social context and interpersonal relationships.[3] There are a lot of internal and external factors influencing one's well-being, in this context, retirees, some of which are religion, education, their children's education, income, physical health, and reputation.[4] According to Park et al.,[5] who researched philosophers and religious figures, gratitude is one of the most potent strengths in improving well-being. According to Watkins et al.,[6] there was a positive correlation

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between gratitude and well-being, happiness, and religiousness. In this context, gratitude is the ultimate source among all the variables.

Gratitude is also a high value among Jewish, Christians, Muslims, Buddhists, and Hindus.[4] Responses to uncomfortable life events, especially ones occurring during retirement, are strongly influenced by how people perceive what happens to them. Some such events can grow hatred and anger due to their interpersonal relations, eventually leading to a lack of well-being. One possible way to cope with this situation is by forgiving or changing negative emotions into such positive ones as empathy, sympathy, love, and caring.[7] Forgiveness is closely related to well-being and helps individuals manage a stable and supportive interpersonal relationship. Empirically, forgiveness also plays an essential role in physical and mental health. In addition to gratitude and forgiveness, social support is crucial to one's retirement well-being, as one under a lot of pressure tends to have bad health and well-being.[8] Social support refers to comfort, attention, appreciation, and help received by someone from either individuals or groups.[9] Those who get social support are usually certain they are loved, cared for, respected, gladly welcomed to be a part of social networking, and have good problem-solving abilities. Besides that, individuals' abilities to strive to face complexities, find a way out, solve problems, and reduce obstacles by changing their paradigms are believed to be influential to their well-being.[10] Such individuals are categorized as having good self-efficacy, also related to happiness and optimism in facing one's life to achieve well-being.[11] It is stated that well-being emerges if there are optimism and self-efficacy.[12] Therefore, the variable of self-efficacy can be a predictor of well-being.

This study aims to test the retirement well-being model in terms of such aspects as gratitude, forgiveness, and social support mediated by self-efficacy.

Methods

A quantitative approach was conducted to study a set of variables considered influencing other variables yet not giving any special treatment. Retired civil servants and non-civil servants in Bandung, Indonesia, served as the objects of this study. As many as 300 questionnaires were distributed online and offline for a month, and only 220 returned. The main factor in not returning the questionnaire was their lack of internet literacy, so the researchers shifted the distribution to offline amid the process. Before filling out the questionnaires, the respondents were informed about the purpose of the study and required to sign an informed consent form to ensure that they were volunteers and that their information was confidential. In addition, demographic data were also needed to identify such background as age, length of retirement, last occupation, current activity, and current address.

This study employed a non-probability sampling technique as the opportunity of the whole population to be selected as samples is unknown. In the meantime, a convenient sampling technique was also administered.[13] This study was conducted over six months, from August 2019 to March 2020.

Well-being measurement was conducted using a standard measuring instrument developed by Butler and Kern[14] based on Seligman.[15] The scale was semantic differential in which the respondents would read statements related to their well-being and choose which represented their condition the most. To measure gratitude, this study used a modified scale of self-report the gratitude questionnaire-six-item form (GQ-6) created by Mccullough et al.[16] This instrument was a Likert model describing approval of the provided statements.

The forgiveness scale used in this study was created based on the Heartland Forgiveness Scale (HFS) by Thompson et al.[17] Four sets of scores were acquired, comprising the total score of HFS and each score for three HFS sub-scales (self-forgiveness, forgiveness of others, and forgiveness of situations). Like the well-being scale, this scale is also semantic differential, with five alternative answers ranging from almost always wrong to almost always right.

The social support scale represents four social support functions: emotional, informational, instrumental, and companionship support.[8] Finally, the self-efficacy measurement instrument represents three self-efficacy dimensions: level, strength, and generality.[18] And data analysis in this study used the structure equation model (SEM) method with the AMOS v.21.0 program. The research was approved by West Java Province National and Political Unity Agency number 070/312/SKP/II/2020.

Results

Table 1 shows that the respondents were 126 males (57.27%) and 94 females (42.73%). In terms of educational background, 58 of them were senior high school graduates (26.36%), 33 of them were diploma graduates (15%), 91 were bachelor graduates (41.37%), and the rest (38) of them were master and doctoral degree graduates (17.27%). Regarding the length of retirement, the respondents varied from 0 to 15 years, of which 90 (40.91%) were civil servants, 125 were non-civil servants (56.82%), and the rest were from military backgrounds. The respondents also showed various salaries ranging from IDR 3 million to IDR 5 million; however, 30% had a side job increasing their wage to IDR 5 million monthly. Currently, what they were doing included religious and social activities (46.36%), taking care of their grandchildren (20.92%), trading or entrepreneurship (17.73%), and farming or gardening.

The hypothesis model proposed is that retirement well-being occurs due to such factors as gratitude, forgiveness, social support, and self-efficacy. Table 2 shows that the score of chi-square=230.24 with the rejection opportunity of the null hypothesis close to zero (p= 0.00) and root mean squared error approximation (RMSEA) by 0.05. The CFA model has a relatively good fit from the chi-square score, even though the RMSEA is smaller than 0.08. Modeling modification is necessary, as inferred by the result; thus, this study gradually modified by adding covariance errors to finally develop the best model (one meeting the criteria of goodness of fit). The final modification of the model by adding eight covariance errors has finally decreased the chi-square score from 230.24 (p=0.00) to 159.17 (p=0.07), indicating that the model fits well. Furthermore, the model can be used in SEM to form the construct.

It is shown in Table 3 that all the variables have good internal consistency. Interestingly, all the

Table 1 Frequency Distribution of Respondent Characteristics

Characteristics	n=220 (%)
Gender	
Male	126 (57.27)
Female	94 (42.73)
Age (years)	
<60	85 (38.64)
60–70	106 (48.18)
>70	29 (13.18)
Education	
Bachelor	129 (58.64)
Diploma	33 (15.00)
Senior high school	58 (26.36)
Length of retirement (years)	
<3	62 (28.18)
3–7	55 (25.00)
8–12	52 (23.64)
>12	51 (23.18)
Retired from	
Civil servant/PNS	59 (26.82)
State-owned enterprises/BUMN	84 (38.18)
Private sector employee	41 (18.64)
Lecturer/teacher	20 (9.09)
Education personnel	11 (5.00)
Indonesian national army/TNI	5 (2.27)
Activities after retirement	
Just stay at home/raise grandchildren	46 (20.92)
Part-time work	12 (5.45)
Gardening/farming	14 (6.36)
Trading/self-employed	39 (17.73)
Religious/social activities	109 (49.55)
Currently living with	
At home alone/with wife and children	189 (85.91)
At the child's house	22 (10)
With relatives/relatives	3 (1.36)
Other	6 (2.73)
Income (million)	
<1	30 (13.63)
1–3	74 (33.64)
4–7	80 (36.36)
8–10	26 (11.82)
>10	10 (4.55)

Table 2 Confirmatory Factor Analysis of Measurement Models: Fit Indices

Variables	χ^2	df	$\Delta\chi^2$	Δdf	NNFI	CFI	IFI	RMSEA	SRMR
Initial CFA	230.24	142	–	–	0.94	0.95	0.95	0.05	0.07
Final CFA	159.17	134	71.07	8	0.98	0.99	0.99	0.03	0.05

Note: n=220, p<0.05, NNFI: non-normed fit index, CFI: comparative fit index, IFI: incremental fit index, RMSEA: root mean square error of approximation, SRMR: standardized root means square residual

Table 3 Descriptive Statistics and Correlation for the Study Variables

Variables	Mean	SD	1	2	3	4	5
Gratitude	15.48	1.45	1				
Forgiveness	16.27	1.86	0.65	1			
Social support	38.73	4.66	0.53	0.64	1		
Self-efficacy	14.99	1.72	0.16	0.23	0.30	1	
Well-being	43.43	4.99	0.49	0.41	0.60	0.42	1

Note: n=220, p<0.05, SD: standard deviation

Table 4 Influence of Exogenous Variables on Well-being

			Estimate	S.E.	C.R.	p
Self-efficacy	←	Forgiveness	0.11	0.09	1.16	0.24
Self-efficacy	←	Gratitude	0.04	0.12	0.28	0.78
Self-efficacy	←	Social support	0.06	0.04	1.66	0.09
Well-being	←	Social support	0.34	0.09	3.66	***
Well-being	←	Self-efficacy	0.79	0.20	3.90	***
Well-being	←	Gratitude	1.06	0.33	3.21	0.00
Well-being	←	Forgiveness	−0.12	0.25	−0.46	0.65

exogenous positively correlate with well-being as each score is less than 0.05. Placed in ranks, the variables with the most significant correlations are gratitude and forgiveness, and those with the most minor correlations are gratitude and self-efficacy.

The hypothesis is accepted in terms of the direct effect of gratitude on well-being (Table 4). The social support and self-efficacy scores also show a significant direct impact of these two variables on well-being. Meanwhile, the immediate effect between forgiveness and well-being was rejected, meaning there is no correlation between forgiveness and well-being.

The hypothesis on the indirect influence of gratitude, forgiveness, and social support on the well-being mediated by self-efficacy as the mediator variable is tested by SEM using AMOS v.21.0. It is found that forgiveness, gratitude, and social support does not significantly influence self-efficacy as the p is higher than 0.05 and neither does forgiveness to the well-being. However, gratitude, social support, and self-efficacy significantly affect well-being, as the p score is lower than 0.05. It has also been empirically proven that the CFA model initially did not fit well, as the chi-square score was 230.24 with p=0.00. However, after the modification, the model showed a good fit as the score of χ^2=159.17, p<0.01, NNFI=0.98, CFI=0.99, IFI=0.99, RMSEA=0.03, SRMR=0.05. Social support's huge influence on self-efficacy is indicated by the score of square multiple correlations (7.22%). Meanwhile, the influence score of gratitude, social support, and self-efficacy to well-being was simultaneously 39.13%, as shown by the model (Figure).

The Figure shows the direct effect of gratitude, social support, and self-efficacy on the well-being of retirees. Gratitude has the most significant effect on social support and self-efficacy. Self-efficacy can only be a mediator for social support and not for gratitude and forgiveness. The forgiveness variable has no direct or indirect influence on the well-being of retirees.

Discussion

The first discussion point in this study is how social support affects well-being mediated by self-efficacy. There is no guarantee that retirees with good social support will have good well-being if their self-efficacy is low. Retirees with high social support and strong self-efficacy will give more meaning to every step they take.[8] Social support will also influence the self and stimulate the thoughts of self, eventually evaluating the self and creating self-efficacy. The better social support one gets, the better their self-efficacy is. It is an excellent factor in creating well-being.[8]

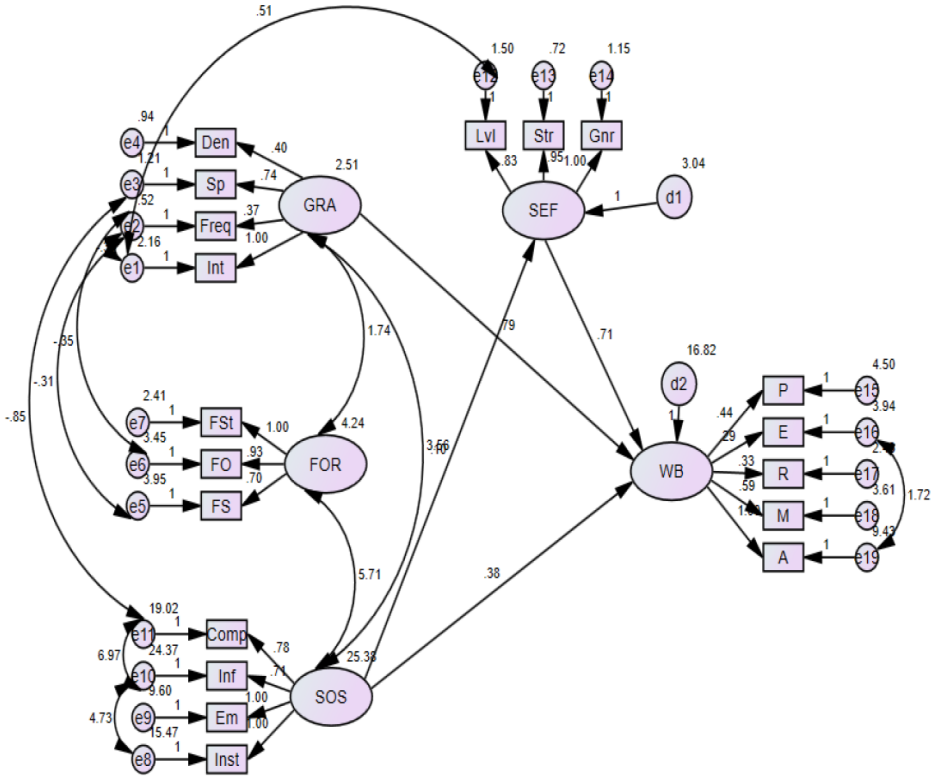

Figure Model Effect of Final Modifications of Gratitude, Forgiveness, Social Support on Self-efficacy and Their Impact on Welfare

GRA: gratitude, FOR: forgiveness, SOS: social support, SEF: self-efficacy, WB: well-being, P: positive emotion, E: engagement, R: relationship, M: meaning, A: accomplishment

It is in line with the results of a previous study highlighting that self-efficacy is a mediator variable for personality factors and subjective components of well-being.[19] In addition, self-efficacy is also a significant mediator for adolescents' happiness11 and can mediate shame and subjective well-being.[20] The demography of the respondents also supports that most retirees are actively involved in various social and religious activities, making them feel welcomed and supported by the community so that they have a meaningful life and well-being. Retirees who found that social resources come from non-professionals commonly have good well-being as they are protected from stress. A study found that support from spouses and friends can avoid loneliness and enhance well-being directly and indirectly.[21] Several studies conclude that people are satisfied with their retirement, healthy, and enjoy their life better when they have good social support.[22,23]

Despite the model's success, there are also some limitations, one of which is related to the influence of gratitude on well-being as part of this study. Although gratitude is closely related to self-efficacy, self-efficacy does not significantly influence it, so when retirees are grateful, they tend to have good well-being, with or without self-efficacy. In other words, self-efficacy, whether high or low, is not a mediator of gratitude for well-being. Retirees who have a disposition of gratitude towards health, family, and work tend to have better well-being due to the indirect influence of these behaviors.[5] Wood et al.[24] found that through simple training, gratitude has a strong potential to improve well-being. Chan[25] also agrees that gratitude substantially and positively correlates to happiness and well-being. Such a finding aligns with previous studies that generally conclude that gratitude directly contributes to well-being.[26,27] In short, the more grateful someone is, the more emotional experiences and positive memories lead to happiness and subjective well-being they have.[28]

Another weakness of this study is that forgiveness did not significantly affect well-being.

Research has shown that forgiveness is a unique predictor positively correlated with emotional well-being and negative affect and indirectly influenced through interpersonal satisfaction.[29–31] However, this study contradicts the result as forgiveness does not significantly influence well-being. This may be due to differences in understanding the definition of forgiveness in the questionnaire the researchers distributed because forgiveness can be interpreted as ignoring bad experiences or pretending to forgive and tolerate them.[32]

Overall, gratitude, forgiveness, and social support significantly influence self-efficacy with various contribution strengths. However, this study proved that self-efficacy is a mediator variable only for social support. It is because self-efficacy is a predictor of something external. In the meantime, such variables as gratitude and forgiveness are internal behavior individuals should work on to reach well-being. Therefore, self-efficacy plays the best role as a moderator variable.

Conclusions

This study concludes that well-being is influenced by gratitude, forgiveness, social support, and self-efficacy. However, self-efficacy is proven only significantly affect social support related to external forces. Most respondents have good well-being as essential aspects such as education, marital status, income, and social and religious activities contribute to retirement well-being are mostly fulfilled.

Conflict of Interest

There is no conflict of interest in this study.

References

1. Wang M, Shi J. Psychological research on retirement. Annu Rev Psychol. 2014;65:209–33.
2. Osborne JW. Psychological effects of the transition to retirement. Can J Couns Psychother. 2012;46(1):45–58.
3. Diener E, Oishi S, Lucas RE. Personality, culture, and subjective well-being: emotional and cognitive evaluations of life. Annu Rev Psychol. 2003;54:403–25.
4. Compton WC. An introduction to positive psychology. San Francisco: Thomson Wadsworth; 2005.
5. Park N, Peterson C, Seligman MEP. Strengths of character and well-being. J Soc Clin Psychol. 2004;23(5):603–19.
6. Watkins PC, Woodward K, Stone T, Kolts RL. Gratitude and happiness: development of a measure of gratitude and relationships with subjective well-being. Soc Behav Pers. 2003;31(5):431–52.
7. Worthington EL Jr, Wade NG. Handbook of forgiveness. 2nd Edition. New York: Routledge; 2020.
8. Cohen S, Underwood LG, Gottlieb BH. Social support measurement and intervention: a guide for health and social scientists. Oxford: Oxford University Press; 2000.
9. Sarafino EP. Applied behavior analysis: principles and procedures in behavior modification. Hoboken: John Wiley & Sons; 2012.
10. Dingemans E, Henkens K. How do retirement dynamics influence mental wellbeing in later life? A 10-year panel study. Scand J Work Environ Health. 2015;41(1):16–23.
11. Loton DJ, Waters LE. The mediating effect of self-efficacy in the connections between strength-based parenting, happiness and psychological distress in teens. Front Psychol. 2017;8:1707.
12. Karademas EC. Self-efficacy, social support, and well-being: the mediating role of optimism. Pers Individ Dif. 2006;40(6): 1281–90.
13. Neuman WL. Social research methods: qualitative and quantitative approaches. 7th Edition. Essex: Pearson Education Limited; 2014.
14. Butler J, Kern ML. The PERMA-Profiler: a brief multidimensional measure of flourishing. Int J Wellbeing. 2016;6(3):1–48.
15. Seligman MEP. Flourish: a visionary new understanding of happiness and well-being. New York: Atria; 2011.
16. Mccullough ME, Emmons RA, Tsang JA. The grateful disposition: a conceptual and empirical topography. J Pers Soc Psychol. 2002;82(1):112–27.
17. Thompson LY, Snyder CR, Hoffman L, Michael ST, Rasmussen HN, Billings LS, et al. Dispositional forgiveness of self, others, and situations. J Pers. 2005;73(2):313–59.
18. Bandura A, Freeman WH, Lightsey R. Self-

efficacy: the exercise of control. J Cogn Psychother. 1999;13(2):158–66.
19. Strobel M, Tumasjan A, Spörrle M. Be yourself, believe in yourself, and be happy: self-efficacy as a mediator between personality factors and subjective well-being. Scand J Psychol. 2011;52(1):43–8.
20. Liu C, Cheng Y, Hsu ASC, Chen C, Liu J, Yu G. Optimism and self-efficacy mediate the association between shyness and subjective well-being among Chinese working adults. PLoS One. 2018;13(4):e0194559.
21. Chen Y, Feeley TH. Social support, social strain, loneliness, and well-being among older adults: an analysis of the health and retirement study. J Soc Pers Relat. 2014;31(2):141–61.
22. Lane JA, Fink RS. Attachment, social support satisfaction, and well-being during life transition in emerging adulthood. Couns Psychol. 2015;43(7):1034–58.
23. Steffens NK, Jetten J, Haslam C, Cruwys T, Haslam SA. Multiple social identities enhance health post-retirement because they are a basis for giving social support. Front Psychol. 2016;7:1519.
24. Wood AM, Froh JJ, Geraghty AWA. Gratitude and well-being: a review and theoretical integration. Clin Psychol Rev. 2010;30(7):890–905.
25. Chan DW. Gratitude, gratitude intervention, and subjective well-being among Chinese school teachers in Hong Kong. Educ Psychol. 2010;30(2):139–53.
26. Aghababaei N, Farahani H. The role of trait gratitude in predicting psychological and subjective well-being. J Dev Psychol. 2012;8(29):75–84.
27. Măirean C, Turliuc MN, Arghire D. The relationship between trait gratitude and psychological wellbeing in university students: the mediating role of affective state and the moderating role of state gratitude. J Happiness Stud. 2019;20(5):1359–77.
28. Diener E, Oishi S, Lucas RE. Subjective well-being: the science of happiness and life satisfaction. In: Snyder CR, Lopez SJ, editors. The Oxford handbook of positive psychology. 2nd Edition. Oxford: Oxford University Press; 2012. p. 187–94.
29. Scheidle LE. Forgiveness and gratitude as predictors of elderly subjective well-being [dissertation]. Virginia Beach: Regent University; 2010 [cited 2022 May 20]. Available from: https://www.proquest.com/openview/ded506be821ccaf127ca3dd1d3c205fc.
30. Liu HC, Wu MX. Relationship among forgiveness, interpersonal satisfaction and subjective wellbeing of college students. Chinese J Clin Psychol [Internet]. 2011;19(4):531–3.
31. Akhtar S, Dolan A, Barlow J. Understanding the relationship between state forgiveness and psychological wellbeing: a qualitative study. J Relig Health. 2017;56(2):450-463.
32. Nashori F, Iskandar TZ, Setiono K, Siswadi AGP, Andriansyah Y. Religiosity, interpersonal attachment, and forgiveness among the Javanese population in Yogyakarta, Indonesia. Ment Health Relig Cult. 2020;23(2):99–112.

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RESEARCH ARTICLE

Effect of Sleep Deprivation on the Number of Prefrontal Cortex Neuroglia Cells in Male White Rats (*Rattus norvegicus*)

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Abstract

Stress induced by sleep deprivation can increase inflammation and oxidative stress, destroying the pyramidal and neuroglia cells in the prefrontal cerebral cortex and interrupting cognitive and behavioral functions. This study aims to observe the difference in the number of pyramidal and neuroglia cells in the prefrontal cortex of male white rats (*Rattus norvegicus*) after stress induction by paradoxical sleep deprivation (PSD) and total sleep deprivation (TSD). This study was conducted in the Anatomy Laboratory of the Faculty of Medicine, Universitas Jenderal Soedirman, from November 2019 to February 2020. The method of this study was a posttest-only design with a control group approach using ten rats for each group; that was control (K.I.), PSD (KII), and TSD (K.I.). PSD and TSD groups received sleep deprivation treatment for eight days for 20 hours/day and 24 hours/day, respectively. The mean pyramidal cell number decreased in the PSD (66.67±24.55) and TSD (65.90±34.91) compared to the control (77.10±26.11) group, but no significant differences were found between all groups ($p>0.05$). The mean neuroglial cell number was lower in the PSD (97.78±28.17) and TSD (75.80±22.39) compared to the control (126.00±48.81). Post-hoc Bonferroni test showed a significant difference between control and TSD ($p<0.05$) but not between control and PSD or PSD and TSD ($p>0.05$). In conclusion, there was a significant difference in the number of neuroglial cells but not pyramidal cells in the prefrontal cortex of male white rats (*Rattus norvegicus*) after stress induction with total sleep deprivation (TSD).

Keywords: Male white rat, neuroglial cells, prefrontal cortex, pyramidal cells, sleep deprivation

Introduction

Sleep is a basic human need to maintain normal body function and support physical and psychological recovery.[1] A good sleep cycle is measured by observing the deepness and quantity of sleep.[2] In adults, the standard sleep duration is 7–9 hours, whereas teenagers need 8–10 hours, and children require 9–11 hours of sleep. Epidemiological data shows that 30% of men and women aged 30 to 64 years sleep less than 6 hours per day,[3] and the survey of the healthy lifestyle index in Indonesia by Taylor Nelson Sofres (TNS) in 2013 in Indonesia, shows that Indonesian people have an average sleep time of 6.8 hours every day due to a lot of activity.[4]

Shorter sleep duration causes sleep deprivation, which can induce disruption of decision-making, repetition of error, and reduction of spontaneity, speed, and motivation to communicate.[3] Sleep deprivation-induced stress in humans can be investigated using animal models by paradoxical sleep deprivation (PSD) or total sleep deprivation (TSD). Sleep deprivation can damage the brain's prefrontal cortex and interrupt cognitive function and behavioral control.[4] Pyramidal and neuroglial cells are primary excitatory neurons in the prefrontal cortex (PFC); therefore, the stress in PFC can be measured by calculating pyramidal and neuroglial cell reduction.[5]

Sleep deprivation can reduce brain glucose metabolism by inducing the hypothalamus-pituitary axis (HPA) and sympatho-adrenomedullary system, further releasing corticotropin-releasing hormone (CRH) and arginine-vasopressin (AVP), increasing adrenocorticotropic hormone (ACTH) and glucocorticoid secretion, and reducing glucocorticoid receptor expression.[6]

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Glucocorticoids increase the release of glutamate in the brain, N-methyl-d-aspartic acid (NMDA) and á-amino-3-hydroxy-5-methyl-4 isoxazole propionic acid (AMPA) in the postsynaptic membrane, magnesium (Mg^{2+}) ion blockade from NMDA receptor, and mobilize plenty of Ca^{2+} ion in the cytosol as an apoptotic signal in a neuron.[7] Neuroglia cells consisting of microglia, astrocytes, and oligodendrocytes are supporting cells in the central nervous system (CNS) that function as a provider of nutrition, protection, and support for neurons and mediate brain metabolism, nerve detoxification, repair, and synaptic plasticity so that they play an essential role in sleep homeostasis.[8] Pyramidal cells are the central neuronal cells that make up the brain and play a role in sensory and motor coordination, especially those related to behavior control and cognition.[9] No research has confirmed whether PSD and TSD can induce pyramidal and neuroglial cell deaths in the prefrontal cortex.

Rahmadhani's[10] research showed that there was a decrease in the number of pyramidal cells in the cerebral cortex of rats induced by monosodium glutamate, with the ecotoxicity mechanism of glutamate similar to that which occurs during exposure to PSD and TSD. Research by Arjadi et al.[11] also showed a decrease in the number of pyramidal cells in the hippocampus as a memory center due to exposure to stress, one of which is PSD. None of the studies can confirm that PSD and TSD can cause neuronal death in the area of the cerebral prefrontal cortex, which is dominated by pyramidal cells. This study aims to observe the difference in the number of pyramidal and neuroglia cells in the prefrontal cortex of male white rats (*Rattus norvegicus*) after stress induction by PSD and TSD.

Methods

This research design is experimental with a posttest-only control group design with a 4-month duration (November 2019–February 2020) conducted in the Anatomy Laboratory of the Faculty of Medicine, Universitas Jenderal Soedirman. Research ethics was approved by the Health Research Ethics Committee, Faculty of Medicine, Universitas Jenderal Soedirman, No. 8395/KEPK/XII/2019.

This study utilized 30 male white rats (*Rattus norvegicus*) of Wistar strain with 3–4 months of age and 100–200 grams of weight from the Animals Laboratory of the Faculty of Medicine, Universitas Jenderal Soedirman. Federer's formula was used for sample size determination; that is (t−1) (n−1) ≥15, in which t is the number of interventions and n is the number of repetitions. Based on this formula, the required sample for each group was nine rats. Since this experiment employed three intervention groups, the total required animal subjects were 27 rats. Ten percent of the total animals were added to avoid dropout, so the samples used in this study were 30 or 10 rats for each group.

The modified multiple platform method (MMPM) was applied for sleep deprivation induction using water-filled tanks measuring 123×44×35 cm containing twelve platforms with 6.5 cm width and 10 cm distance between each platform.[12] The pyramidal and neuroglial cells were measured with a light microscope (Motic) paired with Optilab. Other tools used in this study were a digital weight scale (Dragon 303®), black marker (Snowman®), and surgery set. Experimental materials used in this study were animal feed (Comfeed AD II), water (Aqua®), ether, xylol, alcohol (90% and 95%), ethanol (95%, 90%, 80%, and 70%), gelatin 0.5%, standard formalin buffer 10%, paraffin, aqua dest, and hematoxylin-eosin (HE) staining kit.

Experimental animals were weighed, randomly grouped, acclimatized for seven days, and placed in cages measuring 60×30×30 cm with a temperature of 28±2°C and humidity of 75±5%. The animals were given the same type, amount, and composition of feeds *ad libitum*, namely Comfeed AD II, consisting of protein (19%), water (12%), fat (7%), calcium (1.1%), phosphorus (0.5%), and the rest is crude fiber, then reweighed at the end of acclimatization. The animals were then divided into three groups with a completely randomized design. The animals were grouped by labeling each animal with numbers 1 to 30, and 30 lottery papers were drawn for each group (K.I., KIII, and KIII) and tabulated. The lottery papers were taken one by one and put onto the table to determine control and experiment groups; that is, Group K.I. (control group, without any sleep deprivation intervention); Group KII (PSD, 192 hours total, 20 hours/day, sleep deprivation at 11.00 a.m.–07.00 a.m. local time, and break at 07.00 a.m.–11.00 a.m. local time continuously); and group K.I. (TSD, 192 hours total, 24 hours/day, sleep deprivation at 11.00 a.m.–11.00 a.m. local time continuously).[8]

MMPM equipped with muscle atonia was used to induce sleep deprivation in KII (PSD) and KIII

(TSD) groups.[12] When the animals enter the sleep phase of rapid eye movement, they will fall into the water and wake up. The electric shocks were given every 10 minutes to maintain the animal's awake state.

Animal termination was done after eight days of intervention with ether inhalation. After the rats were dissected, the prefrontal cortex was taken within 2–3 minutes, starting with a skin incision in the middle of the rat head with scissors, followed by a bone incision of the head from the parietal into the frontal bone. Calvaria was then opened using forceps, and the brain was released from its membrane and cranial nerve by cutting to liberate the brain from the cranium base. The brain was fixated using 10% of the standard formalin buffer for at least 24 hours. The fixated brain was then cut coronally to obtain the prefrontal cortex. Darker areas of the prefrontal cortex, the medial prefrontal cortex, were stained with HE.[11]

Pyramidal and neuroglial cells were observed and counted using Image Raster v.2.1 software with 400 times magnification in 10 fields of view. The normal neuroglial cell was defined as a neuroglia cell without pycnotic, karyorrhexis, and karyolysis appearance. The pyramidal cell was described as a cell that has a big cell body with a triangular shape and basophilic cytoplasm.[9] Two independent observers performed the observation, and the interobserver reliability was analyzed by the Bland-Altman test. Specimens were processed in the Anatomic Pathology Laboratory of the Faculty of Medicine, Universitas Jenderal Soedirman.

Univariate data analysis results were presented in maximum and minimum values, mean, median, and standard deviation. Shapiro-Wilk test was used for analyzing data normality, and Levene's test was used for homogeneity. The parametric test was performed with a one-way analysis of variance (ANOVA), followed by post-hoc Bonferroni with a 95% confidence interval (α=0.05).

Results

The interobserver reliability test used the Bland Altman test and showed a range limit of agreement (–5 and 5) between –0.71–0.58 and –1.29–1.36 for the pyramidal and neuroglial cells data that were predominantly distributed around the mean of difference, indicating interobserver reliability is good. The number of neuroglia and pyramid cells was observed using a binocular light microscope, and the number was counted in 10 fields of view for one preparation. The neuroglia cells counted are normal cells with the criteria of not experiencing pycnotic (nucleus condenses, darkens, and shrivels), cariorexis (nucleus tears and forms fragments), karyolysis (the nucleus is pale because it cannot absorb color). Pyramidal cells are neurons with the characteristics of a large cell body, triangular in shape, with basophilic cytoplasm and basophilic cytoplasm (black arrows) and granular cells (red arrows). Histological pictures of neuroglia cells and prefrontal cortex pyramidal cells (Figure 1 and Figure 2) have in same results in all study groups, showing that K.I. (control) had the highest number of pyramidal cells (A), followed by KII (PSD) (B), and the least was owned by

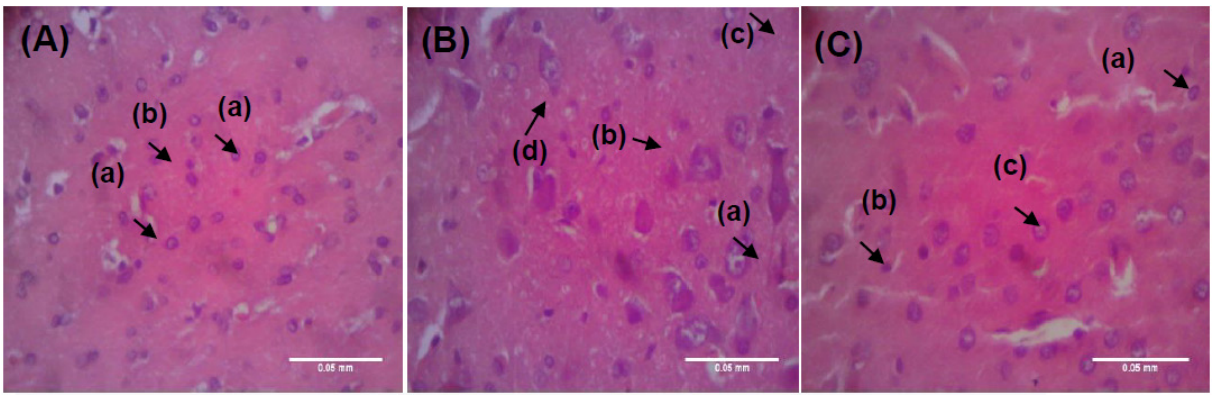

Figure 1 Medial Prefrontal Cortex of the Rat Brain Stained with HE (400× Magnification)
(**A**) control group, (**B**) PSD, (**C**) TSD. Black arrows indicated (**a**) normal neuroglia cell, (**b**) apoptotic neuroglia cell, (**c**) normal granular cell, and (**d**) normal pyramidal cell. Scale bars 0.05 mm

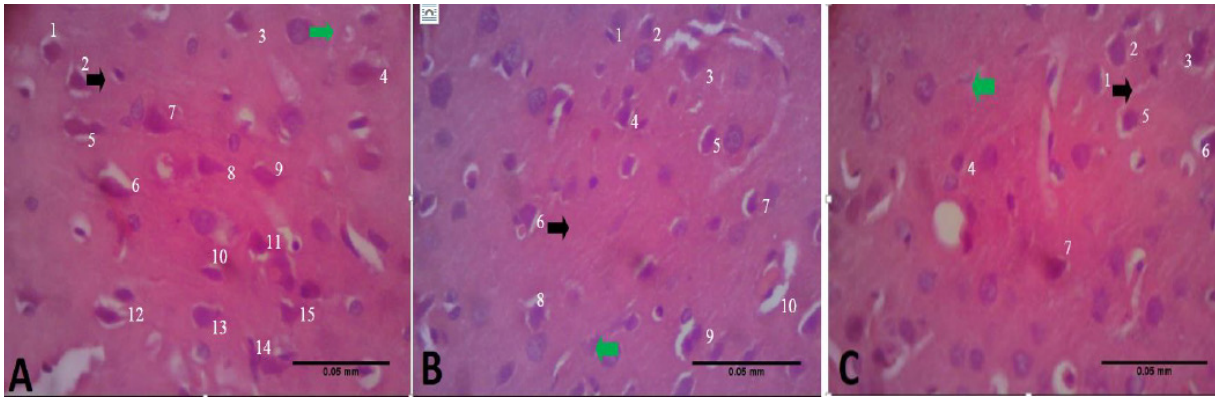

Figure 2 Pyramidal Cell Number in Prefrontal Cortex Pyramidal Stained with HE (400× Magnification)

(**A**) KI (control) showed 15 cells per field, (**B**) KII (PSD) showed 10 cells per field, and (**C**) K III (TSD) showed 7 cells per field. Pyramidal cells exhibited triangular-shaped with basophilic cytoplasm in black arrow and granular cell in green arrow. Scale bars 0.05 mm

group K III (TSD) (C).

Table 1 shows that the highest pyramidal cell number was in the control group (77.10±26.11), and the lowest was in the TSD group (65.90±34.91). Meanwhile, the highest number of normal neuroglia cells was in the control group (126.00±48.81), and the lowest was in the TSD group (75.80±22.39), as shown in Table 2. Shapiro-Wilk analysis showed the data was normally distributed (p>0.05), and Levene's test for homogeneity showed that all data were homogenous in all groups. ANOVA analysis for pyramidal cells showed no significant difference among all groups (p=0.638, p>0.05); therefore, post-hoc analysis was not further performed. Neuroglial cell analysis exhibited a significant difference in at least two groups (p=0.014). Post-hoc Bonferroni test in the mean normal neuroglial cell number showed a significant difference between the control and TSD (p=0.011), while no significant differences between the control and PSD (p=0.280) and between PSD and TSD (p=0.559).

Discussion

Paradoxical sleep deprivation (PSD) is the reduction of human sleep time, which can result

Table 1 Mean Pyramidal Cell Number in Each Group

Groups	n	Pyramidal Cell Number			
		Mean±SD	Min	Max	p
K.I. (Control)	10	77.10±26.11	45	131	0.638*
KII (PSD)	9	66.67±24.55	36	100	
KIII (TSD)	10	65.90±34.91	23	119	

Note: *one-way ANOVA

Table 2 Mean Neuroglia Cell Number in Each Group

Groups	n	Neuroglia Cell Number			
		Mean±SD	Min	Max	p
K.I. (Control)	10	126.00±48.81	50	209	0.014*
KII (PSD)	9	97.78±28.17	57	131	
KIII (TSD)**	10	75.80±22.39	40	113	

Note: *one-way ANOVA, post-hoc Bonferroni test showed a significant result compared to the control (p<0.05)

in the loss of almost all sleep time, and total sleep deprivation (TSD) is a condition in which a person does not sleep at all through one or more periods of actual sleep.[13,14] Paradoxical and total sleep deprivation harm decision-making control and trigger repetition of working memory errors and loss of individual spontaneity in communicating, making them appear humans experience lazy, lethargic, and unmotivated.[15] Sleep deprivation stress, so this research can be used as a preliminary study to determine the effect of sleep deprivation on neuroglia cells as brain neuron support cells and influences various brain functions.

The results of the study indicated a concordance between the hypothesis and the results of the study that there were significant differences in the number of neuroglia cells in male white rats (*Rattus norvegicus*) in the control group, the paradoxical sleep deprivation (PSD) group and the total sleep deprivation (TSD) group. The K1 (control) group showed that the mean pyramidal cell number was higher than that of KII (PSD) and K.I. (TSD) groups, indicating stress induces pyramidal cell death. In addition, the pyramidal cell number of the *cornu ammonis* three hippocampi after PSD was lower than the control. However, there was no statistically significant difference in pyramidal cell number between the control and sleep deprivation groups.

This result did not match recent research, which found a marked difference in pyramidal cell numbers between the control and the stress group induced by immobilization. Immobilization-induced stress is complex, containing physical, psychological, and social stress, while PSD only causes physical and psychological stress.[8] This insignificant result is probably due to the neuroprotective effect of neuroglia activity and brain-derived neurotrophic factor (BDNF) secretion that counter glutamate toxicity caused by cortisol and overactivated glutamate receptors (GluRs) that start neuroglia cell death.[10] Therefore, stress exposure in these experiments reduced apical dendrite complexity and cell size without any pyramidal cell deaths.[5]

Sleep deprivation for 2–4 hours/day can increase the size of mitochondria without damaging their structure.[16] Neuron deaths begin with neuroglia deaths because of neuroglia's role in protecting neurons. For example, an astrocyte, one type of neuroglia, releases BDNF, which regulates neuron proliferation and differentiation to maintain life continuity and neuron defense. The homeostasis mechanism disrupted by 12 hours of sleep deprivation can be preserved by BDNF release for at least one month.[5] Another neuroprotective neuroglia is microglia, which have macrophage-like roles in the central nervous system, clear dead cells and debris, increase neurogenesis, and reduce inflammation.[7]

This study found that the difference in pyramidal cell number between the control and sleep deprivation groups was insignificant. It is speculated that glucocorticoid release due to stress can disrupt the pyramidal cell and neuroprotector functions of neuroglia.[11] Glucocorticoid secretion inhibits glucose uptake and increases glutamate at the extracellular gap, producing excitotoxicity.[12] Glutamate release is responded to by cystine efflux via glutamate-cystine exchanger in neuroglial membrane cells, reducing intracellular glutathione level and elevation of reactive oxygen species (ROS). Glutamate excitotoxicity can induce glutamate receptor (NMDA) overactivity in the pyramidal cell membrane and affect alpha-amino-3-hydroxy-5-methylisoxazole-4-propionic acid (AMPA) and kainite receptors in the neuroglial cell membrane.[7] The glutamate receptor overactivity releases Na^+ influx and activates voltage-gated calcium channel (VGCC) and sodium-calcium exchanger (NCX), causing intracellular calcium ions overload.[17] Calcium overload is absorbed rapidly by mitochondria, causing rapid depolarization and activation of apoptotic cell caspase, ROS elevation, and glutathione reduction.[5]

On the other hand, neuroglia has a role in maintaining glutathione levels and clearing ROS directly. Change in neuroglial cell number in chronic sleep deprivation is regulated by the hypothalamic-pituitary-adrenal (HPA) axis, which elevates plasma cortisol levels. Elevation of cortisol level caused by sleep deprivation inhibits glucose transport in the brain and reduces basal ATP energy. Glucocorticoids also inhibit glucose uptake and increase glutamate levels at the extracellular gap.[8]

The mean neuroglia cell number difference after sleep deprivation treatment was significant in K.I. (TSD) but not in KII (PSD) compared to K.I. (control) group. This result is not consistent with previous studies that demonstrated the notable increase of glutamate and aspartate levels in the hippocampus and brain cortex, reduction of cortex glutathione reductase, and elevation of

malondialdehyde (MDA) after 72 hours of PSD.[18] Elevation of MDA and reduced glutathione reductase make mitochondrial and cytoplasmic antioxidant systems unable to fight free radicals. When animals are awake, their neuron activity is high, causing the oxygen demand to maintain the membrane potential is rising.[19] This condition triggers ROS accumulation, disrupting neuroglia membrane cells in the cortex and hippocampus.[13] Neuroglia acts as a neuroprotector by maintaining glutathione levels and eradicating free radicals directly, but its action does not completely inhibit the effects of oxidative stress on pyramidal cells; even repeated oxidative stress causes >80% damage to neurons that are not protected by neuroglia and 45% to neurons with neuroglial protection.[14]

Paradoxical sleep deprivation implemented for 96 hours can reduce lipid peroxidase by 38% in the cerebral cortex.[15] Oxidative stress reduction in PSD causes an elevation of superoxide dismutase (SOD) level for 40% without glutathione peroxidase (GPx) change. SOD and GPx are antioxidants for transforming free radicals into safe substances for neurons and neuroglia. SOD elevation after PSD indicates compensating responses to control anion superoxide due to oxidation-reduction reaction imbalance in mitochondria.[20]

A study by Inoue et al.[21] showed an elevation of SOD after PSD (68.92±19.08 U/mL) and TSD (82.70±12.93 U/mL) for five days. An elevation of SOD can induce apoptotic signals because of SOD transformation to superoxide reductase (SOR). SOR plays a role as superoxide oxide (SOO) to generate free radicals using alternative pathways. The PSD group had 4 hours of sleep time, so the difference in SOD between the control and PSD group was not as much as between the control and TSD groups. Metabolism is reduced during sleeping, while residual metabolism product inhibits oxidative stress and induces cellular apoptotic. The sleeping period in PSD also inhibits excitatory neuron activity and glutamate neurotransmitters by glutathione disulfide (GSSD). This inhibition reduces extracellular glutamate concentration and minimizes its excitotoxic effect on neuroglia cells.[18]

People who experience sleep deprivation were reported to have a disruption of cognition and behavioral function conducted by the brain's prefrontal cortex, such as a decrease in concentration, reduction of precision work, unsystematic thought, inaccurate decision-making, and emotional disturbance. Continuous disruption of these functions can cause work accidents and decreased performance. Further study by measuring the prefrontal cortex thickness after the induction of PSD and TSD needs to be accomplished to determine the effect of sleep deprivation on the organ level. In addition, sleep recovery needs to be added to the experiment procedure since sleep recovery can improve the condition caused by sleep deprivation.

Conclusions

Total sleep deprivation significantly reduces the neuroglial but not pyramidal cell number in the prefrontal cortex of male white rats (*Rattus norvegicus*). The number of pyramidal and neuroglial cells in the prefrontal cortex of a male white rat (*Rattus norvegicus*) is not significantly reduced after induction of paradoxical sleep deprivation.

Conflict of Interest

The authors declare no conflict of interest.

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References

1. Periasamy S, Hsu DZ, Fu YH, Liu MY. Sleep deprivation-induced multi-organ injury: Role of oxidative stress and inflammation. EXCLI J. 2015;14:672–8.
2. Patrick Y, Lee A, Raha O, Pillai K, Gupta S, Sethi S, et al. Effects of sleep deprivation on cognitive and physical performance in university students. Sleep Biol Rhythms. 2017;15(3):217–25.
3. Hirshkowitz M, Whiton K, Albert SM, Alessi C, Bruni O, DonCarlos L, et al. National Sleep Foundation's sleep time duration recommendations: methodology and results summary. Sleep Health. 2015;1(1):40–3.

4. Taylor Nelson Sofres. Survei indeks pola hidup sehat AIA: fokus penemuan di Indonesia [Internet]. Jakarta: AIA Financial Indonesia; 2013 [cited 2019 August 10]. Available from: https://www.scribd.com/doc/282949216/AIA-Healthy-Living-Index-Survey-2013.
5. Putri DNE, Nasrul E, Masri M. Pengaruh kurang tidur terhadap berat badan pada tikus Wistar jantan. J Kesehat Andalas. 2015;4(1):78–82.
6. Villafuerte G, Miguel-Puga A, Rodríguez EM, Machado S, Manjarrez E, Arias-Carrión O. Sleep deprivation and oxidative stress in animal models: a systematic review. Oxid Med Cell Longev. 2015;2015:234952.
7. Nicolaides NC, Vgontzas AN, Kritikou I, Chrousos G. HPA axis and sleep. In: Feingold KR, Anawalt B, Blackman MR, Boyce A, Chrousos G, Corpas E, et al., editors. Endotext [Internet]. South Dartmouth: MDText.com, Inc.; 2020.
8. Jäkel S, Dimou L. Glial cells and their function in the adult brain: a journey through the history of their ablation. Front Cell Neurosci. 2017;11:24.
9. Wardana RW, Suhesti TS, Arjadi F. Purwoceng (*Pimpinella pruatjan* Molk.) nanosuspension repairs spatial white albino wistar strains' spatial memory degeneration after sleep deprivation. Biogenesis. 2022;10(1):37–43.
10. Rahmadhani KZ. Pengaruh ekstrak daun pepaya terhadap gambaran histopatologi sel piramidal cortex cerebri dan fungsi memori tikus putih jantan yang diinduksi MSG [undergraduate thesis]. Malang: Universitas Muhammadiyah Malang; 2018 [cited 2019 August 18]. Available from: https://eprints.umm.ac.id/42271/
11. Arjadi F, Soejono SK, Maurits LS, Pangestu M. Jumlah sel piramidal CA3 hipokampus tikus putih jantan pada berbagai model stres kerja kronik. MKB. 2014;46(4):197–202.
12. Mônico-Neto M, Giampá SQ, Lee KS, de Melo CM, Souza Hde S, Dáttilo M, et al. Negative energy balance induced by paradoxical sleep deprivation causes multicompartmental changes in adipose tissue and skeletal muscle. Intern J Endocrinol. 2015;2015:908159.
13. Oh MM, Kim JW, Jin MH, Kim JJ, Moon du G. Influence of paradoxical sleep deprivation and sleep recovery on testosterone level in rats of different ages. Asian J Androl. 2012;14(2):330–4.
14. Chennaoui M, Gomez-Merino D, Drogou C, Geoffroy H, Dispersyn G, Langrume C, et al. Effects of exercise on brain and peripheral inflammatory biomarkers induced by total sleep deprivation in rats. J Inflam (Lond). 2015;12:56.
15. Bellesi M, de Vivo L, Chini M, Gilli F, Tononi G, Cirelli C. Sleep loss promotes astrocytic phagocytosis and microglial activation in mouse cerebral cortex. J Neurosci. 2017;37(21):5263–73.
16. Orzeł-Gryglewska J. Consequences of sleep deprivation. Int J Occup Med Environ Health. 2010;23(1):95–114.
17. Arjadi F, Siswandari W, Wibowo Y, Krisnansari D, Muntafiah A. Purwoceng roots ethanol extract make no improvement in leydig cells activity to male white rats (*Rattus norvegicus*) exposed by paradoxical sleep deprivation (PSD) stress models. IOP Conf Ser Earth Environ Sci. 2019;255:012022.
18. Frank MG. The role of glia in sleep-wake regulation and function. Handb Exp Pharmacol. 2019;253:83–96.
19. Kumar V, Abbas A, Aster J. Buku ajar patologi dasar Robbins. 10th Edition. Singapore: Elsevier BV; 2020.
20. Birey F, Kloc M, Chavali M, Hussein I, Wilson M, Christoffel DJ, et al. Genetic and stress-induced loss of NG2 glia triggers emergence of depressive-like behaviors through reduced secretion of FGF2. Neuron. 2015;88(5):941–56.
21. Inoué S, Honda K, Komoda Y. Sleep as neuronal detoxification and restitution. Behav Brain Res. 1995;69(1–2):91–6.

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RESEARCH ARTICLE

Relationship between Knowledge Level and Family Rules with Adolescent Risk Behavior

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Abstract

Health risk behavior emerges due to risk factors within adolescents, family factors, and external factors outside the family. Poor knowledge about risk behavior and parental control may cause adolescents to develop risky behaviors that affect their health. This study aimed to identify the relationship between family factors and knowledge of adolescent risk behavior. It is a cross-sectional study conducted on 271 adolescents aged 17–25 years in Central Java from April to November 2021, taken by random sampling. Data analysis was performed using the chi-square test with a meaning level of 95%. Results show no relationship between knowledge level and adolescent risk behavior (p=0.665), and there was a relationship between family rules and adolescent risk behavior (p=0.001). Family rules significantly prevent adolescent risk behavior; hence, parents must apply family rules to limit teenage behavior, especially in opposite-sex relationships, to avoid sexual risk behavior.

Keywords: Adolescent, family rules, health risk behavior, knowledge

Introduction

Risk behavior is a behavior causing deaths or misbehaviors among adolescents, such as smoking, harassment, alcohol, and drug consumption, an acute diet that potentially causes death, a free destructive lifestyle, and sexual behavior causing pregnancy and fatalities.[1,2]

Adolescents enter the transition period from childhood to adulthood. According to the World Health Organization (WHO), adolescents' ages range from 12 to 24 years, while the National Population and Family Planning Board confirm their age is around 10 to 24 years, and they must be unmarried.[3]

Adolescent lifestyle might produce higher-risk behavior than the adult lifestyle in the community. Adolescents started smoking in Indonesia when ≤13 years old, and most are males. Smoking habit is also influenced by parent or guardian smoking behavior. Thus, a family has a strong influence on adolescent smoking behavior.[4–6]

Alcohol consumption behavior is another adolescent risk behavior. The high prevalence of alcohol consumption among male adolescents aged 15–24 (15.6%) is higher than the national data from the 2007 Basic Health Research (5.5%). In addition, reproductive health is one of the health concerns in adolescence. Research conducted in Central Java, East Java, and Bali showed that most adolescents had inadequate reproductive development knowledge (77.3%).[7]

Health-related risk behavior may be continued to adulthood. One who performs risky behavior in adolescence has a higher chance of stopping schooling, practicing criminal acts, getting addicted to alcoholic drinks, and getting unemployed once they grow up. Besides, adolescent risk behavior may reduce the quality of adolescents and their families at the moment and in the near future. Adolescents with risk behavior may experience physical and psychological problems and even death. Failure to maintain adolescent health and social conditions should be avoided through adolescent interventions.[6,8]

Health risk behavior happens due to intrapersonal risk factors, family factors, and external factors outside of the family.[9,10] Poor knowledge about risk behavior and parental control may cause adolescents to develop risky behavior that impacts their health. According to this background issue, this study aimed to analyze the relationship between knowledge and family rules with adolescent risk behavior. Formulating protective strategies for adolescents to develop and grow to be excellent, healthy, and

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highly qualified generations is essential.

Methods

This study used a cross-sectional quantitative design. Its population is all adolescents aged 17–25 years in Central Java. It used purposive sampling to collect 271 samples.[10,11]

Data were collected through online questionnaires on Google Forms involving two independent variables: knowledge and family rules, and a dependent variable, adolescent risk behavior. Bivariate data analysis was done with a chi-square correlation test to identify correlations between family rules and knowledge level with adolescent risk behavior.

Questionnaires were distributed online from April to November 2021. The Health Research Ethics Committee approved the study in the Faculty of Public Health, Universitas Diponegoro, number 363/EA/KEPK-FKM/2021.

Results

Table 1 shows that the majority of the respondents were female (86%), aged 18 years (72.7%), and pursuing college (93.4%).

Results on the family rule variable (Table 2) explained that most respondents had string family rules (77.1%). Some of the respondents mentioned they did not have rules about hanging out with the opposite sex (82.3%), parental companion for whenever they go out (93.7%), responsibility to introduce friends to their parents (71.2%), and opposite-sex relationships (62.8%). Some strict family rules include not staying overnight outside the home (84.5%), not smoking (91.1%), not going to clubs or bars (94.1%), and not consuming alcoholic drinks and drugs (99.6%).

Table 3 shows that most respondents had high knowledge (72.7%) and strict family rules (77.1%). Most of them mentioned they did not perform any risk behaviors (93%).

The correlation test results in Table 4 showed a relationship between family rules and adolescent risk behavior (p=0.001). Meanwhile, knowledge

Table 1 Frequency Distribution of Respondent Characteristics

Characteristics	n=271 (%)
Age (years)	
16	2 (0.7)
17	32 (11.8)
18	197 (72.7)
19	37 (13.7)
20	3 (1.1)
Gender	
Male	38 (14.0)
Female	233 (86.0)
Education level	
Junior high school	0 (0)
Senior high school	18 (6.6)
College	253 (93.4)

Table 2 Frequency Distribution of Family Rules

Variables	n=271 (%)
Not allowed to hang out with opposite sexes	
No	223 (82.3)
Yes	48 (17.7)
Having night hours	
No	89 (32.8)
Yes	182 (67.2)
Not allowed to stay overnight outside the home	
No	42 (15.5)
Yes	229 (84.5)
Accompanied by parents	
No	254 (93.7)
Yes	17 (6.3)
Dressing codes	
No	115 (42.4)
Yes	156 (57.6)
Not allowed to smoke	
No	24 (8.9)
Yes	247 (91.1)
Not allowed to go to bars/clubs	
No	16 (5.9)
Yes	255 (94.1)
Need to introduce friends to parents	
No	193 (71.2)
Yes	78 (28.8)
Not allowed to be in a romantic relationship	168 (62.0)
No	103 (38.0)
Yes	
Not allowed to consume alcoholic drinks and drugs	
No	1 (0.4)
Yes	270 (99.6)

Table 3 Categories for Knowledge, Family Rules, and Risk Behavior

Variables	n=271 (%)
Knowledge	
Low	74 (27.3)
High	197 (72.7)
Family rules	
Not strict	62 (22.9)
Strict	209 (77.1)
Risk behavior	
Not risky	252 (93.0)
Risky	19 (7.0)

was unrelated to adolescent risk behavior (p=0.665).

Discussion

This study showed no relationship between knowledge and adolescent risk behavior. Knowledge is the basis for the presence of one's action. However, adolescent risk behavior is not only formed and affected by adolescent knowledge and other factors such as socioeconomic status, social support, lifestyle, parenting, and peers. This study confirms the previous research that found a relationship between knowledge and adolescent behavior among female students in Junior High School 1 of Kuto Baro, Aceh Besar.[12]

Actions can be maintained if one knows reasons beyond their efforts.[12,13] Poor knowledge about risk behavior may happen because more information about adolescent risk behavior may be needed. As a result, adolescents tend to seek information themselves on social media. However, they sometimes need to get proper and choppy information and thus tend to develop misbehaviors. Such poor knowledge may cause misperceptions and force adolescents to try risky behaviors.[12,14,15] Adolescents may have inadequate knowledge about risk behavior because they communicate poorly with their parents.[16]

Adolescent risk behavior is influenced by some factors, such as biological, psychological, and social factors, in other words, biopsychological factors. A biopsychological approach provides a simple notion that social and environmental factors may have physical and psychological effects on creating risky behavior.[17]

This model explains that the perception of risk and peer characteristics mediates these four factors. Biological maturation also influences adolescent risk behavior. Its effects include puberty, hormonal impact, and genetic predisposition. Besides, its psychological effects on risk-taking have self-esteem, sensation seeking, and cognitive and affective ability.[17]

A family has the most essential function in adolescent behavior making. It is necessary to create family rules and set specific parenting for decision-making to solve adolescent behavioral problems.[12] If a family cannot run their function well, it may cause "Role Confusion" among its members, including those still young. As a result, adolescents may develop misbehavior and hazardous behavior.[5]

This study showed some respondents had strict family rules about smoking, alcohol, and drug consumption. One of the influencing factors on smoking habit is parenting style. Permissive parenting may lead adolescents to posit smoking behavior. Besides, parents who apply strict rules and supervise their adolescent children tend to prevent them from smoking behavior.[4] Risk factor for the consumption of narcotics, psychotropics, and addictive substances and alcohol comes

Table 4 Correlation Results between Variables

Variables	Risk Behavior Category						p*
	Not Risky		Risky		Total		
	n=252	%	n=19	%	n=271	%	
Knowledge							
Poor	68	91.9	6	8.1	74	100	0.665
High	184	93.4	13	6.6	197	100	
Family rules							
Not strict	52	83.9	10	16.1	62	100	0.001
Strict	200	95.7	9	4.3	209	100	

Note: *p<0.05 significant

from family and is influenced by parenting style. Parenting style and the parent-child relationship are the main factors that cause the consumption of narcotics, psychotropics, and addictive substances among adolescents in their early years. Families who do not apply string rules and control tend to increase the risk of misbehavior among their adolescent members.[18,19]

Some previous studies show a relationship between parents' role, especially in creating rules, with pre-marital sexual behaviors such as having a sex-opposite relationship in adolescence. If families frequently pay attention to their adolescent members, they will develop good pre-marital sexual behaviors.[20] Parents are the ones who give a chance for children to interact with the community. Besides, parenting style also influences the development of risky behavior, such as high-risk sexual behavior among adolescents.[16] Therefore, parental monitoring and family rule-making are required to reduce sexual risk behaviors among adolescents.

Family rules that teach children about life principles and morals are needed. Thus, children, especially adolescents, must obey the rules to form positive behaviors. Unsettled family rules might anticipate any misbehaviors among adolescent members. Besides, parents' control, such as good communication, family rules, and harmonious relationships with adolescent children, will positively impact their behavior.[21,22] These aspects of parental control are essential if social control and parental control are less viable in family-adolescent relationships. Such weakening situations occur due to low-income family protection.[23]

The family rule is one product of parenting styles. Parenting styles have control dimensions such as restrictiveness and strictness.[1,17] Restriction is a preventive action against something a child is interested in, while strictness is strict and assertive parental behavior to make children obey their rules.

Adolescents with beliefs and moral values will be more obedient to rules, and thus they tend not to take any risky behavior. The social control theory explains parental monitoring may reduce adolescent risk behavior. Parents should be present as child controllers when their children transition from childhood to adulthood, where they develop unstable emotional and psychological states. Beliefs invested by children and parents (family) may improve the child's behavior in obeying rules or norms applied in the family.[4,21]

Adolescent misbehaviors happen because of intrapersonal and contextual factors. The intrapersonal factors are developed from self-identity crises when adolescents are still searching for their self-identity and cannot control themselves. Meanwhile, the contextual factors causing adolescent misbehavior are family that contributes to forming their members' self-identify and behavior. Improper parenting styles in the family, such as spoiling children, refusing child existence, and giving less religious education, may cause adolescent misbehaviors.[24] Positive behavior reinforcement among children depends on parents, especially their emotional attachment and behavior towards them.[25]

Conclusions

This study concludes that knowledge level has no relationship with adolescent risk behavior, but family rules do. Family rules are essential for preventing adolescent risk behavior; hence, parents must set rules to restrict adolescent behavior, especially towards opposite-sex relationships or friendships, to avoid sexual risk behaviors.

Conflict of Interest

The authors declare there is no conflict of interest.

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References

1. Hitchcock JE, Schubert PE, Thomas SA. Community health nursing: caring in action. Boston: Cengage Learning; 2002.
2. Hasbi M. Analisis model peer education metode adolescent friendly terhadap peningkatan pengetahuan dan sikap remaja tentang perilaku seksual berisiko. JKT. 2019;1(1):29–37.
3. Yenni Erliza. Remaja ideal generasi perubahan (problematika, perkembangan dan potensi) [Internet]. Mataram: BKKBN Nusa Tenggara Barat; 2021 [cited 2022 March 10]. Available from: https://ntb.

bkkbn.go.id/?p=2127.
4. Rahmawati Y, Raudatussalamah R. Perilaku merokok pada pelajar: peran orang tua dalam pengasuhan. Psikobuletin. 2020;1(1):20–28.
5. Suharyanta D, Widiyaningsih D, Sugiono S. Peran orang tua, tenaga kesehatan, dan teman sebaya terhadap pencegahan perilaku merokok remaja. JMK. 2018;4(1):8–13.
6. Indraswari R, Shaluhiyah Z. Analisis karakteristik remaja terhadap perilaku-perilaku berisiko kesehatan. Higeia. 2022;6(2):144–51.
7. Kusumawardani N, Rachmalina S, Wiryawan Y, Anwar A, Handayani K, Mubasyiroh R, et al. Perilaku berisiko kesehatan pada pelajar SMP dan SMA di Indonesia [Internet]. Jakarta: Badan Litbangkes Kementerian Kesehatan RI; 2015 [cited 2022 May 5]. Available from: https://extranet.who.int/ncdsmicrodata/index.php/catalog/489/download/3800.
8. Fadhila FCN, Febriani Z. Peran parent attachment dan peer attachment terhadap perilaku berisiko remaja serta tinjauannya dalam Islam. In: Nurhayati E, Bagaskara S, editors. Prosiding Konferensi Nasional Psikologi Kesehatan IV; 2021 October 30–31; Jakarta, Indonesia. Jakarta Pusat: Penerbit Universitas YARSI; 2022 [cited 2022 May 10]. p. 42–52. Available from: https://www.yarsi.ac.id/wp-content/uploads/2022/08/11.-Prosiding-Konferensi-Psikologi-Kesehatan-IV-30-31-Oktober-2021.pdf#page=51.
9. Andayani SA, Maghfiroh NF, Anggraini NR. Hubungan self efficacy dan self esteem dengan perilaku berisiko remaja. JKP. 2021;9(2):23–38.
10. Larasati WA, Dwilda FS, Febriyana N. Parental bonding dengan perilaku seksual pada remaja berpacaran di SMKS Persatuan 1 Tulangan Sidoarjo. J Ilkes. 2022;13(1):31–9.
11. Sarita U, Fithria, Hidayati H. Hubungan fungsi afektif keluarga dengan perilaku bullying pada remaja. JIM Keperawatan. 2021;5(2):88–94.
12. Anwar C, Rosdiana E, Dhirah UH, Marniati M. Hubungan pengetahuan dan peran keluarga dengan perilaku remaja putri dalam menjaga kesehatan reproduksi di SMP Negeri 1 Kuta Baro Aceh Besar. J Healthc Technol Med. 2020;6(1):393–403.
13. Mahmudah M, Yaunin Y, Lestari Y. Faktor-faktor yang berhubungan dengan perilaku seksual remaja di Kota Padang. J Kesehat Andalas. 2016;5(2):448–55.
14. Hidayangsih PS. Perilaku berisiko dan permasalahan kesehatan reproduksi pada remaja. J Kesehat Reprod. 2014;5(2):89–101.
15. Lestary H, Sugiharti. Perilaku berisiko remaja di Indonesia menurut Survey Kesehatan Reproduksi Remaja Indonesia (SKRRI) tahun 2007. J Kesehat Reprod. 2011;1(3):136–44.
16. Gustina E. Komunikasi orangtua-remaja dan pendidikan orangtua dengan perilaku seksual berisiko pada remaja. UJPH. 2017;6(2):131–6.
17. Rakhmawati D. Pencegahan perilaku berisiko pada remaja. Pros Semnas FK FIP UPGRIS [Internet]. 2016;2016:15–22 [cited 2022 June 10]. Available from: http://prosiding.upgris.ac.id/index.php/bk_2017/bk_17/paper/viewFile/1470/1364.
18. Mariani NN, Murtadho SF. Hubungan antara peran orang tua, pengaruh teman sebaya, dan sikap terhadap perilaku seksual pranikah pada siswa-siswi SMA Negeri 1 Jamblang Kabupaten Cirebon tahun 2017. Care. 2018;6(2):116–30.
19. Anggraini Y. Hubungan fungsi afektif keluarga dengan perilaku kenakalan remaja di SMK Cendana Padang Panjang. Menara Ilmu. 2017;11(76):155–65.
20. Aunola K, Stattin H, Nurmi JE. Parenting styles and adolescents' achievement strategies. J Adolesc. 2000;23(2):205–22.
21. Wahdini M, Indraswari N, Susanti AI, Sujatmiko B. Faktor-faktor yang berhubungan dengan perilaku berisiko pada remaja. JKM. 2021;7(2):177–84.
22. Kurniadi O. Pengaruh komunikasi keluarga terhadap prestasi belajar anak. Mediator. 2001;2(2):267–90.
23. Nurhayati. Hubungan kekuatan keluarga terhadap perilaku seksual berisiko pada remaja di wilayah Desa Tridaya Sakti Kecamatan Tambun Selatan Kabupaten Bekasi. JKK. 2013;1(2):122–9.
24. Kao TSA, Carter WA. Family influences on adolescent sexual activity and alcohol use. Open Fam Stud J. 2013;5:10–8.
25. Mulya AP, Lukman M, Yani DI. Peran orang tua dan peran teman sebaya pada perilaku seksual remaja. FHJ. 2021;8(2):122–9.

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RESEARCH ARTICLE

Early Impacts of COVID-19 on Nutrition Intake and Household Dietary Diversity in Kupang District, East Nusa Tenggara, Indonesia

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Abstract

One of the social problems solving the direct impact on the community is overcoming household food security due to the COVID-19 pandemic. This study aims to analyze household food security during the COVID-19 pandemic and link it to the nutrient intake and nutritional status of children under five in the Kupang district area. This cross-sectional study is based on a survey conducted on the Timorese population in Kupang, East Nusa Tenggara, Indonesia, from May to October 2021. Data on household dietary diversity was collected through the 24-hour food recall using the household dietary diversity score (HDDS). The study sample was taken from Timorese population families with toddlers under five years, and 1,444 families voluntarily participated in this study. Subjects were taken at each public health using a simple random method. This study analyzes the Spearman correlation test with the HDDS and the proportion of food expenditure. A 63% of households had a balance of less cost (<50%) with an average of 63.9. Generally, households (90.4%) had a pretty good diet diversity score. Food groups that were relatively highly consumed by most households included cereals (100%), sugar and sweeteners (90.2%), oils and fats (93.7%), seasonings, and spices (89.4%). A significant effect with $p<0.05$ was on HDDS during the COVID-19 pandemic. The food consumption score is another indicator widely used in determining household food security. Therefore, it is necessary to revalidate tests in further studies of these indicators.

Keywords: COVID-19, dietary diversity, food security, HDDS

Introduction

As of March 12, 2020, the coronavirus disease 2019 (COVID-19) has been confirmed in 125,048 people worldwide, bringing a mortality rate of around 3–7%, compared to the mortality rate of influenza (less than 1%). There is an urgent need for effective treatment. The current focus is on developing new therapies, including antivirals and vaccines.[1] The first coronavirus case emerged and attacked humans in Wuhan, China. Initially, it was suspected of pneumonia with symptoms similar to the flu, including cough, fever, fatigue, shortness of breath, and no appetite.[1] However, unlike influenza, the coronavirus developed rapidly, resulting in severe infections, organ failure, and death. This emergency condition mainly occurs in patients with previous health problems.[2] It also affects the individual and community levels of the social and food security sectors. The resolution of the COVID-19 problem, especially on social impacts, will involve the minor elements of the community, such as overcoming household food security. Therefore, issues related to food security challenge all countries directly related to improving the economy and achieving the quality of human life.[3,4]

According to FAO, food security is the condition of food fulfillment for everyone, both in quantity and quality. Fulfilling the right to food is the primary key to overcoming hunger. World data from study reports from Rosen et al.[5] stated that the number of people who consumed calories below the recommended in 2015 reached 13.4%. This data generally occurs in developing countries and is projected to increase to 15.1% in 2025.

Food security has been a top priority for the world community for decades in addressing the basic nutritional needs of the poor and vulnerable. Food insecurity still affects hundreds of millions of people in Sub-saharan Africa, where more than one in four people (nearly 218 million) are malnourished. Food and nutrition security is a global challenge and a prerequisite for a healthy and prosperous society. Food

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security occurs when "all people, at all times, have physical, social, and economic access to sufficient, safe, and nutritious food that meets their dietary needs and preferences for an active and healthy life." Nutritional security exists when safe access to an appropriately nutritious diet is coupled with environmental sanitation, adequate health services, and care to ensure a healthy and active life.[6]

Issues and debates about global food security have resurfaced since the 2008 food crisis when prices of essential food commodities spiked dramatically, showing that securing food supply and accessibility to meet the needs of the world's 9 billion people by 2050 is a formidable task. The world population is estimated to increase from 7.3 billion to 9 billion in 2050. Food production requires regular production systems and consumption patterns that need policy action to increase agricultural productivity by 30-40% to fulfill the need for food.[7]

Therefore, programs integrated into joint efforts politically, economically, and socially mobilize awareness of the importance of accurate information systems in providing fast and timely information. Of course, this will help overcome the problem of changing food consumption patterns during the COVID-19 pandemic. This study aims to analyze household food security during the COVID-19 pandemic and link it to the nutrient intake and nutritional status of children under five in the Kupang district area.

Methods

This cross-sectional study is based on a survey conducted on the Timorese population in Kupang district, East Nusa Tenggara, Indonesia, from May to October 2021. The location selection was chosen purposively considering that Kupang district has a high prevalence of nutritional problems. This study involved two subjects: children under five (12–59 months old) and mothers. Population data were obtained from cadre reports from each village recorded at each local health center. Mothers of children were chosen as research subjects because they were fully involved in providing food for all family members. The inclusion criteria considered in determining the child as a subject included children aged 12 to 59 months old, not in severe illness or carrying out routine treatment processes, and the mother's consent as evidenced by signing the informed consent form. The inclusion criteria considered in determining the mother as a subject were: the respondent was the biological mother of the child, had a husband with the status of the household head, the mother was entirely responsible for arranging or preparing family meals, aged 17 to 50 years old, and the subject agreed to interview, evidenced by the signing of the informed consent form. The number of subjects was calculated by proportional allocation by considering each health center's level/stratum of food vulnerability. The subjects totaled 1,444, consisting of mothers and children in the Timorese population. Subjects were taken at each public health using a simple random method without replacement. The randomization process was carried out with the help of the Microsoft Excel 2013 program. The Health Research Ethics Committee of Politeknik Kesehatan Kemenkes Mataram approved the study, number LB.01.03/6/1688/2021.

Data on household dietary diversity was collected through the food recall method 24 hours earlier, using the household dietary diversity score (HDDS) indicator. Interviews were proposed to mothers who were responsible for the preparation of family meals. Subjects were instructed to tell about all types of food consumed by each household, sourced from the purchase process or self-processing at home. In addition, subjects were asked to talk about the food prepared at home for household members outside the home.

The subsequent data was the proportion of food expenditure collected by conducting structured interviews with mothers referring to the questionnaire sheet. Subjects were instructed to explain the average spending for each type of food consisting of staple foods (rice, sugar, cooking oil, coffee, tea); side dishes (chicken eggs, tempeh, tofu, fish, broiled chicken, shrimp, squid); vegetables and fruits; instant noodles; toddler milk; and spices. Subjects explain the average frequency of each type of food purchase in units of time (day/week/month) and state the amount spent on each purchase. Subjects were asked to estimate non-food expenditures paid in one month, such as water, electricity bills, regular installments, fuel, etc.

Results

Table 1 shows the proportion of child subjects by gender. Almost half of the subjects (57.1%) were female, while the proportion of males reached 42.9%.

Table 1 Distribution of Children by Age and Gender

Characteristics	n=1,444 (%)
Age (years)	
1–3	841 (58.2)
3–5	603 (41.8)
Gender	
Male	619 (42.9)
Female	825 (57.1)

Table 2 Characteristics of the Household

Characteristics	n=1,444 (%)
Father's occupation	
Farmer	367 (25.4)
Fisherman	135 (9.4)
Trader	261 (18.1)
Private sector employee	194 (13.4)
Civil servant/military/police officer	487 (33.7)
Mother's occupation	
Housewife	511 (35.4)
Trader	273 (18.9)
Farmer	258 (17.9)
Private sector employee	82 (5.7)
Civil servant/military/police officer	320 (22.1)
Household size (persons)	
Small (≤4)	461 (31.9)
Medium (5–6)	603 (41.8)
Big (≥7)	380 (26.3)

The data on general household characteristics analyzed in this study consisted of fathers' and mothers' occupations and household size. Based on the study results in Table 2, civil servant/military/police was the most dominant type of husband job (33.7%). The proportion of work of the father as a farmer was 25.4%. Meanwhile, almost half of the children's mothers (35.4%) were homemakers or did not work permanently. Some mothers act as private sector employees (5.7%).

Table 3 shows the distribution of parents by education level. Most fathers (39.0%) and mothers (30.4%) had a history of education, having graduated from secondary education. The data shows the low level of parental education.

The study presents the distribution of households based on the proportion of food expenditure described in Table 4. The study results explained that the ratio of lower prices (more than 50% of households) still dominated most families at 59.1%. Meanwhile, the % of households with a proportion of food expenditure categorized as good was 40.1%. The average value of the proportion of food expenditure as a whole household was 60.9%. Table 4 explains

Table 4 Distribution of Households by the Proportion of Food Expenditure

Categories	n=1,444 (%)
Low (>50%)	853 (59.1)
Adequate (≤50%)	591 (40.9)
Average±SD (proportion)	60.9±19.8

Table 5 Distribution of Households based on Diversity of Food Consumption with HDDS

Categories	n=1,444 (%)
Low (≤3 food types)	52 (3.6)
Moderate (4–5 food types)	141 (9.7)
High (≥6 food types)	1,251 (86.6)
Average±SD (proportion)	6.3±1.8

Table 3 Distribution of Parents by Education Level

Education Level	Father		Mother	
	n=1,444	%	n=1,444	%
None	48	3.3	23	1.6
Primary/lower education (elementary school/equivalent)	307	21.3	291	20.1
Junior secondary education (junior high school/equivalent)	564	39.0	439	30.4
Upper secondary education (high school/equivalent)	281	19.5	417	28.9
Higher education (associate degree diploma-3/bachelor degree/master degree/doctoral degree)	244	16.9	274	19.0

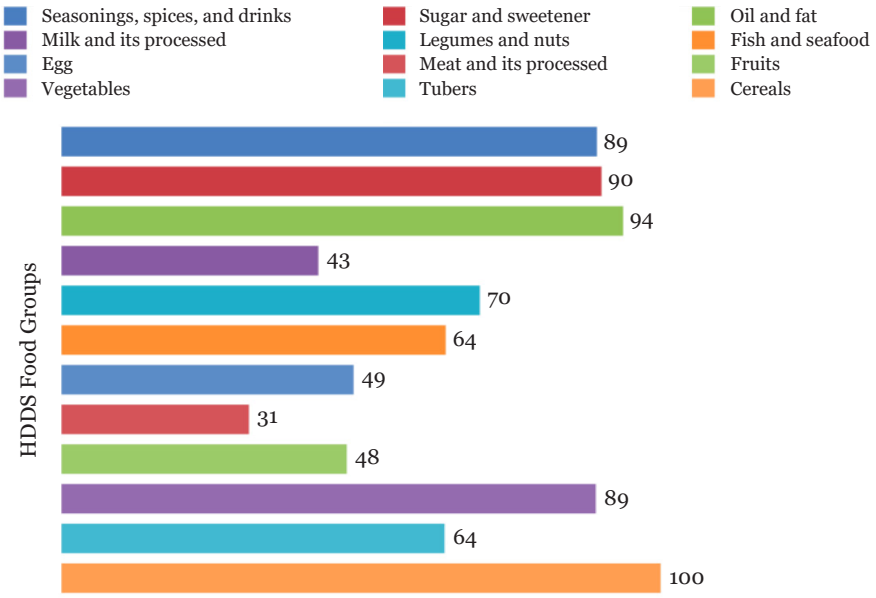

Figure Distribution of Households by Food Group Consumed

that almost half of the households experience food insecurity conditions. Income was the main element that had implications for the proportion of food expenditure.

The distribution of households based on the consumption of food types is described in detail in Figure. Food groups that were relatively highly consumed by most households included cereals (100%), sugar and sweeteners (90.2%), oils and fats (93.7%), seasonings and spices (89.4%).

Dietary diversity illustrates household consumption over a certain period and is an essential indicator of food security. The study results in Table 5 show that as many as 86.6% of households had a reasonably high HDDS.

Discussion

Growth, health, and psychosocial development in children under five are continually occurring, so good nutrition is needed during this period. The general characteristics of children under five in this study were the distribution of subjects based on age and gender. Table 1 explains that most children were aged 1–3 years (58.2%), and the remaining 41.8% were aged 3–5. The grouping of children's age was determined based on the division of the age range in the Table of Indonesian Recommended Dietary Allowances (RDA). Children from early life to 3 years old need nutrients to support brain development which has long-term consequences.[8] Fulfilling nutrition, primarily for toddlers aged 3–5 years (preschool age), is generally used to support children's cognitive and motor development accompanied by stimulation. Children under five who lack nutrient intake can cause nutritional problems/ malnutrition. According to WHO, malnutrition is the main element or factor that causes death and reduces the health status of children under five.[9]

The Economic Survey data analysis showed that employment status and household size determine household food security.[11] According to Ip et al., households with the father's primary occupation as a farmer generally have dynamic food security conditions because they follow the harvest season of agricultural production.[12] The father's role is vital to creating a good food security condition in the household. According to Ochieng et al., children and women in households headed by a father or a man have significantly more diverse diets than in households headed by a woman.[13]

Meanwhile, mothers' work as housewives is strongly correlated with good food security conditions in the family.[14] This is related to the number of times mothers are at home to be involved in the buying process to provide food for household members.[15] Table 2 also presents data on the distribution of households based on the number of family members. Generally, households were classified as medium-sized, with

a proportion of 41.8%. The ratio of small-sized households was 31.9%, and 26.3% were included in large-sized households. According to Mango et al., a small household size can guarantee better food security. The smaller the family size, the more food opportunities for everyone.[16] This becomes important in improving the optimal nutritional status of each individual in the household.[17] The presence of many children in the family usually causes limited resources to meet household needs. In addition, limited access to households in providing nutritional quality food can have implications for suboptimal nutritional conditions in children.

The quality of education greatly determines the quality of human resources because it acts as a means to improve intelligence and human skills. In the food security system, the education level of the head of household and mother is one of the indicators included in social access from the dimension of food access.[18] It will affect the low access of parents in obtaining good jobs to fulfill the needs of family life.[19] The study results of Petralias et al. stated that fathers or mothers who do not complete compulsory education would be more at risk of causing food insecurity conditions. It is due to limited access to nutritious and balanced food. According to Vollmer et al., higher education levels of mothers and fathers are closely related to decreased malnutrition in children. Therefore, education is essential to support socioeconomic status and food and nutrition security conditions at the household level. The proportion of food expenditure is the income allocated to spend on food every month and divided by total household expenditure.

A household with a large proportion of food expenditure is quite at risk of experiencing food insecurity.[19] According to Smith and Subandoro,[34] households can achieve good food security conditions if the average proportion of food expenditure is less than 50%. Impoverished households spend more to access basic needs, reduce food quality, and reduce consumption of the cheapest food.[20] These conditions will impact the achievement of nutritional status that is not optimal in individuals. Expenditure on food can be defined as consumption expenditure at current food prices divided by income. Food is a primary need, so low household income can lead to higher expenditure allocations for food. HDDS indicator provides an overview of the household's ability to access food based on the food group consumed in the previous 24 hours. According to Russel et al., the diversity of food consumption indicates food insecurity in households.[21] The average score of HDDS as a whole was 6.3. Melani supports the results of this study, where most households in agro-ecological areas (72.7%) have high HDDD.[22]

The food consumed by each individual in determining the HDDS can be obtained through several ways, such as self-cooking, buying, and through assistance or giving. Households in this study generally received food for consumption by cooking and buying. The main menu for the family, such as rice and side dishes, naturally came from the processing itself at home through the cooking process. Meanwhile, processed food menus, including snacks, are mostly consumed by children in the household from the nearest food stalls. According to the Ministry of Trade, the Indonesian people's consumption rate in the four food groups is relatively high, the leading national strategic point. Based on the Ministry of Health total diet study, the main staple food in Indonesian society still relies on the cereal group as the primary energy source, and this is in line with a total diet study; cereal and processed groups are foodstuffs with a reasonably high consumption rate by the Indonesian population.[23] While other food groups, households in this study revealed they needed to be better at consuming meat and processed products (41.4%), milk and derivative products (43.1%), and fruits (47.8%).

The sample households' dairy and processed food groups are mainly powdered milk by children under five. The total diet study in 2014 reported that the level of consumption of the vegetable and processed groups in the population in East Nusa Tenggara was relatively high, with an average consumption of 92.7 grams per person per day.[24] This is supported by the high level of community preference for vegetables and their processed products in a geographical environment surrounded by hills and mountains.

The consumption rate of the meat and processed food group needs to be increased because it contributes to meeting the needs for protein, vitamins, and minerals that can support body health.[25] Most households still have relatively low consumption figures for several food groups. About 48% of households consume fruits, meat, and their derivatives, milk, and derivatives. Several factors contributing to this food group's low consumption are income level, type of work, gender, household size, and community

knowledge of food and nutrition.[26] The utilization of local food for root crops, legumes, and nuts needs to be increased to diversify food to find alternative sources of carbohydrates and protein other than rice and meat.

This study has several limitations, such as using a single indicator widely used in determining resilience in household food: food consumption score (FCS), average household energy intake, and the household food insecurity access scale score (HFIAS). Therefore, it is necessary to revalidate these indicators.

Conclusion

There was a change in household food security in the Kupang district community due to the COVID-19 pandemic.

Conflict of Interest

None declared.

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References

1. Chu DK, Akl EA, Duda S, Solo K, Yaacoub S, Schünemann HJ; COVID-19 Systematic Urgent Review Group Effort (SURGE) study authors. Physical distancing, face masks, and eye protection to prevent person-to-person transmission of SARS-CoV-2 and COVID-19: a systematic review and meta-analysis. Lancet. 2020;395(10242):1973–87.
2. Mona N. Konsep isolasi dalam jaringan sosial untuk meminimalisasi efek contagious (kasus penyebaran virus corona di Indonesia). JSHT. 2020;2(2):111–25.
3. Pourreza A, Geravandi S, Pakdaman M. Food security and economic growth. JNFS. 2018;3(3):113–5.
4. Pérez-Escamilla R. Food security and the 2015–2030 sustainable development goals: from human to planetary health: perspectives and opinions. Curr Dev Nutr. 2017;1(7):e000513.
5. Rosen S, Meade B, Murray A. International Food Security Assessment, 2015–2025, GFA-26 [Internet]. Washington, DC: US Department of Agriculture, Economic Research Service; 2015 [cited 2021 May 10]. Available from: https://www.ers.usda.gov/webdocs/outlooks/37264/53198_gfa26.pdf.
6. Augustin MA, Riley M, Stockmann R, Bennett L, Kahl A, Lockett T, et al. Role of food processing in food and nutrition security. Trends Food Sci Technol. 2016;56:115–25.
7. Keating BA, Herrero M, Carberry PS, Gardner J, Cole MB. Food wedges: framing the global food demand and supply challenge towards 2050. Glob Food Sec. 2014;3(3–4):125–32.
8. Cusick SE, Georgieff MK. The role of nutrition in brain development: the golden opportunity of the "first 1000 days". J Pediatr. 2016;175:16–21.
9. World Health Organization. Children: improving survival and well-being [Internet]. Geneva: World Health Organization; 2020 [cited 2021 May 18]. Available from: https://www.who.int/news-room/fact-sheets/detail/children-reducing-mortality.
10. Syamola D, Nurwahyuni A. Determinan ketahanan pangan rumah tangga di daerah pedesaan di Indonesia (analisis data Susenas tahun 2017). MKMI. 2019;15(1):46–54.
11. Ip EH, Saldana S, Arcury TA, Grzywacz JG, Trejo G, Quandt SA. Profiles of food security for US farmworker households and factors related to dynamic of change. Am J Public Health. 2015;105(10):e42–7.
12. Ochieng J, Afari-Sefa V, Lukumay PJ, Dubois T. Determinants of dietary diversity and the potential role of men in improving household nutrition in Tanzania. PLoS One. 2017;12(12):e0189022.
13. Yeganeh S, Motamed N, Boushehri SN, Pouladi S, Ravanipour M. Mothers' knowledge and attitude toward food security in complementary feeding of 1–2 year old children and its relation with demographic indices. Evid Based Care J. 2018;7(4):22–9.
14. Adepoju AA, Ogunniyi LT, Agbedeyi D. The role of women in household food security in Osun state, Nigeria. IJAPR. 2015;3(3):104–13.
15. Mango N, Zamasiya B, Makate C, Nyikahadzoi K, Siziba S. Factors influencing household food security among smallholder farmers in the Mudzi district of Zimbabwe. Dev South Afr. 2014;1(4):625–40.

16. Petralias A, Papadimitriou E, Riza E, Karagas MR, Zagouras AB, Linos A; DIATROFI Program Research Team. The impact of a school food aid program on household food insecurity. Eur J Public Health. 2016;26(2):290–6.
17. Sulaiman AA, Subagyono K, Soetopo D, Sulihanti S, Wulandari S. Kebijakan penyelamat swasembada pangan. 2nd printing. Jakarta: IAARD Press; 2018.
18. Shah AA, Syeda ZF, Bhatti SH. Pocket money as a proxy for family income. IJSSE. 2012;2(4):688–93.
19. Vollmer S, Bommer C, Krishna A, Harttgen K, Subramanian SV. The association of parental education with childhood undernutrition in low- and middle-income countries: comparing the role of paternal and maternal education. Int J Epidemiol. 2017;46(1):312–23.
20. Amalia IN, Mahmudiono T. Hubungan pendapatan, total pengeluaran, proporsi pengeluaran pangan dengan status ketahanan rumah tangga petani gurem (studi di Desa Nogosari Kecamatan Rambipuji Kabupaten Jember). Amerta Nutr. 2017;1(2):143–52.
21. Lele U, Masters WA, Kinabo J, Meenakshi JV, Ramaswami B, Tagwireyi J, et al. Measuring food and nutrition security: an independent technical assessment and user's guide for existing indicators [Internet]. Rome: Food Security Information Network; 2016 [cited 2021 June 2]. Available from: https://sites.tufts.edu/willmasters/files/2016/06/FSIN-TWG_UsersGuide_12June2016.pdf.
22. Russell J, Lechner A, Hanich Q, Delisle A, Campbell B, Charlton K. Assessing food security using household consumption expenditure surveys (HCES): a scoping literature review. Public Health Nutr. 2018;21(12):2200–10.
23. Baliwati YF, Briawan D, Melani V. Validation household dietary diversity score (HDDS) to identify food insecure households in industrial area. Pak J Nutr. 2015;14(4):234–8.
24. Kementerian Kesehatan Republik Indonesia. Buku studi diet total: survei konsumsi makanan individu Indonesia 2014. Jakarta: Badan Penerbitan Badan Penelitian dan Pengembangan Kesehatan Kementerian Kesehatan Republik Indonesia; 2014.
25. Mukherjee A, Paul S, Saha I, Som TK, Ghose G. Dietary diversity and its determinants: a community-based study among adult population of Durgapur, West Bengal. Med J DY Patil Vidyapeeth. 2018;11(4):296–301.
26. Powell B, Bezner Kerr R, Young SL, Johns T. The determinants of dietary diversity and nutrition: ethnonutrition knowledge of local people in the East Usambara Mountains, Tanzania. J Ethnobiol Ethnomed. 2017;13(1):23.

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RESEARCH ARTICLE

Effect of Moringa Leaves and Combination of Fe Tablets on the Increase of Hb in Pregnant Women with Anemia

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Abstract

Anemia during pregnancy can lead to complications during gestation, childbirth, and postpartum. The government recommends administering at least 90 Fe tablets to pregnant women to address this. Additionally, fulfilling nutritional needs is another strategy to combat anemia, with Moringa leaves emerging as a nutrient-rich food source known to elevate hemoglobin levels. This study investigated the impact of Moringa leaves and combined Fe tablet consumption on hemoglobin levels in anemic pregnant women. A quasi-experimental design incorporated pre-test and post-test evaluations with a control group in Bengkulu from June to November 2022. Purposive sampling yielded a cohort of 60 anemic pregnant women, divided equally into intervention and control groups. Data collected over two months were analyzed through univariate and bivariate methods using the Wilcoxon and Mann-Whitney tests at a 5% significance level. Findings indicated that the combination of Moringa leaves and Fe tablet significantly increased hemoglobin levels in pregnant women with anemia ($p<0.05$). Therefore, anemic pregnant women are encouraged to consume Moringa leaves as a potential measure to enhance their hemoglobin levels.

Keywords: Anemia, pregnant women, Moringa, Fe tablets

Introduction

Anemia remains a prevalent health issue among pregnant women in Indonesia. Pregnant women with hemoglobin (Hb) levels below 11 g/dl during their initial visits are diagnosed as anemic. Such women run a heightened risk of delivering infants with iron-deficiency anemia. This deficiency can persist throughout the early years of a child, hindering the growth of the brain and other cells. Consequently, it may delay the child's overall growth and development, potentially leading to stunting or wasting. These developmental setbacks can also have lasting and possibly irreversible impacts on cognitive development.[1–4]

World Health Organization (WHO) reports that around 42% of children under five and 40% of pregnant women worldwide are anemic. This condition contributes to 40% of maternal deaths in developing countries. Between 1990 and 2019, global anemia cases rose from 1.42 billion to 1.74 billion, spanning 204 countries. A 2018 survey showed anemia prevalence in pregnant women at 36.4% in urban settings, 49.5% in rural areas, and a combined rate of 48.9%. In 2020, Bengkulu city documented 308 anemic pregnant women, with the Beringin Raya Public Health Center reporting the most cases at 96.[5–7]

To counteract this, the government introduced the Integrated Antenatal Service program. This strategy involves nutritional counseling during pregnancy, hemoglobin level checks in the 1st and 3rd trimesters, and administering iron (Fe) tablets and at least 90 folic acid tablets throughout gestation. Despite these measures, adherence could be higher. Many pregnant women decline or neglect these guidelines due to adverse effects like nausea and vomiting. Consequently, anemia remains prevalent among them.[8,9]

Supplemental nutritional intake from food is indispensable to satisfy iron needs during pregnancy. A balanced diet during this period is crucial, emphasizing the consumption of both macro and micronutrients to fulfill varied dietary requirements. Factors like calorie intake, protein, carbohydrates, iron, folic acid, vitamin A, zinc, iodine, calcium, and other essential nutrients significantly influence a mother's nutritional status. Rahmawati and Daryanti's[10] study suggested that Fe tablets are most effective when paired with supplements promoting hemoglobin synthesis and iron absorption, such as Moringa leaf extract. Odura et al.[11] further highlighted that 100 grams of Moringa leaves contain an

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impressive 28.29 mg of iron.

Moringa presents as a compelling alternative for alleviating anemia. Its nutritional content outshines many common foods: it has seven times the vitamin C of oranges, ten times the vitamin A of carrots, seventeen times the calcium of milk, fifteen times the potassium of bananas, twenty-five times the iron of spinach, and nine times the protein of yogurt.[12] Besides these, Moringa is enriched with B vitamins, chromium, copper, magnesium, manganese, phosphorus, and zinc. For expectant mothers, Moringa leaves contain essentials: thiamin, riboflavin, niacin, beta-carotene, calcium, iron, phosphorus, magnesium, zinc, vitamin C, antioxidants, and anti-inflammatories. These components are pivotal in staving off the activation of leukocytes and oxidative stress from free radicals.[13–15] A study in Senegal asserted that Moringa leaf powder is beneficial in preventing malnutrition among infants, pregnant women, and nursing mothers, with no proven side effects from Moringa consumption to date.[16]

Many sources advocate for a daily intake of 100 grams of fresh Moringa leaves, citing it as an adequate and safe measure to meet nutritional needs.[17] *Moringa oleifera* is recognized as a natural powerhouse of nutrients. Various parts of this tree—its leaves, fruit, flowers, and pods—are consumed as nourishing vegetables in countries like India, Pakistan, the Philippines, Hawaii, Africa, and Indonesia. Comprehensive studies on Moringa compounds reveal a wealth of essential components, including vitamins, minerals, antioxidants, and amino acids, fulfilling many of the nutritional requirements of expectant mothers. The plant is particularly abundant in micronutrients vital for pregnant women, such as thiamin, riboflavin, niacin, beta-carotene, calcium, iron, phosphorus, magnesium, zinc, and vitamin C. Given its rich content, Moringa can serve as an alternative to conventional multiple micronutrient supplements, enhancing the nutritional well-being of pregnant women. Additionally, Moringa is dense in protein and amino acids and exhibits antioxidant and anti-inflammatory properties.[18–21]

This study investigated the impact of Moringa leaves and combined Fe tablet consumption on hemoglobin levels in anemic pregnant women.

Methods

This study utilized a quantitative approach with a quasi-experimental design (pre-post test with a control group) conducted in Bengkulu city from June to November 2022. Hb levels of both groups were assessed before and after the treatment phase. The intervention for the treatment group entailed administering Moringa leaves and Fe tablets, while the control group received only Fe tablets over eight weeks. Using purposive sampling, the study included 60 anemic pregnant women, equally divided with 30 in the treatment group and 30 in the control group. The research instrument was a data collection form capturing details such as name, age, education, parity, and gestational age. Additionally, a digital Hb measurement tool was used to gauge the Hb levels of the participants. Both univariate and multivariate analyses were employed for data analysis. The Health Research Ethics Committee of the Faculty of Nursing of Universitas Jember approved the study, number 126/UN25.1.14/KEPK/2022.

Bivariate analysis was conducted to determine the difference in the average Hb before and after the intervention in the same group using the Wilcoxon signed ranks test. Meanwhile, the Mann-Whitney test was used to determine the difference in the average Hb before and after the intervention in different groups.

Before the above bivariate analysis, the data normality test was performed using the Shapiro-Wilk test. The results of the Shapiro-Wilk test showed that the data were not normally distributed.

Results

Table 1 shows that most (90%) of intervention respondents with age are not at risk, most (76.6%)) had a high school education, more than some (60%) were multi-gravida, and most (86.7%) were in the 3rd trimester. In the control respondents, most (86.7%) were not at risk, almost half (46 7%) with high school education, most (76.7%) with multi-gravida parity, and some (50%) respondents were in the 1st trimester.

Table 2 shows that the average Hb of respondents in the intervention group before treatment was 10.62 g/dl. The standard deviation was 0.364 g/dl, and it is believed that 95% of the average Hb of respondents before treatment was in the range of 10.34 to 10.62 g/dl. The average Hb of respondents in the control group before being given treatment was 10.44 g/dl, standard deviation of 0.318, and it is believed that 95% of

Table 1 Distribution of Respondents in the Two Groups

Characteristics	IG (n=30)	CG (n=30)
Age		
No risk	27	26
Risk	3	4
Education		
Junior high school	2	5
Senior high school	23	14
D3/S1	5	11
Parity		
Primi gravida	12	7
Multi gravida	18	23
Gestational age		
1st trimester	1	15
2nd trimester	3	2
3rd trimester	26	13

Note: IG: intervention group, CG: control group

Table 2 Distribution of Respondents based on the Average Hb before and after Treatment

Variables	IG (n=30)	CG (n=30)
Hb before		
Mean	10.48	10.44
Median	10.55	10.40
Min	9.6	9.6
Max	10.9	10.8
SD	0.364	0.318
95% CI	10.34–10.62	10.32–10.56
Hb after		
Mean	11.92	10.64
Median	11.90	10.70
Min	10.7	10.0
Max	13,5	11.0
SD	0.724	0.290
95% CI	11.64–12.19	10.53–10.75

Note: IG: intervention group, CG: control group

the average Hb of respondents before being given treatment was in the range of 10.32 to 10.56 g/dl.

In the intervention group, the average Hb after being given treatment was 11.92 g/dl, the standard deviation was 0.724 g/dl, and it is believed that 95% of respondents' average Hb before being given treatment was in the range of 11.64 to 12.19 g/dl. The average Hb of respondents in the control group after being given treatment was 10.64 g/dl, the standard deviation was 0.290, and it is believed that 95% of the average Hb of respondents before being given treatment was in the range of 10.53 to 10.75 g/dl.

The results of the data normality test with Shapiro-Wilk showed $p<0.05$, meaning that the Hb data before the treatment had an abnormal distribution in the intervention and control groups. Meanwhile, the Hb variable after treatment in the intervention group had $p>0.05$, meaning that the Hb data after treatment had a normal distribution; in the control group, $p<0.05$, indicating that the Hb data after treatment had an abnormal distribution. So the test used is non-

Table 3 Differences in Hb levels of Response before and after Moringa Leaves Combination with Fe Tablets in the Intervention Group

Hemoglobin (Hb)	n	Median (Min–Max)	Z	p
Before intervention	30	10.55 (9.6–10.9)	–4.785	0.000*
After intervention	30	11.90 (10.7–13.5)		

Note: *Wilcoxon test, p>0.05 significant

Table 4 Differences in Hb Levels of Respondents before and after Giving Fe Tablets in the Control Group

Hemoglobin (Hb)	n	Median (Min–Max)	Z	p
Before intervention	30	10.40 (9.6–10.8)	–4.899	0.000*
After intervention	30	10.70 (10.0–11.0)		

Note: *Wilcoxon test, p>0.05 significant

Table 5 Effect of Moringa Leaf and Fe Tablet Combination on the Increase of Hb in Pregnant Women with Anemia

Hemoglobin (Hb)	Median (Min–Max)	U	p
Intervention	1.350 (0.20–3.00)	32,500	0.000*
Control	0.300 (0.10–3.00)		

Note: *Mann-Whitney test, p>0.05 significant

parametric.

Table 3 shows difference in the intervention group's median Hb before and after treatment Moringa leaves combination with Fe tablets (p=0.000, p<0.05). Table 4 shows difference in the control group's median Hb before and after giving Fe tablets (p=0.000, p<0.05).

Table 5 illustrates the analysis results using the Mann-Whitney test, which shows a difference in the median increase in Hb levels before and after the intervention in the intervention and control groups (p=0.000, p<0.05). So, there is an effect of giving Moringa leaves and a combination of Fe tablets to increase Hb in anemic pregnant women.

Discussion

The data reveals that most participants in both groups were within an age range considered safe for pregnancy: 90.0% in the intervention group and 86.7% in the control group. The optimal age for gestation is between 20 and 35 years, when the reproductive system is at its peak, thus minimizing pregnancy and delivery complications.[22] Sjahriani and Faridah's[23] study underscores this by showing that pregnant women below 20 years or above 35 are 1.8 times more likely to develop anemia than those aged between 20–35 years. The heightened risk of anemia in women of reproductive age is attributed to iron loss during menstruation and childbirth and increased iron demands during pregnancy.[24]

Education significantly impacts one's cognitive processes and information acquisition. A higher educational level facilitates better assimilation of health-related knowledge. Conversely, limited education among pregnant women can hinder efforts to address nutritional and family health issues, as emphasized by Hidayati and Andyarini.[25] Economic status also plays a crucial role in determining access to quality nutrition. While knowledge can be derived from education, personal experiences, media, and one's environment, well-educated pregnant women better understand iron deficiency anemia and its treatment, leading to better adherence to recommendations.[26,27]

Parity, the number of live births a woman has had, significantly influences the likelihood of anemia in pregnant women. The National Population and Family Planning Board defines parity as the total number of live births a woman has had during her reproductive years.[28] Multiple pregnancies heighten the risk of anemia. This is of concern as parity is a dominating factor for anemia during pregnancy. Women who have given birth more than twice or frequently face physical and mental demands. With every successive pregnancy, the woman's body requires more iron to support her well-being and fetal growth. However, repeated pregnancies can deplete the body's optimal iron stores, as the mother and fetus continually utilize the iron.[26] This is consistent with Purwandari et al.'s[27] study, which found a significant correlation between a woman's parity and her risk of anemia.

In the intervention group, a significant majority (86.7%) of the respondents were in their third trimester, while in the control group, half (50%) of the respondents were in their first trimester and experienced anemia. These findings agree with a study by Hidayati and Andyarini,[25] which identified a correlation between gestational age and the prevalence of anemia in pregnant women. Anemia can manifest in both the 1st and 3rd trimesters. Specifically, anemia is 20% in the first, 70% in the second, and 70% in the third. The iron requirement is minimal in the first trimester due to the absence of menstruation and slow fetal growth. However, from the second trimester onward, a woman's blood volume escalates by up to 35%, necessitating an equivalent of 450 mg of iron for red blood cell production, supporting the increased oxygen demand of the growing fetus. Furthermore, childbirth results in blood loss that requires an additional 300–350 mg of iron. Overall, by the time of delivery, a pregnant

woman's daily iron needs approximately double to around 40 mg, compared to when she is not pregnant.[29]

Pregnancy leads to increased blood volume, termed hypervolemia, which dilutes hemoglobin concentration. This phenomenon, known as hemodilution, is characterized by a 30–40% surge in plasma volume, an 18–30% increase in red blood cells, and a 19% increase in hemoglobin. If a mother's pre-pregnancy hemoglobin level is roughly 11g%, hemodilution can decrease to 9.5–10g%, resulting in anemia.[30]

The results showed that the average Hb of the respondents in the intervention group before treatment was 10.62 g/dl, and the standard deviation was 0.364. The average Hb of the control group respondents before treatment was 10.44 g/dl, and the standard deviation was 0.318. This increase in Hb occurs because Moringa leaves are rich in iron and other essential nutrients needed for iron metabolism. These results are in line with research by Shija et al.[31] on the effect of *Moringa oleifera* leaf powder supplementation on reducing anemia in children under two years in Kisarawe district, Tanzania. It was found that there was a change in the average hemoglobin (Hb) concentration, and the prevalence of anemia was compared between the two groups.

The results showed differences in the increase in Hb in anemic pregnant women before and after the intervention of giving Moringa leaves and a combination of Fe tables. It was higher in anemic pregnant women who only consumed Fe tablets. In line with the results of Fauziandari,[32] it showed that there was a significant difference between the levels before and after the administration of Moringa leaf extract. Moringa is an alternative in reducing anemia because Moringa contains seven times more vitamin C than oranges, ten times vitamin A from carrots, 17 times calcium from milk, 15 times more than bananas, 25 times iron from spinach. And nine times the protein of yogurt. Differences in Hb levels of respondents before and after being given Fe tablets in the control group.[12]

The study highlighted the positive impact of administering Moringa leaves with Fe tablets on elevating Hb levels in pregnant women. Moringa leaves are packed with nutrients, vitamins, minerals, antioxidants, and amino acids essential for expecting mothers. These findings echo the research of Shija et al.,[31] which demonstrated a notable shift in mean hemoglobin concentration and anemia prevalence between the intervention and control groups after the Moringa administration. Similarly, Rahmawati and Daryanti's[10] study documented the beneficial effect of Moringa leaf extract on augmenting hemoglobin levels in expectant mothers during their 2nd and 3rd trimesters, with $p<0.05$. Another study by Sindhu et al.[33] in Bangalore found that *Moringa oleifera* notably enhanced hemoglobin levels in anemic women.

Anemia remains a prevalent health challenge for pregnant women. Iron deficiency can impede brain development during this crucial phase and potentially damage cognitive growth. Furthermore, iron plays a pivotal role in forming myoglobin (an oxygen-carrying protein for muscles), collagen (a protein present in bones, cartilage, and connective tissues), and vital enzymes. Iron also fortifies the body's defense mechanisms.[12]

Moringa leaves, beneficial in modest and higher dosages, have proven particularly effective for anemic patients. These leaves are frequently incorporated as vegetables in diets. They house phytosterols, potent agents for boosting breast milk production in lactating mothers, and are also instrumental in addressing anemia issues in children and pregnant women. Moringa leaf extract is enriched with Fe 5.49 mg/100 g, sitosterol 1.15%/100 g, and stigmasterol 1.52%/100 g. The observed substantial increase in red and white blood cell counts upon Moringa leaf consumption emphasizes its potential as a dietary supplement. It holds promise as an alternative iron source, especially beneficial for anemic pregnant women.[13,34]

Conclusion

Findings indicated that the combination of Moringa leaves and Fe tablet significantly increased hemoglobin levels in pregnant women with anemia.

Conflict of Interest

The authors declare no conflicts of interest in this article.

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References

1. Ewusie JE, Ahiadeke C, Beyene J, Hamid JS. Prevalence of anemia among under-5 children in the Ghanaian population: estimates from the Ghana demographic and health survey. BMC Public Health. 2014;14:626.
2. Kementerian Kesehatan Republik Indonesia. Pedoman program pemberian pemantauan mutu tablet tambah darah untuk ibu hamil di wilayah program kesehatan dan gizi berbasis masyarakat. Jakarta: Kementerian Kesehatan Republik Indonesia; 2015.
3. Kementerian Kesehatan Republik Indonesia. Pedoman penatalaksanaan pemberian tablet tambah darah. Jakarta: Kementerian Kesehatan Republik Indonesia; 2015.
4. Direktorat Jenderal Kesehatan Masyarakat, Kementerian Kesehatan Republik Indonesia. Pedoman pemberian tablet tambah darah (TTD) bagi ibu hamil pada masa pandemi COVID-19 bagi tenaga kesehatan. Jakarta: Kementerian Kesehatan Republik Indonesia; 2020.
5. Badan Penelitian dan Pengembangan Kesehatan, Kementerian Kesehatan Republik Indonesia. Laporan nasional Riskesdas 2018. Jakarta: Lembaga Penerbit Badan Penelitian dan Pengembangan Kesehatan; 2019.
6. World Health Organization. The global prevalence of anaemia in 2011. Geneva: World Health Organization; 2015.
7. World Health Organization. WHO guideline on use of ferritin concentrations to assess iron status in individuals and populations. Geneva: World Health Organization; 2020.
8. Sivanganam S, Westa W. Gambaran tingkat kepatuhan ibu hamil mengkonsumsi tablet besi di wilayah kerja Puskesmas Sidemen tahun 2015. ISM. 2017;8(2):135–8.
9. Mutiarasari D. Hubungan status gizi dengan kejadian anemia pada ibu hamil di Puskesmas Tinggede. HTJ. 2019;5(2):42–8.
10. Rahmawati M, Daryanti MS. Pengaruh ekstrak daun kelor terhadap peningkatan kadar hemoglobin ibu hamil trimester 2 dan 3 di Puskesmas Semanu I [Internet]. Yogyakarta: Universitas 'Aisyiyah; 2017 [cited 2022 June 10]. Available from: http://digilib.unisayogya.ac.id/2776/1/NASKAH%20PUBLIKASI%20ibu%20mutia.pdf.
11. Oduro I, Ellis WO, Owusu D. Nutritional potential of two leafy vegetables: *Moringa oleifera* and *Ipomoea batatas* leaves. SRE. 2008;3(2):057–60.
12. Rani KC, Ekajayani NI, Darmasetiawan NK, Dewi ADR. Modul pelatihan: kandungan nutrisi tanaman kelor. Surabaya: Fakultas Farmasi Universitas Surabaya; 2019.
13. Kristina NN, Siti FS. Pemanfaatan tanaman kelor (*Moringa oleifera*) untuk meningkatkan produksi air susu ibu. War Penelit Pengemb Tanam Ind. 2014;20(3):26–9.
14. Khuzaimah A, Hadju V, As S, Abdullah N, Bahar B, Riu DS, et al. Effect of honey and *Moringa oleifera* leaf extracts supplementation for preventing DNA damage in passive smoking pregnancy. IJSBAR. 2015;24(1):138–45.
15. Sujatha BK, Patel P. *Moringa oleifera*—nature's gold. IJIR. 2017;3(5):1175–9.
16. Idohou-Dossou N, Diouf A, Gueye A, Guiro A, Wade S. Impact of daily consumption of Moringa (*Moringa oleifera*) dry leaf powder on iron status of Senegalese lactating women. AJFAND. 2011;11(4):4985–99.
17. Hanif F, Berawi KN. Literature review: daun kelor (*Moringa oleifera*) sebagai makanan sehat pelengkap nutrisi 1000 hari pertama kehidupan. J Kesehat. 2022;13(2):398–407.
18. Islam Z, Islam SMR, Hossen F, Mahtab-Ul-Islam K, Hasan MR, Karim R. *Moringa oleifera* is a prominent source of nutrients with potential health benefits. Int J Food Sci. 2021;2021:6627265.
19. Gopalakrishnan L, Doriya K, Kumar DS. *Moringa oleifera*: a review on nutritive importance and its medicinal application. Food Sci Hum Wellness. 2016;5(2):49–56.
20. Koul B, Chase N. *Moringa oleifera* Lam.: panacea to several maladies. J Chem Pharm Res. 2015;7(6):687–707.
21. Udikala M, Verma Y, Sushma S, Lal S. Phytonutrient and pharmacological significance of *Moringa oleifera*. Int J Life Sci Sci Res. 2017;3(5):1387–91.
22. Manuaba IAC, Manuaba IBGF, Manuaba IBG. Ilmu kebidanan, penyakit kandungan, dan KB untuk pendidikan bidan. 2nd editiion. Jakarta: EGC; 2012.
23. Sjahriani T, Faridah V. Faktor-faktor yang berhubungan dengan kejadian anemia pada

ibu hamil. JKM. 2019;5(2):106–15.
24. Abioye AI, Park S, Ripp K, McDonald EA, Kurtis JD, Wu H, et al. Anemia of inflammation during human pregnancy does not affect newborn iron endowment. J Nutr. 2018;148(3):427–36.
25. Hidayati I, Andyarini EN. Hubungan jumlah paritas dan umur kehamilan dengan kejadian anemia ibu. J Health Sci Prev. 2018;2(1):42–7.
26. Afriyanti D. Faktor risiko yang berhubungan dengan kejadian anemia pada ibu hamil di Kota Bukittinggi. Menara Ilmu. 2020;14(1):6–23.
27. Purwandari A, Lumy F, Polak F. Faktor-faktor yang berhubungan dengan kejadian anemia. J Ilm Bidan. 2016;4(1):62–8.
28. Badan Kependudukan dan Keluarga Berencana Nasional. Laporan kinerja BKKBN 2018 [Internet] Jakarta: Badan Kependudukan dan Keluarga Berencana; 2019 [2022 July 10]. Available from: https://www.bkkbn.go.id/storage/files/1/LAKIP%20BKKBN/LAKIP_BKKBN_2018.pdf.
29. Susiloningtyas I. Pemberian zat besi (Fe) dalam kehamilan. Maj Ilm Sultan Agung. 2012;50(128):73–99.
30. Wiknjosastro H. Ilmu kebidanan. Jakarta: Yayasan Bina Pustaka Sarwono Prawirohardjo; 2012.
31. Shija AE, Rumisha SF, Oriyo NM, Kilima SP, Massaga JJ. Effect of *Moringa oleifera* leaf powder supplementation on reducing anemia in children below two years in Kisarawe district, Tanzania. Food Sci Nutr. 2019;7(8):2584–94.
32. Fauziandari EN. Efektifitas ekstrak daun kelor terhadap peningkatan kadar hemoglobin pada remaja putri. JKKH. 2019;7(2):185–90.
33. Sindhu S, Mangala S, Sherry B. Efficacy of *Moringa oleifera* in treating iron deficiency anemia in women of reproductive age group. Int J Phytother Res. 2013;3(4):15–20.
34. Samuel SA, AO Francis AO, Onyinyechi UO, Ayomide O. Effects of *Moringa oleifera* leaf extract on red and white blood cells counts. IJCMPR. 2015;1(9):150–61.

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RESEARCH ARTICLE

Screening for Latent Tuberculosis Infection using Interferon-Gamma Release Assay Test among Healthcare Workers

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Abstract

Healthcare workers (HCWs) represent a significant demographic for screening latent tuberculosis infection (LTBI) due to their potential exposure to infectious patients. Tests based on immunology detection, such as the tuberculin skin test (TST) and the interferon-gamma release assay (IGRA), have been pivotal in diagnosing LTBI. The objective of this study was to evaluate the efficacy of the IGRA test in detecting LTBI compared to the TST among HCWs in an infectious disease hospital. In a cross-sectional study conducted in August 2019 at the Sulianti Saroso Infectious Disease Hospital, we examined 84 HCWs selected through consecutive sampling. Participants were assessed using questionnaires, and the IGRA and TST tests were performed. The findings revealed that 42 (50%) HCWs tested positive for LTBI based on the IGRA test. Most were female, aged 36–45 years, had direct exposure to TB patients, and had been in the healthcare profession for over a decade. The concordance between the TST and IGRA test, as indicated by a κ value, was 0.234. Furthermore, a significant correlation was observed between the incidence of LTBI and the duration of the healthcare profession (p=0.016). In conclusion, our research suggests that both TST and IGRA tests can effectively detect LTBI. The IGRA test had a higher positivity rate among HCWs with over ten years of service.

Keywords: Interferon-gamma release assay, latent tuberculosis infection

Introduction

Indonesia ranks third in global tuberculosis (TB) burden, following India and China.[1] Prioritizing TB management is imperative.[2] Early diagnosis and treatment of pulmonary TB are paramount to curtail TB transmission.[1,3] The risk of TB infection among healthcare workers (HCWs) consistently surpasses that of the general population across the globe.[4] Systematic reviews have revealed that the median estimated annual TB incidence among HCWs in regions with high TB incidence is 1,180/100,000 persons (IQR 91–3,222), in stark contrast to 311/100,000 persons (IQR 168–405) in the general population.[5] In light of this, the CDC guidelines advocate for a comprehensive TB screening program tailored for all HCWs.[4]

Mycobacterium tuberculosis infection can often be contained by the immune system, causing the bacterium to become dormant, leading to latent infection.[4] Latent tuberculosis infection (LTBI) can progress to an active infection or undergo reactivation. Hence, pinpointing and treating LTBI is crucial to minimize the emergence of new active infections within hospital environments.[6,7] Diagnosing LTBI presents a challenge, given the indeterminate bacterial count and the inherent difficulties of direct examination. Consequently, immunological assessments, such as the tuberculin test and the Interferon-gamma release assay (IGRA), have become the cornerstone for LTBI diagnosis.[8,9] This study seeks to evaluate the efficacy of the IGRA test in diagnosing LTBI, juxtaposed against the tuberculin test, among HCWs at the Sulianti Saroso Infectious Disease Hospital.

Methods

A cross-sectional investigation was undertaken at the Sulianti Saroso Infectious Disease Hospital (SSIDH), recognized as a center of excellence in managing infectious diseases, particularly tuberculosis. Eligible participants for the study were healthcare workers who underwent a medical evaluation in 2018, encompassing a tuberculin test and chest X-ray results. Moreover, participation was contingent upon their consent to undergo the interferon-gamma (IFN-γ) release assay (IGRA). We omitted those currently undergoing TB treatment or diagnosed with an active TB infection. The sample size was

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ascertained using the Lameshow formula, and 84 HCWs were accrued through a consecutive sampling technique.

Data accumulated from August to September 2019, the primary information using a designated questionnaire and the IGRA test. We extracted Secondary data from both the laboratory and radiology departments. Categorical variables were presented in percentages and frequencies, with a comparative analysis facilitated by either the chi-square or Fisher's exact test. To gauge the consistency between the two diagnostic methods, we employed the Kappa Test. Our study was sanctioned by the Health Research Ethics Committee of the Sulianti Saroso Infectious Disease Hospital, as evidenced by Ethical Clearance Number 17/38/XXXVI.10/VI/2019—informed written consent procured from all participants.

Results

Our study encapsulated 84 participants who satisfied the inclusion prerequisites. This cohort included both medical and non-medical professionals. The age bracket of these participants ranged from 19 to 56 years, with an average age of 34.58±8.16 years. Their tenure at the SSIDH spanned from 1 to 29 years, averaging 9.32±6.93 years. Table 1 delineates the detailed characteristics of the participants.

Table 1 Characteristic of Participants

Variables	n=84	%
Gender		
Male	22	26.2
Female	62	73.8
Education		
High school	8	9.5
College study	45	53.6
Undergraduate school	26	31.0
Graduate school	5	6.0
Duration of healthcare profession (years)		
≥10	40	47.6
<10	44	52.4

We amassed data, juxtaposing the IGRA and tuberculin test results (as depicted in Table 2). From the pool of 84 participants, 42 (50%) were flagged positive for LTBI using the IGRA test, whereas the tuberculin skin test (TST) only identified 14 as positive. In evaluating the concordance between the two testing methodologies, we derived a κ statistic of 0.234. Despite the modest κ value, it underscores that both the TST and IGRA tests can be deployed as viable detection tools for LTBI.

We delved into the risk factors associated with positive IGRA results (as detailed in Table 3). Our study substantiated that one's tenure in the healthcare profession emerged as the sole determinant correlated with a positive IGRA outcome ($p<0.05$). Contrarily, the bivariate analysis didn't discern any statistically significant disparity between LTBI and potential risk determinants such as age, gender, educational background, presence of a BCG scar, past instances of TB contact outside the hospital environment, or the utilization of respiratory protection like the N95 mask.

Discussion

In our study, the proportion of LTBI in HCWs at the infectious disease hospital was 50%. The precise prevalence of latent tuberculosis infection in Indonesia is challenging, potentially indicating a gap in awareness regarding the importance of screening and testing for LTBI in HCWs. Furthermore, specific guidelines need to be added on which groups should be targeted for these procedures in countries with high TB incidence countries. The World Health Organization (WHO) has suggested that screening for LTBI should primarily focus on adults in contact with TB patients.[8] Previous research has shown that the prevalence of LTBI among HCWs varies widely, ranging from 9% to 86%.[9–12] In high TB incidence countries, HCWs are at an increased risk of LTBI due to their repeated exposure

Table 2 Comparison between IGRA and Tuberculin Test

IGRA	Tuberculin Test			κ Score	p
	Positive	Negative	Total		
Positive	24	18	42	0.234	0.028
Negative	14	28	42		

Table 3 Risk Factors Related to Positive IGRA Result

Variables	IGRA Result			p
	Positive n=42 (%)	Negative n=42 (%)	Total n=84 (%)	
Age (years)				
≥35	27 (58.7)	19 (41.3)	46 (100)	0.125
<35	15 (39.5)	23 (60.5)	38 (100)	
Gender				
Male	11 (50)	11 (50)	22 (100)	1.000
Female	31 (50)	31 (50)	62 (100)	
Education				
High school	3 (37.5)	5 (62.5)	8 (100)	0.294
College study	20 (44.4)	25 (55.6)	45 (100)	
Undergraduate school	17 (65.4)	9 (34.6)	26 (100)	
Graduate school	2 (40)	3 (60)	5 (100)	
Duration of healthcare profession (years)				
≥10	26 (65)	14 (35)	40 (100)	0.016
<10	16 (36.4)	28 (63.6)	44 (100)	
BCG scar				
No	9 (39.1)	14 (60.9)	23 (100)	0.328
Yes	33 (54.1)	28 (45.9)	61 (100)	
History of contact				
Yes	28 (50.9)	27 (49.1)	55 (100)	1.000
No	14 (48.3)	15 (51.7)	29 (100)	
Use of respirator masks				
No*	27 (46.6)	31 (53.4)	58 (100)	0.479
Yes	15 (57.7)	11 (42.3)	26 (100)	

Note: *use of surgical masks

to TB cases and inconsistent implementation of control practices.[9] Compared to household exposures, HCWs are subjected to more frequent, albeit shorter, risk periods. Moreover, there's the concern that infected HCWs could become transmission vectors to patients in healthcare environments.[4]

LTBI is a persistent immune response to stimulation without clinically evident active TB. Clinicians should employ a combination of anamnesis, physical examinations, and chest X-rays to rule out active *Mycobacterium tuberculosis* infections. According to WHO guidelines, no single test is the gold standard for diagnosing LTBI.[8] Studies from the USA indicate that conversions (from negative to positive) and reversions (from positive to negative) were more frequently detected using the IGRA test as compared to the tuberculin skin test.[8,13] IGRA boasts several advantages, including needing a single sample (thus requiring only one patient visit), reduced cross-reactivity with non-tuberculosis bacteria and BCG vaccinations, rapid results, objectivity in measurements, and the lack of boosting.[14,15] IGRAs are pricier and more technically intricate than the TST.[8] We did not derive a definitive conclusion in our study, as the agreement between the TST and IGRA was a mere 0.234. Rafiza et al.,[16] in their Malaysian study, found results mirroring ours and linked these findings to the mandatory BCG vaccinations in their nation. Indonesia's vaccination program mandates BCG vaccinations for newborns. Cross-reactivity with other members of the *Mycobacterium* family could lead to false-positive TST results.[13,16]

Our study found no difference in the proportion of LTBI between older and younger HCWs. While some past research indicated that HCWs over 50 were a risk factor,[6,10,13,15] other studies found that health workers aged 30–39 were more susceptible.[7,16] This suggests that

age might be interlinked with other factors like contact history and employment duration.[13,15]

In our research, the only significant factor related to a positive IGRA test was the duration of the healthcare profession. Contrary to HCWs with an employment duration under ten years, our study indicated a higher positivity rate among those with over ten years of service (p=0,016). It aligns with findings from prior studies.[9,16] Both Apriani et al.[9] and Rafiza et al.,[16] in their systematic reviews, highlighted work duration as an independent occupational risk factor for LTBI, as measured by the IGRA test. They also noted other factors like the history of contact with TB patients and the average daily time of direct patient contact in previous years. Joshi et al.[13] documented a threefold rise in the prevalence of LTBI with employment exceeding ten years. Joshi et al.[13] highlighted that attending physicians were more susceptible than medical students and that an individual's risk of infection increased with their time in healthcare. It suggests that both age and years in healthcare mirror cumulative exposure to *M. tuberculosis*.

Our findings showed that consistent use of respirator masks (N95 masks) wasn't a standalone factor in preventing LTBI. However, in Thailand, a hospital's multi-pronged administrative control measures resulted in a significant decline (from 9.3% to 2.2%) in the annual incidence of LTBI among its HCWs. A similar administrative control study in Brazil across two hospitals underscored the importance of respiratory masks in successfully reducing the incidence of LTBI.[14] These cases emphasize the significance of employing personal protective equipment and maintaining strict administrative controls to thwart LTBI among HCWs.[13,14] Contrastingly, our data indicated that 57.7% of participants who wore a respirator mask tested positive on the IGRA test, suggesting the need for the correct and snug fit of the mask.

Our study does have limitations—the sample size needed to be more significant to represent the entire HCW community in the hospital. Additionally, potential biases exist in classifying risk factors, given that many HCWs had histories of working in various departments before their current roles. Also, the IGRA test and tuberculin test were performed separately. Given that we sourced Tuberculin test data from earlier medical check-up reports, and with TB's incubation period being under a month, biases are plausible. More rigorously designed studies are needed.

Conclusions

Our study indicates that both TST and IGRA tests can be employed for LTBI detection. The IGRA positivity rate was higher among HCWs with over a decade of service. Screening for latent tuberculosis infection is crucial to prevent transmission that could escalate into severe and potentially fatal outcomes for patients and HCWs. Yet, while screening, the cost-effectiveness must be weighed, and primary transmission triggers should be addressed.

Conflict of Interest

We declare no conflict of interest concerning this study.

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References

1. National Tuberkulosis Programme, World Health Organization. The Republic of Indonesia joint external monitoring mission for tuberculosis. Jakarta: Kementerian Kesehatan Republik Indonesia; 2020 [cited 2022 June 12]. Available from: https://tbindonesia.or.id/wp-content/uploads/2021/06/INDONESIA-JEMM-2020-Eng-1.pdf.
2. Erawati M, Andriany M. The prevalence and demographic risk factors for latent tuberculosis infection (LTBI) among healthcare workers in Semarang, Indonesia. J Multidiscip Healthc. 2020;13:197–206.
3. Muñoz L, Stagg HR, Abubakar I. Diagnosis and management of latent tuberculosis infection. Cold Spring Harb Perspect Med. 2015;5(11):a017830.
4. Bar-Meir M, Pariente G, Romem A, Wiener-Well Y. Identifying factors affecting latent tuberculosis treatment acceptance among healthcare workers: a retrospective analysis in a tertiary care center. BMJ Open. 2021;11(9):e047444.
5. Baussano I, Nunn P, Williams B, Pivetta E, Bugiani M, Scano F. Tuberculosis among

health care workers. Emerg Infect Dis. 2011;17(3):488–94.
6. Chen B, Gu H, Wang X, Wang F, Peng Y, Ge E, et al. Prevalence and determinants of latent tuberculosis infection among frontline tuberculosis healthcare workers in southeastern China: a multilevel analysis by individuals and health facilities. Int J Infect Dis. 2019;79:26–33.
7. Almufty HB, Abdulrahman IS, Merza MA. Latent tuberculosis infection among healthcare workers in Duhok province: from screening to prophylactic treatment. Trop Med Infect Dis. 2019;4(2):85.
8. World Health Organization. Latent tuberculosis infection: updated and consolidated guidelines for programmatic management. Geneva: World Health Organization; 2018.
9. Apriani L, McAllister S, Sharples K, Alisjahbana B, Ruslami R, Hill PC, et al. Latent tuberculosis infection in healthcare workers in low- and middle-income countries: an updated systematic review. Eur Respir J. 2019;53(4):1801789.
10. Almohaya A, Aldrees A, Akkielah L, Hashim AT, Almajid F, Binmoammar T, et al. Latent tuberculosis infection among healthcare workers using Quantiferon-TB Gold-Plus in a country with a low burden for tuberculosis: prevalence and risk factors. Ann Saudi Med. 2020;40(3):191–9.
11. Rosamarlina, Jahiroh, Lisdawati V, Hendrawati N, Sundari T, Rusli A, et al. Duration of work improves risk of latent tb infection in healthcare workers. Adv Health Sci Res. 2020;22:279–82.
12. Han SS, Lee SJ, Yim JJ, Song JH, Lee EH, Kang YA. Evaluation and treatment of latent tuberculosis infection among healthcare workers in Korea: a multicentre cohort analysis. PLoS One. 2019;14(9):e0222810.
13. Joshi R, Reingold AL, Menzies D, Pai M. Tuberculosis among healthcare workers in low- and middle-income countries: a systematic review. PLoS Med. 2006;3(12):e494.
14. Prado TND, Riley LW, Sanchez M, Fregona G, Nóbrega RLP, Possuelo LG, et al. Prevalence and risk factors for latent tuberculosis infection among primary health care workers in Brazil. Cad Saude Publica. 2017;33(12):e00154916.
15. Pai M, Gokhale K, Joshi R, Dogra S, Kalantri S, Mendiratta DK, et al. Mycobacterium tuberculosis infection in health care workers in rural India: comparison of a whole-blood interferon gamma assay with tuberculin skin testing. JAMA. 2005;293(22):2746–55.
16. Rafiza S, Rampal KG, Tahir A. Prevalence and risk factors of latent tuberculosis infection among health care workers in Malaysia. BMC Infect Dis. 2011;11:19.

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RESEARCH ARTICLE

Perception of Acupuncture Compared with Biomedicine among Health Practitioners

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Abstract

Compared with biomedicine held by medical experts, perspectives on acupuncture may impact how the general populace uses acupuncture. Therefore, research on the opinions of medical professionals regarding acupuncture therapy is crucial. This cross-sectional study was conducted from July to September 2022 using a questionnaire. The study participants are doctors and nurses from three clinics in Bali province who had at least one year of working experience and were willing to be research respondents. Descriptive analysis and multiple logistic regression are used to determine the participants' perceptions and predictors of their perception. Of 155 participants, the majority (64%) have a positive perception of acupuncture compared with biomedicine. Participants with prior acupuncture usage were 9.01 times more likely than those without previous acupuncture use to have positive perceptions of acupuncture compared to biomedicine (Adj OR=9.01; 95% CI; p=0.001). The results of this study show that acupuncture is seen positively by health practitioners as an effective modality, has few side effects, and is supported by science. Health practitioners' perceptions are affected by their prior acupuncture experience. It is crucial to understand how medical professionals feel about acupuncture. Medical professionals' opinion impacts every patient's decision to seek therapy because one of their duties as specialists is to offer patients clinical judgment, information, and suggestions.

Keywords: Acupuncture, biomedicine, complementary and alternative medicine, health practitioners, perceptions

Introduction

As patient-centered care, integrative medicine blends the utilization of biomedicine based on scientific evidence with complementary and alternative medicine (CAM) modalities, like acupuncture.[1] The World Health Organization has recognized acupuncture, one of traditional Chinese medicine's (TCM) main procedures, as a successful treatment for some ailments.[2]

Acupuncture therapy is a treatment therapy by inserting needles at mapped acupuncture points in the human body. Acupuncture points (acupoints) are electrically active cells with low electrical resistance and high electrical conductivity, so acupuncture points will conduct electricity faster than other cells.[3] Acupuncture is beneficial when used with conventional medicine to treat cancer, pediatric pain, and knee osteoarthritis. Improvements in physical and psychological symptoms, quality of life, and the doctor-patient relationship were all associated with these benefits. Reports have also been of improving immunological function, lowering medicine adverse effects, and taking charge of patient well-being.[4–7]

The World Health Organization (WHO) has acknowledged acupuncture's efficacy and urges the National Health Systems (NHS) to adopt it to alleviate the burden of some conventional therapies' high prices. It is also believed to be beneficial in response to the rise in chronic and degenerative illnesses.[8] Despite its numerous advantages, the viewpoint of health practitioners may affect the utilization of acupuncture by the general population.[9]

The general public's usage of acupuncture can be influenced by health professionals' perspectives, particularly in Indonesia. The view of health professionals plays a significant part in every patient's choice to seek treatment because one of their jobs as experts is to give clinical judgment, information, and recommendations to patients. Therefore, studying how healthcare professionals feel about acupuncture therapy is essential. Only a few studies have examined how health professionals think about acupuncture therapy.[8–10] Most studies just concentrated on the

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therapeutic effects of acupuncture.

This research is designed to overcome these gaps. This is the first study that examines the perceptions of health professionals related to acupuncture compared to biomedicine in Indonesia, especially in the province of Bali. The purpose of this research is to identify the perceptions of health workers about acupuncture compared to biomedicine.

Methods

This cross-sectional study used a three-part questionnaire from July to September 2022. The questionnaire was adapted and obtained permission from a previous study in Hong Kong by Chan et al.[11] The questionnaire was then translated by a certified translator and distributed via Google Forms to all respondents in three clinics. The first part of the questionnaire is demographic characteristics, the second part is previous experience with acupuncture, and the third part is the ten statements assessing the perceptions of acupuncture compared with biomedicine. All those ten items used a Likert scale of strongly agree, agree, neutral, disagree, and strongly disagree to assess the perception. The health practitioner's perception was classified into positive and negative categories.

The study population involved all doctors and nurses from three clinics in Bali province who had at least one year of working experience and were willing to be respondents. Doctors and nurses who did not fill out the questionnaire completely were excluded. SPSS version 26 was used to enter data and analysis. The characteristics of participants and perception of health practitioners were presented as frequency and proportion using descriptive statistics. The chi-square test analyzed the association between the independent and dependent variables, and the determinant factors affecting the health practitioners' perceptions of acupuncture compared with biomedicine were analyzed by multiple logistic regression.

This research was approved by the Committee of Research of the Institute of Technology and Health Bali with an ethical clearance letter number 04.0458/KEPITEKES-BALI/VII/2022.

Results

Based on the results of this study, from a total sample of 255 health workers consisting of doctors and nurses, 155 health workers were willing to fill out the questionnaires that had been distributed. The response rate of this study was 60.78%. Table 1 shows that among 155 health workers, the majority of participants are 29 years old and above (52.3%), female (67.7%), have an education level bachelor's or above (80.6%), have a job as a nurse (65.8%), never used acupuncture previously (75.5%) and never learned acupuncture once (80.0%). The Figure shows that, out of 155 health practitioners, most participants have a positive perception of acupuncture compared with biomedicine 64%. An analysis of related factors affecting the perceptions of acupuncture compared with biomedicine is presented in Table 2. Among several factors that were analyzed,

Table 1 General Characteristics of the Health Practitioner

Characteristics	n=155 (%)
Age (years)	
<29	74 (47.7)
≥29	81 (52.3)
Gender	
Male	50 (32.3)
Female	105 (67.7)
Education	
Diploma	30 (19.4)
Bachelor or above	125 (80.6)
Job	
Doctor	53 (34.2)
Nurse	102 (65.8)
Used acupuncture previously	
Yes	38 (24.5)
No	117 (75.5)
Learned acupuncture previously	
Yes	31 (20.0)
No	124 (80.0)

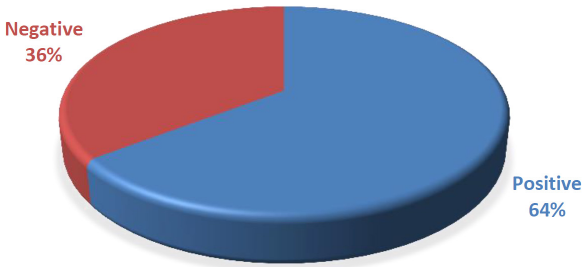

Figure Perceptions of the Health Practitioners of Acupuncture Compared with Biomedicine (n=155)

Table 2 Related Factors Affecting Participants' Perception of Acupuncture Compared with Biomedicine

Factors	Perception		χ^2	p
	Positive n=100 (%)	Negative n=55 (%)		
Age (years)				
≥29	44 (59.5)	30 (40.5)	1.58	0.20
<29	56 (69.1)	25 (30.9)		
Gender				
Male	31 (62)	19 (38)	0.20	0.65
Female	69 (65.7)	36 (34.3)		
Education				
Diploma	20 (66.7)	10 (33.3)	0.07	0.78
Bachelor or above	80 (64)	45 (36)		
Job				
Doctor	28 (52.8)	25 (47.2)	4.80	0.02*
Nurse	72 (70.6)	30 (29.4)		
Used acupuncture previously				
Yes	35 (92.1)	3 (7.9)	16.73	0.00*
No	65 (55.6)	52 (44.4)		
Learned acupuncture previously				
Yes	22 (71)	9 (29)		
No	78 (62.9)	46 (37.1)	0.70	0.40

Note: *p<0.05 significant

two factors related significantly to participants' perceptions of acupuncture compared with biomedicine: participants' jobs and experience of using acupuncture previously. Both showed significant relationships (p<0.05).

Furthermore, these factors relating to the participant's perception of acupuncture compared with biomedicine are analyzed by multiple linear regression, and the result is shown in Table 3. Participants who had experience using acupuncture previously were 9.01 times more likely to have positive perceptions of acupuncture compared with biomedicine than those who never used acupuncture before (Adj OR=9.01; 95% CI; p=0.001).

Discussion

This research found that most health practitioners (64%) perceived acupuncture more positively than biomedicine. This finding also aligns with a previous study where health professionals viewed acupuncture favorably. They stated that acupuncture completes conventional medicine shortages by providing preventive and individualistic treatments and a patient-centered approach.[8,9] The perceptions of acupuncture compared with biomedicine in this study included trust in acupuncture compared to biomedicine, the effectiveness of acupuncture, and side effects and costs.

Table 3 Factors Affecting Participants' Perception of Acupuncture Compared with Biomedicine

Characteristics	Adj OR	p
Job	0.49	0.06
Used acupuncture previously	9.01	0.001*

Note: multiple logistic regression analysis, *p<0.05 significant

Trust in acupuncture is assessed because this modality has a scientific basis and is under government regulation. Many studies have been conducted to give scientific evidence related to the therapeutic effect of acupuncture. According to a recent analysis of acupuncture systematic reviews, acupuncture had a moderate to considerable efficacy with medium to high confidence evidence in eight diseases or conditions out of the 77 ailments examined: improvement in functional communication of patients with post-stroke aphasia; relief of neck and shoulder pain; relief of myofascial pain; relief of fibromyalgia-related pain; relief of non-specific lower back pain; increased lactation success rate within 24 hours of delivery; reduction in the severity of vascular dementia symptoms; and improvement

of allergic rhinitis nasal symptoms.[12,13]

Besides the fact that this modality had been scientifically proven, trust in acupuncture was also earned because this therapy is under government regulation. Acupuncture practice is regulated under the Indonesian Ministry of Health decree No. 34 of 2018 regarding the licensing and training of acupuncture therapists. This regulation stated that acupuncture treatment can only be delivered by an acupuncturist with a minimum of three years of formal education. Acupuncture health professionals who hold practice licenses can be considered qualified and competent since they have completed at least three years of school, passed the competence exam, and participated in seminars and workshops to further their education.[14]

Related to a side effect of this modality, the fact that acupuncture experiences fewer adverse effects than pharmaceuticals is one of its benefits.[15] A review study also supports it shows that acupuncture for migraine prevention is just as effective as many of the presently prescribed pharmaceuticals and has fewer adverse effects.[16] Not only fewer side effects, but the mean costs of acupuncture treatment are also less than the cost of biomedicine in treating specific illnesses, for instance, chronic low back pain. Regarding usefulness and overall cost, acupuncture significantly differs from non-steroidal anti-inflammatory drugs (NSAIDs). The results show that acupuncture has a better cost-effectiveness ratio than NSAIDs, making it a viable alternative treatment for CLBP with a good cost-utility ratio.[17]

This current research reveals that among several related factors that might affect the perception of acupuncture compared with biomedicine, two factors are associated with participants' perception: job and acupuncture experience. However, based on logistic regression analysis, the most significant factor that affected the participants' perception was the experience of using acupuncture previously. It was found that health practitioners who used acupuncture once had a more positive perception of acupuncture than biomedicine.

People who have a positive perception are more likely to adopt healthy behaviors.[18] In this study, health practitioners with a positive perception of acupuncture compared with biomedicine might encourage them to integrate acupuncture into their practice. Acupuncture attitudes and practices have been influenced by a variety of circumstances, according to previous research. One of the main determinants is clinical or individual exposure to acupuncture therapy.[19] The individuals' prior acupuncture treatment experiences influenced their present acupuncture usage.[20] The use of acupuncture was also influenced by prior success with the treatment. According to a recent study from New Zealand, people who have successfully used acupuncture are more inclined to do so in the future for a comparable problem.[21] According to a different study, those who have had successful acupuncture treatments are more likely to benefit from acupuncture for chronic pain.[22]

According to the findings of this study, acupuncture was seen by the participants who have a positive perception as a modality that is efficient, has few adverse effects, and is validated by science. Previous acupuncture experience has become the predictor that affected the health practitioners' perception of acupuncture compared with biomedicine. Health professionals who have used acupuncture in the past have a higher favorable perception of it than those who have never tried it.

Conclusions

In conclusion, this study found that most health practitioners had a positive perception of acupuncture compared with biomedicine. Experience of using acupuncture previously is a factor that influences participants' perceptions. Health practitioners' perception of acupuncture is essential, affecting how patients use acupuncture.

Conflict of Interest

The authors affirm that they don't have any conflicts of interest in this research.

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References

1. Silver Highfield E, Longacre M, Chuang YH, Burgess JF Jr. Does acupuncture treatment affect utilization of other hospital services

at an urban safety-net hospital? J Altern Complement Med. 2016;22(4):323–7.
2. World Health Organization. Acupuncture: review and analysis of reports on controlled clinical trials. Geneva: World Health Organization; 2002.
3. Widowati R, Murti B, Pamungkasari EP. Efektivitas terapi akupunktur dan inframerah dalam menurunkan nyeri muskuloskeletal pada lanjut usia. IJM. 2017;2(1):41–51.
4. Feng S, Han M, Fan Y, Yang G, Liao Z, Liao W, et al. Acupuncture for the treatment of allergic rhinitis: a systematic review and meta-analysis. Am J Rhinol Allergy. 2015;29(1):57–62.
5. Zhou J, Fang L, Wu WY, He F, Zhang XL, Zhou X, et al. The effect of acupuncture on chemotherapy-associated gastrointestinal symptoms in gastric cancer. Curr Oncol. 2017;24(1):e1–5.
6. Landgren K, Hallström I. Effect of minimal acupuncture for infantile colic: a multicentre, three-armed, single-blind, randomized controlled trial (ACU-COL). Acupunct Med. 2017;35(3):171–9.
7. MacPherson H, Vickers A, Bland M, Torgerson D, Corbett M, Spackman E, et al. Acupuncture for chronic pain and depression in primary care: a programme of research. Southampton (UK): NIHR Journals Library; 2017.
8. García-Escamilla E, Rodríguez-Martín B. What can acupuncture bring to western medicine? The perspective of health professionals also trained in traditional Chinese medicine-based acupuncture. Eur J Integr Med. 2017;12:108–16.
9. García-Escamilla E, Rodríguez-Martín B, Martínez-Vizcaíno V. Integration of acupuncture into conventional medicine from health professionals' perspective: a thematic synthesis of qualitative studies. Health (London). 2016;20(2):176–200.
10. Zhang NM, Vesty G, Zheng Z. Healthcare professionals' attitudes to integration of acupuncture in western medicine: a mixed-method systematic review. Pain Manag Nurs. 2021;22(6):684–93.
11. Chan K, Tsang L, Fung TKF. Attitudes toward acupuncture in Hong Kong. Int J Pharm Healthc Mark. 2015;9(2):158–74.
12. Lu L, Zhang Y, Ge S, Wen H, Tang X, Zeng JC, et al. Evidence mapping and overview of systematic reviews of the effects of acupuncture therapies. BMJ Open. 2022;12(6):e056803.
13. Lu L, Zhang Y, Tang X, Ge S, Wen H, Zeng J, et al. Evidence on acupuncture therapies is underused in clinical practice and health policy. BMJ. 2022;376: e067475.
14. Wijanto C, Tamtomo D, Joebagyo H. Recognizing acupuncture therapist and services. J Health Policy Manag. 2019;4(2):128–38.
15. Mortara L, Coco G, Pozzi C. Biomedicine and traditional Chinese medicine: a fruitful scientific and cultural interaction. Acta Biomed. 2022;93(1):e2022070.
16. Zhang N, Houle T, Hindiyeh N, Aurora SK. Systematic review: acupuncture vs standard pharmacological therapy for migraine prevention. Headache. 2020;60(2):309–17.
17. Toroski M, Nikfar S, Mojahedian MM, Ayati MH. Comparison of the cost-utility analysis of electroacupuncture and nonsteroidal antiinflammatory drugs in the treatment of chronic low back pain. J Acupunct Meridian Stud. 2018;11(2):62–6.
18. Dananjaya R, Wisaksana R, Sudjana P, Iskandar S. Perception of health workers on preventing COVID-19 transmission behavior based on work area and exposure. GMHC. 2022;10(2):144–51.
19. Chan K, Siu JYM, Fung TK. Perception of acupuncture among users and nonusers. Health Mark Q. 2016;33(1):78–93.
20. Patel A, Chen Y. Patients' reasons for seeking traditional Chinese medicine: a qualitative study. J Prim Health Care. 2018;10(4):338–42.
21. Patel A, Toossi V. Traditional Chinese medicine practitioners in New Zealand: differences associated with being a practitioner in New Zealand compared to China. N Z Med J. 2016;129(1444):35–42.
22. Witt CM, Schützler L, Lüdtke R, Wegscheider K, Willich SN. Patient characteristics and variation in treatment outcomes which patients benefit most from acupuncture for chronic pain? Clin J Pain. 2011;27(6):550–5.

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RESEARCH ARTICLE

Diphtheria Outbreak among Children in 2017–2018: a Single Centre Study in Indonesia

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Abstract

Diphtheria is an acute infectious disease caused by the bacterium *Corynebacterium diphtheriae*. Accurate and prompt diagnosis is essential for effective case management, predicting disease prognosis, preventing complications, and ensuring cost-effective medical intervention. This study aimed to assess the variety of clinical symptoms exhibited by pediatric diphtheria cases during an outbreak. An observational cross-sectional study was conducted using data from the medical records of pediatric diphtheria cases at Sulianti Saroso Infectious Disease Hospital from November 1, 2017, to February 28, 2018. The study involved 202 cases, and statistical analysis was performed using the chi-square test. Out of the 202 cases, 58.4% were male. Age distribution was <1 year: 7.4%, 1–2 years: 3.5%, >2–5 years: 24.8%, >5–12 years: 45.5%, and >12 years: 18.8%. Anamnestic findings revealed the presence of fever in 88.1% of patients, pain upon swallowing in 73.3%, and cough in 55.4%. Clinically, every patient exhibited pseudomembrane formations. Other findings included bilateral tonsillar involvement in 53%, lymphadenopathy in 40.1%, bullneck in 17.8%, and snoring in 7.9%. Four significant variables were associated with the diphtheria diagnosis: fever, snoring, bullneck, and snoring ($p<0.05$) respectively. Clinical signs and symptoms are pivotal in establishing a diphtheria diagnosis in pediatric cases.

Keywords: Children, diphtheria, outbreak

Introduction

Diphtheria is an acute disease primarily affecting the upper respiratory tract, instigated by the bacterium *Corynebacterium diphtheriae*. Remarkably, this bacterium can subsist in dust or the ambient air for durations extending to six months, enabling its propagation via droplets or direct contact.[1,2] Clinical manifestations typically encompass fever, malaise, cough, and painful swallowing. A prominent clinical feature observed upon examination is the formation of a pseudomembrane.[3,4] The criticality of laboratory investigations, such as culture or polymerase chain reaction (PCR), cannot be understated, as they detect the toxic strains that not only assail the respiratory tract, skin, and eyes but can also remain as asymptomatic carriers.[5,6] Alarmingly, toxins from 54 out of the 57 identified bacterial strains mandate prompt diagnostic and laboratory interventions to stave off dire outcomes such as cardiac failures or even sudden death.[5,7,8]

According to the World Health Organization (WHO) data, Indonesia ranks second globally, only surpassed by India, in the number of diphtheria cases and is the frontrunner amongst ASEAN countries.[9,10] 2011, there were 806 reported cases, yielding a case fatality rate (CFR) of 4.71%. In the subsequent year we showed up to 1,192 cases, with a CFR pegged at 6.38%. However, 2013 marked a reduction with 778 cases and a CFR of 5.01%. In 2017, diphtheria outbreaks spanned 170 districts/cities across 30 provinces, accounting for 954 cases and 44 deaths. The data from the onset of 2018 until January 9 indicates 14 cases spread across 11 regencies/cities in four provinces (DKI Jakarta, Banten, West Java, and Lampung), with zero mortality. The Sulianti Saroso Infectious Disease Hospital's inpatient data over the previous three years suggests a rising trend in diphtheria cases.[11,12]

Although all strains of *C. diphtheria* can instigate both endemic and epidemic diphtheria, the mitis strains typically demonstrate reduced toxicity and result in milder symptomatic presentations. Genesis of diphtheria symptoms

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can be attributed to localized inflammation of the skin or airways coupled with the systemic ramifications of exotoxins. These toxins instigate the formation of pseudomembranes—a conglomerate of fibrin, leukocytes, erythrocytes, epithelial cells, and the causative organisms—which adhere tenaciously to the underlying tissues. The ensuing pseudomembranes and concomitant tissue edema can potentially lead to airway obstructions. Toxins disseminating within the body can compromise various organs, with the heart, nerves, and kidneys particularly vulnerable. The toxin's synthesis is contingent upon lysogenic bacteriophages that house the genes responsible for the toxin's encoding. This toxin comprises three domains: one within fragment A, the catalyst unit, and two within fragment B, designated for receptor binding and insertion. Intracellularly active, the toxin precipitates cellular death.[13] Initial diphtheria presentations are typically ambiguous, marked by symptoms such as low-grade fevers, vomiting, coughs, and sore throats. Physical examinations may reveal cervical lymphadenopathy and pharyngeal erythema, which can evolve into a grayish-white exudate before culminating in pseudomembrane formation. A hallmark sign is the pseudomembrane's dirty, grayish-white appearance, which can lead to blockages due to inflamed tonsils, extending to adjacent structures, presenting the "bull neck" appearance. Dislodging these membranes is challenging, often accompanied by bleeding.[2,14]

Rapid diagnosis should be immediately based on clinical symptoms and laboratory (culture or PCR) for early treatment. The treatment used a specific antitoxin and antibiotic. The variety of symptoms that appear varies and sometimes is not typical. Pseudomembranes, as the primary symptom, can be small and do not bleed easily but give the results of culture and elective tests as toxigenic diphtheria. The discrepancy between the patient's clinical theory and therapy causes information about the clinical symptoms of diphtheria, which still needs to be improved and results in optimal case management. Therefore, this study aims to evaluate the diversity of clinical signs of diphtheria cases in pediatrics found during outbreaks.

Methods

This research is an observational study with a cross-sectional study design. The data was taken from patients' medical records diagnosed with diphtheria and diphtheria suspects from November 1, 2017, to February 28, 2018, at Sulianti Saroso Infectious Disease Hospital, which is a reference hospital for new emerging diseases in Indonesia.

Based on WHO guidelines, the clinical case definition in diphtheria is laryngitis, pharyngitis, or tonsillitis with pseudomembranes in the tonsils, pharynx, and nose. Isolation of *C. diphtheriae* from throat swabs is a laboratory diagnostic criterion.[8] The diagnosis of diphtheria is based on history, physical examination, and investigations. Based on the 2017 WHO guidelines explain that the diagnostic criteria for probable diphtheria include laryngitis, pharyngitis, tonsillitis, membranes in the nose, tonsils, and larynx or severe lymphadenopathy. A supporting examination of electrification and culture supports a confirmed diagnosis. The criteria for diphtheria for surveillance purposes are divided into suspect, probable, and confirmed diagnoses. Determination of early diagnosis is needed to determine the accuracy and speed of case management, disease prognosis, and prevent complications and other benefits, namely so that the costs incurred are practical and efficient.11 Patients with suspected diphtheria should receive anti-diphtheria serum (ADS) and antibiotics at treatment. The determination of the provision of ADS is based on the history and clinical symptoms reported by the doctor in charge of service (DPJP) to a team of experts appointed by the Ministry of Health. This study recorded as many as 202 medical records of patients who met the criteria and were diagnosed with suspected diphtheria from November 1, 2017, to February 28, 2018, meeting the ICD 10 criteria (A36, A36.0, A36.1, A36.2, A36.3, A36.8, A36.9).

The diagnosis of diphtheria is made clinically based on history, physical examination, and culture results. Inclusion criteria were pediatric patients <18 years diagnosed with suspected diphtheria, clinical diphtheria, or confirmed diphtheria. The sample size in this study was 202 samples. After the analysis, the power study was 71.70%, with a 95% confidence interval.

This study uses a questionnaire to record the data in the case medical records. The research questionnaire consisted of 3 parts: the anamnesis results, clinical symptoms, and signs. Questions about anamnesis data included age, gender,

education, place of residence, length of illness before hospital admission, immunization history, and contact history. Furthermore, questions about symptoms include weight, low fever, sore throat, runny nose, cough, hoarseness, snoring, nausea and vomiting, chest pain, shortness of breath, and palpitations. Clinical signs studied in this questionnaire such as temperature, pseudo membrane, membrane location, concha hyperemesis, pharyngeal hyperemesis, tonsil hypertrophy, lymphadenopathy, site of lymphadenopathy, "bull neck", snore, heart murmur, dysrhythmia, tachycardia, bradycardia, distant heart sounds. The researcher and the team recorded all the information needed in the questionnaire. They validated the answers in the medical record through the doctor or nurse on duty for the case. This study uses simple data analysis such as frequency and proportion to describe the patient's clinical condition, clinical signs, and demographic characteristics. The chi-square test determines the factors associated with clinical symptoms of diphtheria cases. This study received an ethical review (exempt) from the Health Research Ethics Committee of the Sulianti Saroso Infectious Disease Hospital Number 26/XXXVIII.10/VII/2018.

Results

This study involved as many as 202 (60%) respondents of child diphtheria in the period (November 2017–February 2018) diphtheria outbreaks in Indonesia in 2018 from a total of 337 cases in 2016–2018 (Figure). A total of 126 (63.4%) patients were diagnosed with clinical siphtheria, 12 (5.9%) were confirmed diphtheria patients, and 64 (30.7%) were non-diphtheria patients. In the period of diphtheria outbreaks, most cases were dominated by males, with 118 cases (58.4%) and 84 (41.6%) female cases. Table 1 shows that more than half of the respondents were from DKI Jakarta (58.9%). Most of the 87 (69.0%) clinical diphtheria patients came to the hospital three days after feeling sick symptoms—likewise, 9 (75.0%) patients with confirmed diphtheria. Most of the data/information regarding the contact history of patients with diphtheria before illness, 109 (86.5%) clinical diphtheria patients and 9 (75.0%) confirmed diphtheria patients.

Table 2 showed that most patients aged <1 year received complete immunizations according to age, namely 7 (46.7%) patients. Of 7 patients aged 1–2 years, most of them received complete immunizations 3 (42.8%); from 50 patients aged >2, Most of those five years old received incomplete immunization, namely 61 (66.3%), and of 38 patients aged >12 years, most of them received incomplete vaccination, 22 (57.9%). Table 3 showed a relationship between fever symptoms and the diagnosis of diphtheria (p=0.040). Meanwhile, there was no relationship between symptoms of shortness of breath, chest pain, and a diagnosis of diphtheria (p=0.565; 1,000, respectively). Sign of suspected diphtheria

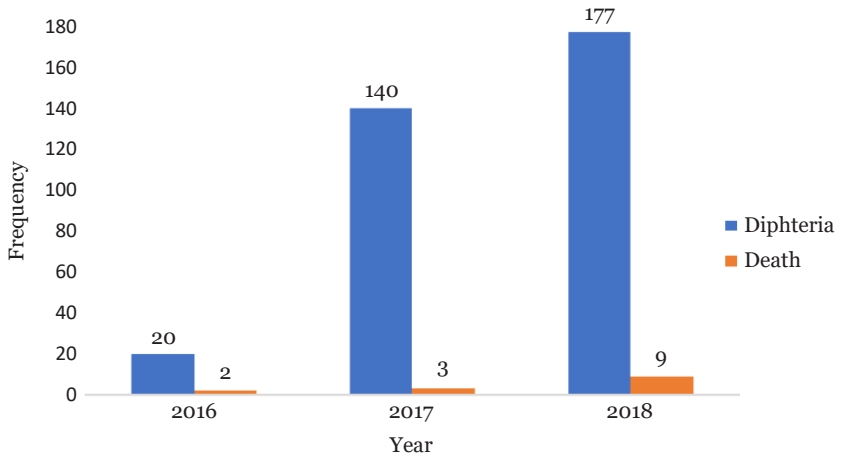

Figure Diphtheria Outbreak among Children Patients in 2016–2018 at Sulianti Saroso Infectious Disease Hospital

Table 1 Characteristics of Suspect Diphtheria Children

Variables	Suspect Diphtheria			Non-diphtheria n=64 (%)
	Clinical Diphtheria n=126 (%)	Confirm n=12 (%)	Total n=202 (%)	
Demographic				
Sex				
Male	76 (60.3)	4 (33.3)	118 (58.4)	38 (59.4)
Female	50 (39.7)	8 (66.7)	84 (41.6)	26 (40.6)
Domicile				
DKI Jakarta	72 (57.1)	8 (66.7)	119 (58.9)	39 (60.9)
Outside DKI Jakarta	54 (42.9)	4 (33.3)	83 (41.1)	25 (39.1)
History of contact				
Yes	1 (0.8)	0 (0)	5 (2.5)	4 (6.2)
No	125 (99.2)	12 (100)	197 (97.5)	60 (93.8)
Clinical onset (days)				
<3	39 (31.0)	3 (25.0)	66 (32.7)	24 (37.5)
≥3	87 (69,0)	9 (75.0)	136 (67.3)	40 (62.5)

Table 2 History of Vaccination of Suspected Diphtheria Cases

Age (Years)	History of Vaccination			
	Unvaccinated Children n=9 (%)	No Data n=42 (%)	Fully Vaccinated Children based on Age n=35 (%)	Partially Vaccinated Children n=116 (%)
<1	2 (13.3)	2 (13.3)	7 (46.7)	4 (26.7)
1–2	1 (14.3)	2 (28.6)	3 (42.8)	1 (14.3)
>2–5	3 (6.0)	10 (20.0)	9 (18.0)	28 (56.0)
>5–12	3 (3.3)	14 (15.2)	14 (15.2)	61 (66.3)
>12	0 (0)	14 (36.8)	2 (5.3)	22 (57.9)

in children is shown in Table 4. There was a relationship between the "bull neck", snore, and the diagnosis of diphtheria (p=0.011; 0.023, respectively).

Discussion

This study showed that among the 202 cases, 5–12 years were the most common age group, namely 92 (45.5%) patients. Patients aged 5–12 years with clinical diphtheria were 46.8%, and 58.3% with confirmed diphtheria. A study in Delhi found a similar picture, with 93% of patients aged less than nine years.[15,16] Meanwhile, reports on outbreaks of research in the USA and ex-Soviet countries found an epidemiological shift in the age of diphtheria sufferers from pre-school age to school age and adulthood which illustrates the low level of antibodies in this age group, so that during outbreaks, this group becomes susceptible to diphtheria.[17] In contrast to the study in Surabaya, which stated that most diphtheria patients were under the age of 5 years, namely 61.5%, followed by ages 5–10 years, as many as 31.8% and the rest at the age of more than ten years.[18] Regarding domicile, most clinical and confirmed diphtheria patients reside in Jakarta, while those outside Jakarta are satellite cities of the capital city (Bekasi, Depok, Bogor, and Tangerang).

Most patients aged 2–5 years, >5–12 years, and >12 years had incomplete immunization status. This case of no data could be caused by not being asked in the anamnesis or not remembering the child's immunization history. Incomplete immunization is generally due to not repeating immunization after 12 months of age. DPT repeat immunization only entered the national program in 2014, so most patients over the age of 5 years will have incomplete immunizations if they are

Table 3 Symptoms of Suspected Diphtheria in Children

Variables	Diagnosis		Total n=202 (%)	p	OR (95% CI)
	Diphtheria* n=138 (%)	Non-diphtheria n=64 (%)			
Fever					
Yes	126 (70.8)	52 (29.2)	178 (100)	0.040**	2.42 (1.02–5.74)
No	12 (50.0)	12 (50.0)	24 (100)		
Painful swallow					
Yes	106 (71.6)	42 (28.2)	148 (100)	0.095	1.74 (0.91–3.32)
No	32 (59.3)	22 (40.7)	54 (100)		
Dysfagia					
Yes	38 (73.1)	14 (26.9)	52 (100)	0.392	1.36 (0.67–2.73)
No	100 (66.7)	50 (33.3)	150 (100)		
Rhinopharyngitis					
Yes	46 (65.7)	24 (34.3)	70 (100)	0.563	0.83 (0.45–1.55)
No	92 (69.7)	40 (30.3)	132 (100)		
Cough					
Yes	82 (73.2)	30 (26.8)	112 (100)	0.095	1.66 (0.91–3.02)
No	56 (62.2)	34 (37.8)	90 (100)		
Hoarse					
Yes	5 (55.6)	4 (44.4)	9 (100)	0.468[a]	0.56 (0.15–2.17)
No	133 (68.9)	60 (31.1)	193 (100)		
Dyspnea					
Yes	9 (60.0)	6 (40.0)	15 (100)	0.565[a]	0.67 (0.23–1.98)
No	129 (69.0)	58 (31.0)	187 (100)		
Chest pain					
Yes	3 (75.0)	1 (25.0)	4 (100)	1.000[a]	–
No	135 (68.2)	63 (31.8)	198 (100)		
Pounding chest					
Yes	1 (100)	0 (0)	1 (100)	1.000[a]	–
No	137 (68.2)	64 (31.8)	201 (100)		
Nausea/vomiting					
Yes	19 (70.4)	8 (29.6)	27 (100)	0.805	1.12 (0.46–2.71)
No	119 (68.0)	56 (32.0)	175 (100)		

Note: *clinical diphtheria and confirm cases, **p<0.05 significant, [a]Fisher's exact

Table 4 Signs of Suspected Diphtheria in Children

Variables	Diagnosis		Total n=202 (%)	p	OR (95% CI)
	Diphtheria* n=138 (%)	Non-diphtheria n=64 (%)			
Lymphadenopathy					
Yes	60 (74.1)	21 (25.9)	81 (100)	0.150	1.57 (0.85–2.93)
No	78 (64.5)	43 (35.5)	121 (100)		
Bullneck					
Yes	31 (86.1)	5 (13.9)	36 (100)	0.011**	3.42 (1.26–9.26)
No	107 (64.5)	59 (35.5)	166 (100)		
Snore					
Yes	15 (93.8)	1 (6.3)	16 (100)	0.023**	7.68 (0.99–59.49)
No	123 (66.1)	63 (33.9)	186 (100)		

Note: *clinical diphtheria and confirm cases, **p<0.05 significant

immunized at *posyandu*, *puskesmas*, or schools.

These results are similar to the diphtheria outbreak in Kolkata, India. Outbreaks caused by low immunization coverage at age replicates.[19,20] A history of contact with diphtheria sufferers was experienced in 2% of cases. This may be because most diphtheria carriers are asymptomatic.[21] In fact, these data are needed to support the diagnosis of patients. All household contacts or people who have had contact with diphtheria patients should be monitored closely during the incubation period, which is seven days.[22,23] Diphtheria can be prevented by immunization, and immunization has been a national program since 1976.[24] Diphtheria immunization is given five times between the ages of 6 weeks to 6 years: 3 times before the period of 12 months as a basic immunization and repeated at the age of 18–24 months, and 5–6 years after that every ten years. The coverage of DPT basic immunization in Jakarta based on *Riskesdas* 2013 is 79.1%. The highest is between Banten (63.3%) and West Java (71.5%) which are directly adjacent.[25]

The interval between the clinical onset and hospitalization was ≥3 days in both clinical diphtheria and confirmed diphtheria cases. Most of the data are unavailable in clinical and confirmed cases of diphtheria. This may be because most diphtheria carriers are asymptomatic,[20–22,26] so patients do not realize that people around them can transmit these germs. However, the data is essential to support the diagnosis of patients.

The anamnesis results showed that the most common patient complaint was fever, which was significantly associated with the diagnosis of diphtheria ($p<0.05$). As with a study in Andhra Pradesh, India, Meera found all patients diagnosed with diphtheria complained of fever. Most diphtheria patients feel pain when swallowing.[27–29] Sore throat, runny nose, hoarseness, shortness of breath, chest pain, palpitations, nausea, and vomiting are rarely found in cases of diphtheria. In contrast to a study in Andhra Pradesh, India Meera, most diphtheria patients experience sore throat, runny nose, nausea, and vomiting.[28] These symptoms are not specific because they are also found in non-diphtheria disease. Test results ($p>0.05$). In contrast to cough, which diphtheria patients mostly feel. The chi-square test results showed that the results were insignificant ($p>0.05$). However, these symptoms are variations that each diphtheria patient feels.

Clinical signs found that all patients suspected of diphtheria had pseudomembranes. It was found in all diphtheria patients, with the most locations in the tonsils. Bleeding membranes were only found in 6 cases, in contrast to the basic concept that pseudomembranes in diphtheria bleed easily. As many as 18.8% of cases also showed the form of a membrane in the form of detritus, not thick plaque. It may be due to the early phase of the disease. Three out of 18.8% cases with detritus membrane form also gave confirmatory results for diphtheria examination, so caution must be exercised in diagnosing diphtheria based on the membrane shape.[30]

Lymphadenopathy is found in most diphtheria patients, while there was no relationship between lymphadenopathy and the diagnosis of diphtheria ($p>0.05$). "Bull neck" and snore are primarily found in diphtheria patients. "Bull neck" is one of the complications of diphtheria, so these symptoms can help establish a clinical diagnosis.[28,31,32] The same applies to snore, which occurs due to the "bull neck" experienced by diphtheria patients. The chi-square test results obtained $p<0.05$, so it can be concluded that "bull neck" or snore patients as symptoms of diphtheria. Research in Andhra Pradesh, India Meera, proved that most "bull necks" were found in patients diagnosed with diphtheria.[28] Meanwhile, snore was only found in patients diagnosed with diphtheria. Soft tissue edema (pseudomembrane) and enlarged lymph nodes (lymphadenopathy) can cause a "bull neck." This condition will block the airway, which is characterized by the presence of snore.[5,15]

Conclusions

Diphtheria in pediatric patients often presents with fever as a notable symptom. Furthermore, complications such as "bull neck" and snore are significant indicators and are closely linked to the diagnosis of diphtheria. These clinical manifestations can aid healthcare professionals in promptly identifying and managing diphtheria cases, especially during outbreaks. Recognizing these symptoms early on is crucial for timely intervention and reducing potential complications associated with this infectious disease.

Conflict of Interest

We declare no conflict of interest in this study.

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References

1. Soedarmo SSP, Garna H, Hadinegoro SRS, Satari HI, editors. Buku ajar infeksi dan pediatri tropis. 2nd edition. Jakarta: Badan Penerbit Ikatan Dokter Anak Indonesia; 2015.
2. Hadfield TL, McEvoy P, Polotsky Y, Tzinserling VA, Yakovlev AA. The pathology of Diphtheria. J Infect Dis. 2000;181(Suppl 1):S116–20.
3. Asher MI, Grant CC. Infections of the upper respiratory tract. In: Taussig LM, Landau LI, editors. Pediatric Respiratory Medicine. 2nd edition. Philadelphia: Mosby Elsevier; 2009. p. 453–80.
4. Tanz RR. Sore throat. In: Kliegman RM, Lye PS, Bordini BJ, Toth H, Basel D, editors. Nelson pediatric symptom-based diagnosis. Philadelphia: Elsevier; 2018. p. 1–14.e2.
5. Hartoyo E. Difteri pada anak. Sari Pediatr. 2018;19(5):300–6.
6. Williams MM, Waller JL, Aneke JS, Weigand MR, Diaz MH, Bowden KE, et al. Detection and characterization of diphtheria toxin gene-bearing Corynebacterium species through a new real-time PCR assay. J Clin Microbiol. 2020;58(10):e00639–20.
7. World Health Organization. Diphtheria: WHO laboratory manual for the diagnosis of diphtheria and other related infections [Internet]. Geneva: World Health Organization; 2010 [cited 2022 March 12]. Available from: https://cdn.who.int/media/docs/default-source/immunization/diphtheria_lab_manual_v2.pdf.
8. Gillespie SH, Hawkey PM. Principles and practice of clinical bacteriology. 2nd ed. Chichester: John Wiley & Sons; 2006.
9. Clarke KEN, MacNeil A, Hadler S, Scott C, Tiwari TSP, Cherian T. Global epidemiology of diphtheria, 2000–2017. Emerg Infect Dis. 2019;25(10):1834–42.
10. Clarke KEN. Review of the epidemiology of diphtheria, 2000–2016. Atlanta: Centers for Disease Control and Prevention; 2017 [cited 2022 May 6]. Available from: https://terrance.who.int/mediacentre/data/sage/SAGE_Docs_Ppt_Apr2017/10_session_diptheria/Apr2017_session10_diphtheria_2000-2016.pdf.
11. Kementerian Kesehatan Republik Indonesia. Pemerintah optimis KLB difteri bisa teratasi [Internet]. Jakarta: Kementerian Kesehatan Republik Indonesia; 2018 [cited 2022 May 6]. Available from: https://www.kemkes.go.id/article/view/18011500004/pemerintah-optimis-klb-difteri-bisa-teratasi.html.
12. Epidemiology Surveillance Unit RSPI Prof. Dr. Sulianti Saroso. Diphtheria surveillance report. Jakarta: RSPI Prof. Dr. Sulianti Saroso; 2018.
13. Parveen S, Bishai WR, Murphy JR. *Corynebacterium diphtheriae*: diphtheria toxin, the tox operon and its regulation by Fe^{2+}-activation of apo-DtxR. Microbiol Spectr. 2019;7(4):gpp3-0063-2019.
14. Sharma K, Das S, Goswami A. A study on acute membranous tonsillitis, its different etiologies and its clinical presentation in a tertiary referral centre. Indian J Otolaryngol Head Neck Surg. 2022;74(Suppl 3):4543–8.
15. Sharma NC, Banavaliker JN, Ranjan R, Kumar R. Bacteriological and epidemiological characteristics of diphtheria cases in and around Delhi-a retrospective study. Indian J Med Res. 2007;126(6):545–52.
16. Murhekar M. Epidemiology of diphtheria in India, 1996–2016: implications for prevention and control. Am J Trop Med Hyg. 2017;97(2):313–8.
17. Lumio J. Studies on the epidemiology and clinical characteristics of diphtheria during the Russian epidemic of the 1990s [Internet]. Helsinky: University of Tampere; 2003 [cited 2022 March 23]. Available from: https://trepo.tuni.fi/bitstream/handle/10024/67110/951-44-5750-1.pdf.
18. Puspitasari D, Ernawati, Husada D. Gambaran klinis penderita difteri anak di RSUD dr. Soetomo. J Ners. 2012;7(2):136–41.

19. Kole AK, Roy R, Kar SS, Chanda D. Outcomes of respiratory diphtheria in a tertiary referral infectious disease hospital. Indian J Med Sci. 2010;64(8):373–7.
20. Truelove SA, Keegan LT, Moss WJ, Chaisson LH, Macher E, Azman AS, et al. Clinical and epidemiological aspects of diphtheria: a systematic review and pooled analysis. Clin Infect Dis. 2020;71(1):89–97.
21. Wagner KS, White JM, Crowcroft NS, De Martin S, Mann G, Efstratiou A. Diphtheria in the United Kingdom, 1986–2008: the increasing role of *Corynebacterium ulcerans*. Epidemiol Infect. 2010;138(11):1519–30.
22. World Health Organization. Diphtheria [Internet]. Geneva: World Health Organization; 2018 [cited 2022 January 25]. Available from: https://cdn.who.int/media/docs/default-source/immunization/vpd_surveillance/vpd-surveillance-standards-publication/who-surveillancevaccinepreventable-04-diphtheria-r2.pdf.
23. Centers for Disease Control and Prevention. Diphtheria [Internet]. Atlanta: Centers for Disease Control and Prevention; 2020 [cited 2022 March 23]. Available from: https://www.cdc.gov/diphtheria/index.html.
24. Pusat Pendidikan dan Pelatihan Tenaga Kesehatan, Kementerian Kesehatan Republik Indonesia. Buku ajar imunisasi. 2nd printing. Jakarta: Pusat Pendidikan dan Pelatihan Tenaga Kesehatan, Kementerian Kesehatan Republik Indonesia; 2015.
25. Badan Penelitian dan Pengembangan Kesehatan, Kementerian Kesehatan Republik Indonesia. Riset kesehatan dasar (Riskesdas) 2013. Jakarta: Kementerian Kesehatan Republik Indonesia; 2013 [cited 2022 January 30]. Available from: https://repository.badankebijakan.kemkes.go.id/id/eprint/4467/1/Laporan_riskesdas_2013_final.pdf.
26. Jané M, Vidal MJ, Camps N, Campins M, Martínez A, Balcells J, et al. A case of respiratory toxigenic diphtheria: contact tracing results and considerations following a 30-year disease-free interval, Catalonia, Spain, 2015. Euro Surveill. 2018;23(13):17-00183.
27. Arfijanto MV, Mashitah SI, Widiyanti P, Bramantono. A patient with suspected diphtheria. IJTID. 2010;1(2):69–76.
28. Meera M, Rajarao M. Diphtheria in Andhra Pradesh-a clinical-epidemiological study. Int J Infect Dis. 2014;19:74–8.
29. Kandi V, Vaish R. Diphtheria or streptococcal pharyngitis: a case report highlighting the diagnostic dilemma in the post-vaccination era. Cureus. 2019;11(11):e6190.
30. World Health Organization. Operational protocol for clinical management of diphtheria. Geneva: World Health Organization; 2017 [cited 2022 February 10]. Available from: https://www.who.int/docs/default-source/documents/publications/operational-protocol-for-clinical-management-of-diphtheria.pdf.
31. Arguni E, Karyanti MR, Satari HI, Hadinegoro SR. Diphtheria outbreak in Jakarta and Tangerang, Indonesia: epidemiological and clinical predictor factors for death. PLoS One. 2021;16(2):e0246301.
32. Quick ML, Sutter RW, Kobaidze K, Malakmadze N, Strebel PM, Nakashidze R, et al. Epidemic diphtheria in the Republic of Georgia, 1993–1996: risk factors for fatal outcome among hospitalized patients. J Infect Dis. 2000;181(Suppl 1):S130–7.

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RESEARCH ARTICLE

Indoxyl Sulfate Levels and Its Relation with Executive Function in Routine Hemodialysis Patients

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Abstract

Executive function is a crucial cognitive domain that can be adversely affected by various toxic substances, including the uremic toxin indoxyl sulfate. Although it's known that indoxyl sulfate has harmful effects on intra or extra-kidney organs, its impact on executive function remains unclear. This study aimed to evaluate indoxyl sulfate levels in patients with chronic kidney disease (CKD) undergoing hemodialysis and to understand its correlation with executive function impairments. This observational cross-sectional study was conducted at the Dr. M. Djamil General Hospital Padang Hemodialysis Unit from March to July 2022; 60 patients undergoing hemodialysis and 20 healthy controls participated. Executive function was assessed using the Trail Making Test B (TMT-B). Indoxyl sulfate levels were quantified using an ELISA assay with the Assay Genie kit. The Mann-Whitney test set statistical significance at a $p<0.05$. The average age of the subjects was 51.4±11.4 years, with 53% being male. The mean indoxyl sulfate levels were considerably higher in the CKD group (118.79 ng/ml, range: 11–1,709 ng/ml) compared to the control group (6.028±1.829 ng/ml), with a significant difference ($p<0.001$). Impaired executive function was observed in 75% of the CKD patients. The average indoxyl sulfate level was 165.12 ng/ml (range: 29–1,709 ng/ml) in the impaired executive function group and 71.22 ng/ml (range: 11–333 ng/ml) in the group with normal executive function, indicating a significant difference ($p=0.013$). Patients with CKD undergoing hemodialysis exhibit elevated serum indoxyl sulfate levels compared to healthy individuals. Moreover, CKD patients with impaired executive function have notably higher indoxyl sulfate levels than those with normal executive function. Further research is needed to elucidate the mechanistic links between indoxyl sulfate and cognitive impairments.

Keywords: Executives renal functions, hemodialysis, indoxyl sulfate

Introduction

Chronic kidney disease (CKD) is often associated with a spectrum of neurological disorders, one of the most notable being cognitive impairment. It has been observed that CKD patients face a heightened risk of cognitive dysfunction when compared to the general population, with the likelihood of cognitive decline rising as renal function deteriorates.[1] One of the most critical aspects of cognitive processes is executive function, which is central to diverse problem-solving tasks and achieving complex goals. Given its rapid evolution as a cognitive domain, executive function becomes particularly susceptible to impairments from structural or metabolic abnormalities in the brain. A study by Sánchez-Fernández et al.[2] highlighted discernible differences in the executive functions between CKD patients on hemodialysis (HD) and healthy controls.

While CKD has many complications, these aren't solely attributable to underlying diseases. A significant contributor to these complications is the accumulation of uremic toxins owing to the kidney's compromised filtration capacity. Indoxyl sulfate stands out among these uremic toxins.[3] Indoxyl sulfate is primarily excreted via secretion in the kidney tubules in individuals with healthy kidney function. However, hemodialysis machines need to catch up in replicating this intricate process. Hemodialysis is chiefly effective in clearing indoxyl sulfate forms that remain soluble and unbound to plasma proteins, allowing them to traverse the dialysis membrane. Since the clearance rate of dialysis is significantly subpar compared to a fully functioning kidney, there's a marked buildup of indoxyl sulfate in the plasma over time.[4–6]

Indoxyl sulfate has been implicated in many pathologies, from kidney and vascular diseases to bone disorders and central nervous system ailments. Research by Kuo et al.[7] provided evidence suggesting that the unbound, accessible

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form of indoxyl sulfate present in plasma might be linked to cognitive dysfunction. Yet, the influence of indoxyl sulfate when complexed with other proteins remains obscure.

While numerous studies have underscored the potentially harmful effects of uremic toxins, including indoxyl sulfate, on cognitive health,[8] the specific contribution of indoxyl sulfate to executive function anomalies in patients subjected to hemodialysis has yet to be extensively probed. This investigation sought to elucidate the association between serum indoxyl sulfate concentrations and compromised executive function in individuals routinely undergoing hemodialysis. A distinctive feature of this research was its focus on discerning how the concurrent presence or absence of depression in these patients could modulate the said relationship.

Methods

This comparative observational study was conducted at the Dr. M. Djamil General Hospital Padang Hemodialysis Unit. The study targeted chronic kidney disease patients who underwent hemodialysis from March to July 2022.

Sixty patients were recruited for the study and met the inclusion and exclusion criteria. Additionally, 20 healthy individuals were included as control subjects due to the absence of baseline data on indoxyl sulfate levels in a typical healthy population. Notably, all selected patients were beneficiaries of health insurance protection, ensuring that they did not bear any financial burdens due to their participation. The hemodialysis regimen was standardized, with each patient undergoing the procedure twice weekly.

The Research Ethics Committee of the Faculty of Medicine, Universitas Andalas, reviewed and approved the study protocol under reference number 888/UN.16.2/KEP-FK/2022.

The neuropsychological tool Trail Making Test B (TMT-B) evaluated participants' executive functions. This assessment was conducted one hour before their hemodialysis session to ensure patients were in an optimal state. In TMT-B, patients were instructed to sequentially connect numbers and corresponding letters displayed on the test sheet. Before the official test, participants underwent a brief practice session. Executive function was deemed normal if a participant could complete the TMT-B in under 80 seconds (for those below 55 years) or within 120 seconds (for those aged 55–69 years).

The depression status of the participants was ascertained using the Patient Health Questionnaire 9 (PHQ-9).[9] This tool generates a score between 0 and 27. A score exceeding 4 indicated the presence of depression, while a score of 4 or below was indicative of its absence.

Venous blood samples (approximately five ml) were collected from participants and placed in vacutainer tubes. These samples were then centrifuged at speeds between 2,000 and 3,000 rpm for a duration of 20 minutes. The resulting serum was transferred to microtubes and stored at –80°C. Once all samples were amassed, indoxyl sulfate concentrations were determined using an enzyme-linked immunosorbent assay (ELISA) reader, with the Assay Genie ELISA kit employed for the assay.

Results

A total of 80 participants were involved in the study, consisting of 60 patients with chronic kidney disease undergoing routine hemodialysis and 20 healthy control subjects. The age range for hemodialysis patients was between 21 and 69 years. These patients had been on hemodialysis for a period ranging from 6 to 108 months. The average age of the hemodialysis patients was 51.4±11.4 years. Males constituted 53% of the patient group, slightly outnumbering the

Table 1 Baseline Data of Research Subjects

Characteristics	n=60 (%)
Age (years)	
≤50	26 (43)
≥50	34 (57)
Gender	
Male	32 (53)
Female	28 (47)
Underlying disease	
Hypertension	48 (80)
Diabetes mellitus	4 (7)
None	8 (13)
Result of PHQ-9	
Depression	37 (62)
Normal	23 (38)
TMT-B	
Impaired	45 (75)
Normal	15 (25)

Table 2 Relationship between Baseline Characteristics with Impaired Executive Function

Variables	Executive Function		p
	Impaired n=45	Not Impaired n=15	
Age (years)			
≤50	24	5	0.179
≥50	21	10	
Gender			
Male	23	9	0.550
Female	22	6	
Education level (years)			
≤9	14	0	0.013
≥9	31	15	
Hypertension			
Yes	35	13	0.456
Normal	10	2	
Diabetes mellitus			
Yes	3	1	1.000
Normal	42	14	
Depression			
Yes	26	11	0.283
Normal	19	4	

females. The most common underlying disease is hypertension. Depression was found in 61% of the patients, and impaired executive function in 75% (Table 1).

From Table 2, there was a significant relationship between educational level and impaired executive function (p=0.013, p<0.05), and there was no association of other baseline characteristics with executive dysfunction (>0.05).

The average indoxyl sulfate level for the patients was 118.79 ng/ml, with a range spanning from 11 ng/ml to 1,709 ng/ml. The intermediate indoxyl sulfate level in the healthy control group was 6.028±1.829 ng/ml). The difference in indoxyl sulfate levels between the CKD patients and healthy controls was statistically significant (p<0.001), where the level of indoxyl sulfate in the case group was around 19 times that of the control group (Table 3).

Impaired executive function was observed in 75% of the patient group, represented by 45 individuals (Table 1). When comparing the indoxyl sulfate levels in the impaired executive function group, the average level was 165.12 ng/ml, ranging from 29 ng/ml to 1,709 ng/ml. The average level in the not-impaired executive function group was 71.22 ng/ml, varying between 11 ng/ml and 333 ng/ml. There was a significant difference in indoxyl sulfate levels between the impaired and without executive function with p=0.013 (p<0.05, Table 4). The results indicate that hemodialysis patients exhibited significantly higher indoxyl sulfate levels than healthy

Table 3 Difference of Indoxyl Sulfate Level in Case and Control Groups

Variable	Groups		p
	Control n= 20	Case n=60	
Indoxyl sulfate	6.028±1.829	118.79 (11–1,709)	<0.001

Table 4 Differences Between Indoxyl Sulfate Level in Impaired and Without Executive Function in Hemodialysis Patients

Variable	Executive Function		p
	Impaired (n = 45)	Without Impaired (n = 15)	
Indoxyl sulfate	165.12±(29–1,709)	71.22 (11–333)	<0.013

controls. Furthermore, those with impaired executive function showed markedly elevated levels of indoxyl sulfate when contrasted with patients showcasing normal executive functions.

Discussion

Chronic kidney disease (CKD) is characterized by persistent renal abnormalities, such as a glomerular filtration rate (GFR) of below 60 ml/min/1.73 m^2, albuminuria lesser than 30 mg per 24 hours, or visible signs of kidney damage (like hematuria or structural anomalies) persisting for more than three months.[10]

Cognitive impairment is frequently observed in CKD patients.[11,12] The risk of cognitive deficits in CKD patients is notably higher than in the general population.[13] As kidney function deteriorates, the likelihood of cognitive dysfunction rises.[14] Numerous uremic toxins, including uric acid, parathyroid hormone, and indoxyl sulfate, have been implicated in cognitive anomalies.[8,15,16]

Executive function embodies an intricate interplay of goal-oriented behavioral processes, tightly interwoven with the prefrontal cortex's structure.[17] Among CKD patients, executive function is a particularly vulnerable cognitive domain, with significant deficits observed even in hemodialysis recipients. Research by Kurella Tamura et al.[18] in 2017 and corroborated by Murthy and Shukla[19] in 2020 underscores the vulnerability of executive function in CKD patients.

In our study, indoxyl sulfate levels in hemodialysis patients were markedly elevated—almost 19-fold compared to the control group. This elevation underscores the inefficiency of hemodialysis in removing indoxyl sulfate from the bloodstream. Indoxyl sulfate's extensive protein binding makes its clearance via hemodialysis exceptionally challenging.[20] Conventional treatments show that indoxyl sulfate clearance significantly lags behind ureas.[21]

These heightened levels of indoxyl sulfate in dialysis patients—sometimes reported to be up to 80 times higher than in healthy controls[22]—have grave implications for cognitive health. The impaired renal transport mechanisms in CKD facilitate the accumulation of indoxyl sulfate in the brain. Its neurotoxic effects, accelerated by vascular calcification and aging, are hazardous for dementia patients.

Extensive research has outlined indoxyl sulfate's harmful effects on renal and extrarenal organs. Elevated indoxyl sulfate has been linked to declining glomerular filtration rates,[23,24] enhanced coronary atherosclerosis,[25] and more.

A significant finding of our study was the correlation between heightened indoxyl sulfate levels and impaired executive function in hemodialysis patients. While several factors can influence executive function, our results suggest a significant role of indoxyl sulfate levels in shaping the cognitive landscape of CKD patients on hemodialysis.

Conclusions

CKD patients on routine hemodialysis exhibit substantially elevated serum indoxyl sulfate levels compared to a healthy cohort. Among these patients, those with compromised executive function have even higher indoxyl sulfate concentrations.

Conflict of Interest

All contributing authors confirm no conflict of interest associated with this investigation.

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References

1. Xie Z, Tong S, Chu X, Feng T, Geng M. Chronic kidney disease and cognitive impairment: the kidney-brain axis. Kidney Dis (Basel). 2022;8(4):275–85.
2. Sánchez-Fernández MDM, Reyes Del Paso GA, Gil-Cunquero JM, Fernández-Serrano MJ. Executive function in end-stage renal disease: acute effects of hemodialysis and associations with clinical factors. PLoS One. 2018;13(9):e0203424.
3. Lano G, Burtey S, Sallée M. Review indoxyl sulfate, a uremic endotheliotoxin. Toxins (Basel). 2020;12(4):229.
4. Nigam SK, Wu W, Bush KT, Hoenig MP, Blantz RC, Bhatnagar V. Handling of drugs, metabolites, and uremic toxins by kidney proximal tubule drug transporters. Clin J Am Soc Nephrol. 2015;10(11):2039–49.
5. Jansen J, Fedecostante M, Wilmer MJ, Peters JG, Kreuser UM, van den Broek PH, et al. Bioengineered kidney tubules effificiently excrete uremic toxins. Sci Rep. 2016;6:26715.
6. Sirich TL, Funk BA, Plummer NS, Hostetter TH, Meyer TW. Prominent accumulation in hemodialysis patients of solutes normally cleared by tubular secretion. J Am Soc Nephrol. 2014;25(3):615–22.
7. Kuo YT, Li CY, Sung JM, Chang CC, Wang JD, Sun CY, et al. Risk of dementia in patients with end-stage renal disease under maintenance dialysis—a nationwide population-based study with consideration of competing risk of mortality. Alzheimers Res Ther. 2019;11(1):31.
8. Vanholder R, Pletinck A, Schepers E, Glorieux G. Biochemical and clinical impact of organic uremic retention solutes: a comprehensive update. Toxins (Basel). 2018;10(1):33.
9. Kroenke K, Spitzer RL, Williams JB. The PHQ-9: validity of a brief depression severity measure. J Gen Intern Med. 2001;16(9):606–13.
10. Levey AS, Eckardt KU, Tsukamoto Y, Levin A, Coresh J, Rossert J. Definition and classification of chronic kidney disease: a position statement from kidney disease: improving global outcomes (KDIGO). Kidney Int. 2005;67(6):2089–100.
11. Bronas UG, Puzantian H, Hannan M. Cognitive impairment in chronic kidney disease: vascular milieu and the potential therapeutic role of exercise. Biomed Res Int. 2017;2017:2726369.
12. Foster R, Walker S, Brar R, Hiebert B, Komenda P, Rigatto C, et al. Cognitive impairment in advanced chronic kidney disease: the Canadian frailty observation and interventions trial. Am J Nephrol. 2016;44(6):473–80.
13. Zhang CY, He FF, Su H, Zhang C, Meng XF. Association between chronic kidney disease and Alzheimer's disease: an update. Metab Brain Dis. 2020;35(6):883–94.
14. Szerlip HM, Edwards ML, Williams BJ, Johnson LA, Vintimilla RM, O'Bryant SE. Association between cognitive impairment and chronic kidney disease in Mexican Americans. J Am Geriatr Soc. 2015;63(10):2023–8.
15. Niwa T. Indoxyl sulfate is a nephro-vascular toxin. J Ren Nutr. 2010;20(Suppl 5):S2–6.
16. Yeh YC, Huang MF, Liang SS, Hwang SJ, Tsai JC, Liu TL, et al. Indoxyl sulfate, not p-cresyl sulfate, is associated with cognitive impairment in early-stage chronic kidney disease. Neurotoxicology. 2016;53:148–52.
17. Diamond A. Executive functions. Annu Rev Psychol. 2013;64:135–68.
18. Kurella Tamura M, Vittinghoff E, Hsu CY, Tam K, Seliger SL, Sozio S, et al.; CRIC Study Investigators. Loss of executive function after dialysis initiation in adults with chronic kidney disease. Kidney Int. 2017;91(4):948-953.
19. Murthy VS, Shukla VS. A study of executive function in patients with chronic kidney disease before and after a single session of hemodialysis. J Neurosci Rural Pract. 2020 Apr;11(2):250-255.
20. Niwa T. Removal of protein-bound uraemic toxins by haemodialysis. Blood Purif. 2013;35(Suppl 2):20–5.
21. Eloot S, Schneditz D, Cornelis T, Van Biesen W, Glorieux G, Dhondt A, et al. Protein-bound uremic toxin profiling as a tool to optimize hemodialysis. PLoS One. 2016;11(1):e0147159.
22. Niwa T. Indoxyl sulfate, a tryptophan metabolite, induces nephro-vascular toxicity. Biotechnol Biotechnol Equip. 2012;26(Suppl 1):129–33.
23. Wu IW, Hsu KH, Lee CC, Sun CY, Hsu

HJ, Tsai CJ, et al. p-cresyl sulphate and indoxyl sulphate predict progression of chronic kidney disease. ol Dial Transplant. 2011;26(3):938–47.
24. Lin CJ, Liu HL, Pan CF, Chuang CK, Jayakumar T, Wang TJ, et al. Indoxyl sulfate predicts cardiovascular disease and renal function deterioration in advanced chronic
25. Hsu CC, Lu YC, Chiu CA, Yu TH, Hung WC, Wang CP, et al. Levels of indoxyl sulfate are associated with severity of coronary atherosclerosis. Clin Invest Med. 2013;36(1):E42–9.

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RESEARCH ARTICLE

Effect of Moringa Leave Ethanol Extract on Accelerating Wound Healing Process

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Abstract

TGF-β and VEGF are vital in cell proliferation and regeneration, as evidenced in processes like wound healing. The leaves of *Moringa oleifera* Lam exhibit anti-inflammatory and cell regenerative properties that may facilitate the transition from the inflammatory to the proliferative phase, enhancing wound repair. This research sought to discern the potential of orally administered moringa leaf extract in augmenting systemic wound healing, focusing on TGF-β and VEGF serum as *in vivo* molecular markers. This research was conducted at the Animal Laboratory of the Faculty of Medicine, Universitas Padjadjaran, and the Laboratory of Molecular Genetics, Universitas Padjadjaran, from January to March 2022. We divided thirty Swiss Webster mice into two categories: healthy and wound-treated. Wounded mice received 100 mg/kgBW Na CMC as a negative control, 500 mg/kgBW zinc syrup as a positive control, and *M. oleifera* leaves ethanol extract (MOLE) in doses of 280 and 560 mg/kgBW orally from day 3 to day 6. Wound progression was documented and measured on days 0, -1, -3, and -6. Day-6 blood samples were obtained, and TGF-β and VEGF serum levels were gauged using ELISA. Results from day 6 revealed that wound coverage in the 280 and 560 mg/kgBW MOLE groups was 13.76±5% and 13.38±4%, respectively. These percentages notably surpassed that of the negative control group (p=0.005). However, the TGF-β and VEGF serum levels in the MOLE-treated groups did not differ significantly from the negative control (p=0.081 and p=0.149, respectively). Thus, the study concludes that while MOLE expedites wound closure, it does so without the systemic involvement of TGF-β and VEGF *in vivo*.

Keywords: *Moringa oleifera* leaves extract, TGF-β, VEGF, wound healing

Introduction

Wounds are defined as a loss or damage of body tissue due to a sharp or blunt trauma, temperature changes, chemical exposure, or electric shock.[1] They cause damage to the skin due to loss of epithelial tissue continuity, with or without loss of other underlying tissues, such as muscles, bones, blood vessels, and nerves.[2] According to the National Health Service (NHS), the annual prevalence of injuries in the United Kingdom increased by 71% between 2012/2013 and 2017/2018.[3] There is no epidemiology data on wounds in Indonesia. Still, it can be estimated that they are almost the same in number. The wounds that are difficult to heal affect the health costs incurred.[4] Wound healing treatments optimize controllable healing factors, such as infection clearance, mechanical protection, and nutritional support.[5]

Wound healing is a dynamic and complex process in response to injury. The skin cells are activated to promote healing by attracting other cells and substances from different body parts. The healing process has four overlapping phases: hemostasis, inflammatory proliferative, and remodeling. The inflammatory phase begins in 24 hours, lasting three days after wound onset.[5] In the proliferative phase, granulation tissue is formed by transforming growth factor β (TGF-β) and vascular endothelial growth factor (VEGF).[6] Some wound healing processes involve these factors, including inflammation, stimulation of angiogenesis, the proliferation of fibroblast, synthesis, and deposition of collagen, and remodeling of new extracellular matrix (ECM). Additionally, an increase in these factors on day 6 of onset accelerates wound closure, seven, and the disruption of this signaling causes impaired healing. Wound healing disorders are abnormal scarring or chronic injuries characterized by itching and pain. They may cause functional impairment, aesthetic, and psychological problems, leading to decreased quality of life.[8]

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Synthetic and natural medicines accelerate wound healing, and tropical regions rich in biological resources can be used as herbal medicines, including *Moringa oleifera* Lam, which has a high economic value and spread in many tropical and subtropical regions. Moringa has a range of medicinal uses with high nutritional value.[9] The leaves contain beta-carotene, vitamin C, vitamin E, flavonoids including quercetin, kaempferol, vicenin-2, and natural antioxidants. Therefore, they are reported to improve various biological functions, including anti-inflammatory, antimicrobial, anti-cancer, and wound healing properties.[10] The flavonoids increase the growth factor required for wound healing, such as epidermal growth factor (EGF), transforming growth factor α (TGF-α), TGF-β, platelet-derived growth factor (PDGF), VEGF, and fibroblast growth factor (FGF), making it faster. These benefits accelerate the inflammatory phase, resulting in an earlier proliferative phase and faster healing.[6,11] Histologically, the wound tissue of rats given Moringa leaves showed increased growth, proliferation, and migration of fibroblasts in palatal wounds.[11] The diabetic rat group given Moringa leave aqueous extract orally demonstrated faster wound healing by increasing the inflammatory substance.[13] However, the proliferative effect of Moringa leaves on the levels of TGF-β and VEGF has not been elucidated well before. This study aimed to investigate the ability of oral Moringa leave extract to improve the wound healing process systemically using TGF-β and VEGF serum as molecular targets.

Methods

A laboratory experiment with a case-control design was conducted at the Animal Laboratory of the Faculty of Medicine, Universitas Padjadjaran, and the Laboratory of Molecular Genetics, Universitas Padjadjaran, from January to March 2022. This study was approved by the Research Ethics Committee, Faculty of Medicine, Universitas Padjadjaran, with Protocol No. 1064/ UN6.KEP/ EC/2021.

Swiss Webster (*Mus musculus*) male mice from the Institut Teknologi Bandung, aged 5–10 weeks and weighing 20–25 grams, were used and adapted for at least seven days before the study. The exclusion criteria include weight loss >10% during the adaptation period, death, or illness. Mice were housed in polypropylene cages at 22°C with a 12-hour light and dark cycle and ad libitum access to water and pallets.

The Moringa leaves powder (PT Moringa Organik Indonesia, Blora, Indonesia) is a fine powder (500 mesh) that contains 100% organic Moringa leaves without additives, which, based on laboratory tests, contains minerals, beta carotene, thiamine, riboflavin, niacin, pyridoxine, biotin, ascorbic acid, cholecalciferol, tocopherol, vitamin K, amino acids, polyphenols, oleic acid, zeatin, folic acid, and chlorophyll. The Moringa leaves powder was extracted using the maceration method with 96% ethanol (Merck, Rahway, NJ, USA) and water in a 1:3 ratio for 24 h and then filtered. This process was repeated three times. The entire filtrate was homogenized and evaporated in a rotatory evaporator until it was one-third of the initial volume. The filtrate was frozen at −20°C for 24 hours and dried further using the freeze-drying method until it turned into a greenish concentrate. The extract was kept in the refrigerator until treatment use. The ethanol extract was dissolved in 1% Na CMC for oral administration.[14]

The mouse on the left side was wounded after the fur was shaved and the skin was disinfected using 70% alcohol. Then, an intraperitoneal injection of 10 µl/gBW ketamine/xylazine solution (1:1:8) was used to anesthetize the mice. Furthermore, a punch biopsy with a diameter of 5 mm and a depth of 2 mm was used to make a wound, which was treated according to the procedure.[15]

The mice were divided into five groups, containing six mice each. Group 1 was unwounded and received Na CMC (PT Anggana Catur Prima, Jakarta, Indonesia) at 100 mg/kg BW. Groups 2 and 3 were wounded and treated with 100 mg/kgBW Na CMC and 500 mg/kgBW zinc syrup (PT Darya-Varia Laboratoria Tbk, Jakarta, Indonesia), representing the normal, positive and negative controls, respectively.[16,17] Meanwhile, groups 4 and 5 were wounded and treated with *M. oleifera* leaves ethanol extract (MOLE) with a dose of 280 and 560 mg/kgBW mixed with 1% Na CMC, respectively, given orally each day from day-3 to -6.[14] The wound area was photographed on day-0, -1, -3, and -6 using an iPhone 11 Pro camera (Apple, Cupertino, CA, USA), then analyzed with ImageJ version 1.53k (National Institute of Health, Bethesda, MD, USA) was used to quantify the wound area. The wound area percentage was calculated using the

formula described as the initial wound area minus the current, divided by the initial in percent, and then the wound area percentage between groups on day six was compared.

The mice were anesthetized and sacrificed on day 6, and the blood was collected using cardiac puncture. Then, the blood was centrifuged at 1,000 × g for 15 minutes to assemble the serum. Furthermore, the enzyme-linked immunosorbent assay (ELISA) kit was used to measure the TGF-β and VEGF serum levels based on the manufacturer's instructions (EliKineTM kits, Abbkine Scientific Co., Ltd, Wuhan, China, cat. no. KET7014 and KET7016, respectively).

The data were analyzed for the normality distribution using the Shapiro-Wilk normality test. A normally distributed data set was analyzed using one-way analysis of variance (ANOVA), followed by the Bonferroni post hoc test. Meanwhile, Kruskal-Wallis analysis was used when the data was not normally distributed, followed by the Mann-Whitney test. The differences were statistically significant at $p<0.05$. Statistical analyses were performed using SPSS for Windows software version 20 (IBM, Armonk, NY, USA).

Results

The wound healing process for all groups was followed by visual monitoring of the wound size at day 0, -1, -3, and -6 (Figure 1), which was then measured and analyzed under ImageJ. On day 0, -1, and -3, the mean wound area of the group treated with MOLE at doses of 280 and 560 mg/kg was not significantly different from the negative control group ($p>0.05$). The mean area of wounds on day 6 in the positive control group had a lower percentage ($p=0.018$) than the opposing group, constituting 13.62±4% vs 21.93±5%, respectively. Similarly, in groups treated with 280 and 560 mg/kgBW MOLE, there was a lower percentage of wound area compared to the negative control group, accounting for 13.76±5% and 13.38±4%

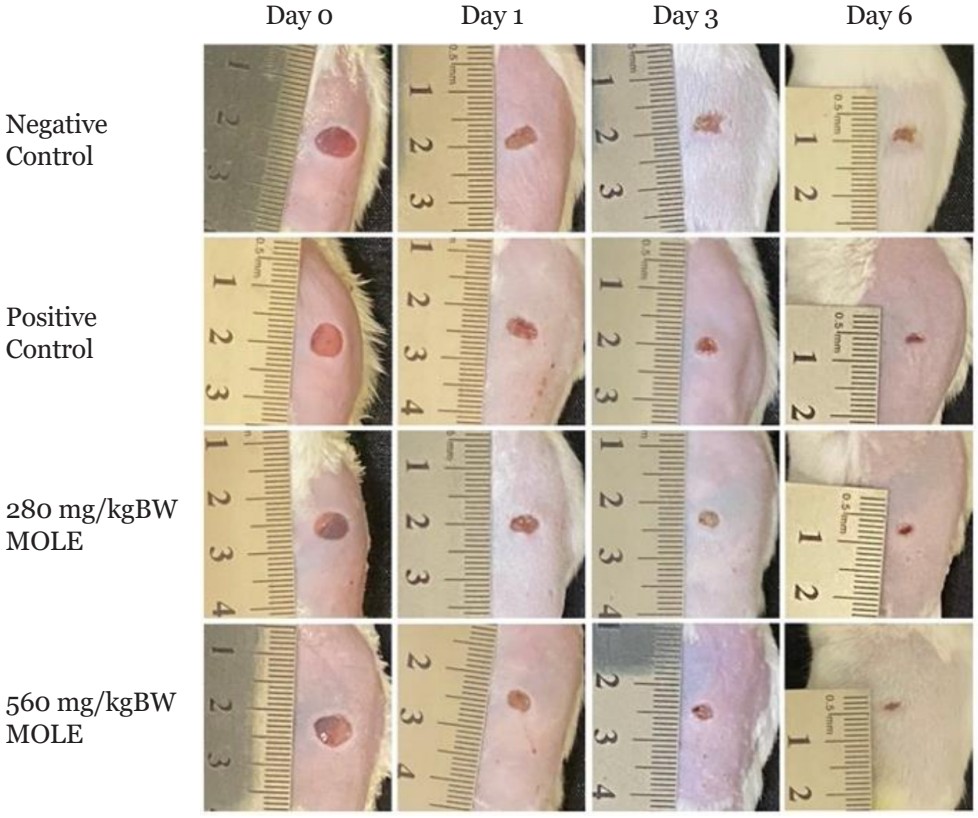

Figure 1 Photographically Recorded the Wound Area on Days 0, 1, 3, and 6 after Wounding

Note: The wound areas in 280 mg/kgBW MOLE and 560 mg/kgBW MOLE on days 1 and 3 were slightly smaller than in the negative control and showed significantly smaller wound areas than in the negative control on day 6

vs 21.93±5% (p=0.021, p=0.015, respectively). However, the groups treated with MOLE were insignificantly statistical compared to the positive control group, 13.76±5% and 13.38±4% vs 13.62±4%, respectively (p=1.000), indicating that both doses had a similar effect to the positive group, as shown in Figure 2.

In the positive control group, the mean TGF-β serum level was higher than the negative and normal control group, 178.2 pg/ml vs 121.4 pg/ml and 98.2 pg/ml (p=0.674, p=0.124, respectively). Meanwhile, in groups treated with 280 mg/kgBW MOLE, it was lower than the positive and negative control, generating 101.2 pg/ml versus 178.2 pg/ml and 121.4 pg/ml (p=0.157, p=1.000, respectively), though higher than the normal control group, 101.2 pg/ml vs 98.2 pg/ml, (p=1.000). A similar result was obtained at a dose of 560 mg/kgBW, generating 118.2 pg/ml vs 178.2 pg/ml and 121.4 pg/ml, when compared to the positive and negative control (p=0.541, p=1.000 respectively), but higher than the normal control group, 118.2 pg/ml vs 98.2 pg/ml (p=1.000) as indicated in Figure 3.

The median VEGF serum level in the normal group was higher than the negative and positive control group, producing 171.6 pg/ml vs 96.7 pg/ml and 67.9 pg/ml (p=0.262, p=0.078, respectively). In groups treated with 280 mg/kgBW MOLE, it was lower than the normal, negative, and positive control, generating 59.5 pg/ml vs 171.6 pg/ml, 96.7 pg/ml, and 67.9 pg/ml (p=0.016, p=0.200, p=0.522, respectively). Also, at a dose of 560 mg/kgBW, the serum level decreased compared to the normal and negative control, yielding 72.2 pg/ml vs 171.6 pg/ml and 96.7 pg/ml (p=0.150, p=0.749, respectively), but higher than the positive control group, 72.2 pg/ml vs 67.9 pg/ml (p=1.000). Hence, there was no significant difference in VEGF expression in groups treated with 280 and 560 mg/kgBW MOLE, 59.5 pg/ml, and 72.2 pg/ml (p=0.262), as indicated in Figure 4.

Discussion

Skin trauma is shared globally, and studies have shown that more than one million people experience skin injuries yearly. Therefore, effective drugs with low side effects are required urgently.[18] The *M. oleifera* leaves ethanol extract (MOLE), with its flavonoid compounds, is a novel candidate for skin wound healing with minimum side effects.[19]

The gross wound size (Figure 1) significantly reduced after oral MOLE administration and was accompanied by a dose-dependent wound area reduction (Figure 2). This was in line with a previous study, where topical MOLE accelerated excisional wound healing in diabetic rats by reducing wound size, increasing wound contraction and tissue regeneration, down-regulating inflammatory mediators, antibacterial activity, and regulating VEGF angiogenic

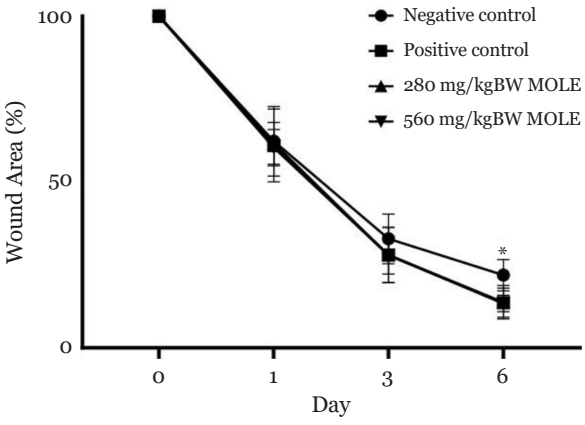

Figure 2 The Average Wound Area Percentage in Mice Treated with *Moringa oleifera* Leaves Extract

Note: *p<0.05 negative control vs positive control and MOLE groups. Data were presented as mean±SD, n=6 for each group

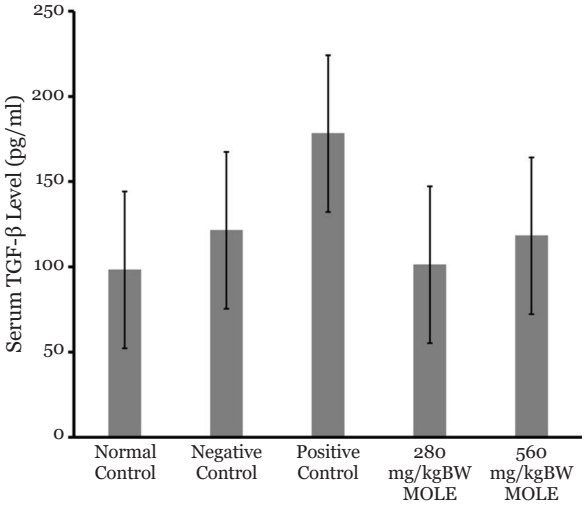

Figure 3 Serum TGF-β Levels

Note: serum TGF-β levels were measured using the ELISA method from serum samples obtained on day 6 in mice treated with *Moringa oleifera* leaf extract. Data were presented as mean+SD (n=6)

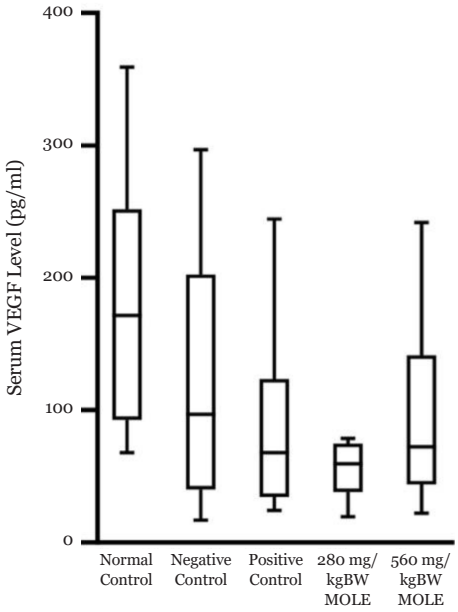

Figure 4 Serum VEGF Levels

Note: serum VEGF levels were measured using the ELISA method from serum samples obtained on day 6 in mice treated with *Moringa oleifera* leaves extract. Data were presented as median (n=6)

markers.[20] There was no significant difference in the percentage of wound contraction between the positive and MOLE groups. Hence, MOLE can be an alternative to wound healing therapy.

Skin re-epithelialization begins after injury, as growth factors are released by cells to induce keratinocytes, macrophages, and fibroblasts proliferation and migration into the wound space. TGF-β plays a critical role by directing inflammatory cells into the wound, accelerating ECM deposition and granulation tissue formation, and increasing the expedition of collagen type 1 to replace type 3 during the inflammation, proliferation, and remodeling phase, respectively. Meanwhile, VEGF is the angiogenetic factor regulated to promote angiogenesis and revascularization. Therefore, MOLE accelerates wound healing through TGF-β and VEGF signaling pathways.[21]

The presence of vicenin-2 and quercetin in MOLE increases the expression of TGF-β and VEGF by activating the critical transcription factor of the VEGF gene, hypoxia-inducible factor 1α (HIF-1α), reducing the expression of MMP-2, MMP-9, cathepsin. B, and cathepsin K, and increasing tissue inhibitory MMP-1 gene expression.[21,22] In this study, the increase in TGF-β levels in the dosage groups of MOLE was insignificant compared to the negative and the positive control groups (Figure 3) because MOLE acts locally in the wound.[23,24] A previous study showed that the expression of TGF-β in injuries treated with topical lavender oil increased significantly compared to the control.[25]

The VEGF levels decreased in the wounded group compared to the average (Figure 4). When a wound occurs on the skin of a healthy human, there is a spike in the local VEGF expression in response to hypoxia and local inflammation conditions.[26] The results were inconsistent with the previous study, where topical administration of *Callicarpa nudiflora* showed increased VEGF serum levels in rats with scald wounds.[27] In another study, using curcumin ointment for skin ulcers in a diabetic rat showed higher VEGF expression compared to the control group.[28] However, other studies demonstrated that oral MOLE reduces VEGF expression in Wistar rats because the isothiocyanates in the leaves lower the amount of VEGF through inhibitory pathways in the transcription of hypoxia-inducible factor (HIF).[29] Flavonoid-based compounds in Moringa leaves and seed residue extracts, such as isoquercetin, zeatin, rutin, quercetin, β-sitosterol, caffeoylquinic acid, and kaempferol, have potential antiangiogenic activity. These compounds act as inhibitors of CaN, blocking the CaN/NFAT pathway, which promotes cancer growth, migration, as well as angiogenesis, and suppresses angiogenesis.[30]

Other active substances play a role in the wound-healing process. Further studies should be conducted using flavonoids from Moringa leaf extract (quercetin, kaempferol, and vicenin-2) for wound healing. This study also did not perform histological research to confirm the fibroproliferative effect of Moringa leaf extract. Therefore, a histological examination is necessary to determine the number of fibroblasts and the level of granulation tissue formation in the wound. It is also suggested to measure VEGF and TGF-β protein levels in wound tissue to confirm the effect of Moringa leaf extract in the local wound area.

Conclusions

MOLE improves wound closure macroscopically, and the results showed that it is a promising alternative for therapy. However, MOLE may not

affect systemic TGF-β and VEGF levels. Further studies are required to examine the histology of fibroblast cells and VEGF and TGF-β protein levels in wound tissue.

Conflict of Interest

None declared.

Acknowledgments

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References

1. Laut M, Ndaong N, Utami T, Junersi M, Seran YB. Efektivitas pemberian salep ekstrak etanol daun anting-anting (*Acalypha indica* Linn.) terhadap kesembuhan luka insisi pada mencit (*Mus musculus*). J Kaji Vet. 2019;7(1):1–11.
2. Wintoko R, Yadika ADN. Manajemen terkini perawatan luka. JK Unila. 2020;4(2):183–9.
3. Guest JF, Fuller GW, Vowden P. Cohort study evaluating the burden of wounds to the UK's National Health Service in 2017/2018: update from 2012/2013. BMJ Open. 2020;10(12):e045253.
4. Meiliana A, Dewi NM, Wijaya A. Stem cell therapy in wound healing and tissue regeneration. Indones Biomed J. 2016;8(2):61–70.
5. Landén NX, Li D, Ståhle M. Transition from inflammation to proliferation: a critical step during wound healing. Cell Mol Life Sci. 2016;73(20):3861–85.
6. Wang L, Qin W, Zhou Y, Chen B, Zhao X, Zhao H, et al. Transforming growth factor β is essential in enhancing wound healing by topical application of povidone-iodine. Sci Rep. 2017;7(1):991.
7. Putra A, Alif I, Hamra N, Santosa O, Kustiyah AR, Muhar AM, et al. MSC-released TGF-β regulates α-SMA expression of myofibroblast during wound healing. J Stem Cells Regen Med. 2020;16(2):73–9.
8. Ghazawi FM, Zargham R, Gilardino MS, Sasseville D, Jafarian F. Insights into the pathophysiology of hypertrophic scars and keloids: how do they differ? Adv Skin Wound Care. 2018;31(1):582–95.
9. Gopalakrishnan L, Doriya K, Kumar DS. *Moringa oleifera*: a review on nutritive importance and its medicinal application. Food Sci Hum Wellness. 2016;5(2):49–56.
10. Kusmiyati, Keman S, Amin M, Suwarno, Nugroho HSW. The role of *Moringa oleifera* leaves against oxidative stress and chronic inflammation: a review. Indian J Public Health Res Dev. 2018;9(6):257–62.
11. Walton KL, Johnson KE, Harrison CA. Targeting TGF-β mediated SMAD signaling for the prevention of fibrosis. Front Pharmacol. 2017;8:461.
12. Amaliya A, Muhaimina RK, Susanto A, Sutjiatmo AB. Histological assessment of palatal donor site wound healing after application of *Moringa oleifera* Lamarck leaf extract in rats. Eur J Dent. 2019;13(2):248–54.
13. Azevedo ÍM, Araújo-Filho I, Teixeira MMA, Moreira MDFC, Medeiros AC. Wound healing of diabetic rats treated with *Moringa oleifera* extract. Acta Cir Bras. 2018;33(9):799–805.
14. Syamsunarno MRAA, Alia F, Anggraeni N, Sumirat VA, Praptama S, Atik N. Ethanol extract from *Moringa oleifera* leaves modulates brown adipose tissue and bone morphogenetic protein 7 in high-fat diet mice. Vet World. 2021;14(5):1234–40.
15. Tan NS, Wahli W. Studying wound repair in the mouse. Curr Protoc Mouse Biol. 2013;3(3):171–85.
16. Wang C, Lu J, Zhou L, Li J, Xu J, Li W. Effects of long-term exposure to zinc oxide nanoparticles on development, zinc metabolism and biodistribution of minerals (Zn, Fe, Cu, Mn) in mice. PLoS One. 2016;11(10):e0164434.
17. Dev D, Sarkar A, Roy B. *Acanthus leucostachyus* leaf extracts promote excision wound healing in mice. Asian Pac J Trop Biomed. 2022;12(11):475–82.
18. Pang Y, Zhang Y, Huang L, Xu L, Wang K, Wang D, et al. Effects and mechanisms of total flavonoids from *Blumea balsamifera* (L.) DC. on skin wound in rats. Int J Mol Sci. 2017;18(12):2766.
19. Gothai S, Muniandy K, Zarin MA, Sean TW, Kumar SS, Munusamy MA, et al. Chemical composition of *Moringa oleifera* ethyl acetate

fraction and its biological activity in diabetic human dermal fibroblasts. Pharmacogn Mag. 2017;13(Suppl 3):S462–9.
20. Al-Ghanayem AA, Alhussaini MS, Asad M, Joseph B. *Moringa oleifera* leaf extract promotes healing of infected wounds in diabetic rats: evidence of antimicrobial, antioxidant and proliferative properties. Pharmaceuticals (Basel). 2022;15(5):528.
21. Tan WS, Arulselvan P, Ng SF, Taib CNM, Sarian MN, Fakurazi S. Improvement of diabetic wound healing by topical application of vicenin-2 hydrocolloid film on Sprague Dawley rats. BMC Complement Altern Med. 2019;19(1):20.
22. Taskan MM, Yuce HB, Karatas O, Gevrek F. Topical quercetin gel application improved wound healing in Wistar rats. Ann Med Res. 2019;26(10):2397–404.
23. Chin CY, Ng PY, Ng SF. *Moringa oleifera* standardised aqueous leaf extract-loaded hydrocolloid film dressing: in vivo dermal safety and wound healing evaluation in STZ/HFD diabetic rat model. Drug Deliv Transl Res. 2019;9(2):453–68.
24. Tofiq SA, Azeez HA, Othman HH. Wound healing activities of *Moringa oleifera* leaves extract cultivated in Kurdistan region-Iraq. Jordan J Biol Sci. 2021;14(4):637–45.
25. Mori HM, Kawanami H, Kawahata H, Aoki M. Wound healing potential of lavender oil by acceleration of granulation and wound contraction through induction of TGF-β in a rat model. BMC Complement Altern Med. 2016;16:144.
26. Honnegowda TM, Kumar P, Udupa EGP, Kumar S, Kumar U, Rao P. Role of angiogenesis and angiogenic factors in acute and chronic wound healing. Plast Aesthet Res. 2015;2(5):243–9.
27. Zhang XG, Li XM, Zhou XX, Wang Y, Lai WY, Liu Y, et al. The wound healing effect of *Callicarpa nudiflora* in scalded rats. Evid Based Complement Alternat Med. 2019;2019:1860680.
28. Zhou J, Ni M, Liu X, Ren Z, Zheng Z. Curcumol promotes vascular endothelial growth factor (VEGF)-mediated diabetic wound healing in streptozotocin-induced hyperglycemic rats. Med Sci Monit. 2017;23:555–62.
29. Hartono DRN, Sulisetyawati TIB, Jularso E. The potential effect of *Moringa oleifera* leaves extract on vascular endothelial growth factor expression in Wistar rat oral cancer cells. Dent J. 2019;52(2):71–5.
30. Lim WF, Mohamad Yusof MI, Teh LK, Salleh MZ. Significant decreased expressions of CaN, VEGF, SLC39A6 and SFRP1 in MDA-MB-231 xenograft breast tumor mice treated with *Moringa oleifera* leaves and seed residue (MOLSr) extracts. Nutrients. 2020;12(10):2993.

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