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Distributions of Breast Cancer Primary Tumor Locations in Indonesian Patients

Helenia Putri¹, Maria A. Kristina¹, Devita Widjaja¹, Bernard A. Baskoro², Erna Kristiani^{3*}, Rusli Muljadi⁴

¹Faculty of Medicine, Pelita Harapan University, Tangerang, Banten, Indonesia

²Department of Surgical Oncologist, Siloam Hospital Lippo Village, Tangerang, Banten, Indonesia

³Department of Pathology Anatomy, Siloam Hospital Lippo Village, Tangerang, Banten, Indonesia

⁴Department of Radiology, Siloam Hospital Lippo Village, Tangerang, Banten, Indonesia

Abstract

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Keywords: Breast Cancer; Distribution; Laterality

***Correspondance:** Erna Kristiani
Department of Pathology Anatomy,
Siloam Hospital Lippo Village,
Tangerang, Banten, Indonesia.
E-mail: erna.kristiani@uph.edu
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Introduction: Overseas studies have shown various distributions of breast cancer primary tumor locations based on stages and histopathologic types. Based on them, breast cancer was consistently reported to be found on the left breast more than the right. Breast cancer laterality was estimated to be one of the determinant factors in prognosis. In Indonesia, there are only a few studies on the laterality of breast cancer, as well as the characteristics that accompany it. The aim of this study is to know the distributions of primary breast cancer tumor locations in Indonesian patients.

Material and Methods: A cross-sectional design study was done and the data was collected from Siloam Hospital Lippo Village radiology and pathology anatomy department within the 2014-2018 period. The results were presented using descriptive statistics.

Results: A total of 74 breast cancer patients from various ages and stages were enrolled in this study. Based on the histopathological types, 84.2% patients left breast tumors and 72.2% patients with right breast tumors had invasive ductal carcinoma of no special type. Based on quadrants, 50% tumors on the left breast are in the superolateral quadrant, followed by 31.6% in superomedial, 13.2% in inferomedial, and the rest in inferolateral. Conclusion: Most tumors are located in the superolateral quadrant and the most histopathological types are non-specific invasive carcinomas.

Introduction

Overseas studies have shown various distributions of breast cancer primary tumor locations based on stages and histopathologic types. Based on them, breast cancer was consistently reported to be found on the left breast more than the right. Superolateral quadrant has the most dense tissue because of the fibroglandular and adipose, which then became the most frequent site for the primary tumor occurrence. Breast tumors in older patients have the tendency to occur in the left breast, whereupon the radiotherapy treatment will greatly affect the cardiovascular system and mortality.

Breast cancer laterality was estimated to be one of the determinant factors in prognosis. In Indonesia, there are only a few studies on the laterality of breast cancer, as well as the characteristics that accompany it. The aim of this study is to know the distributions of primary breast cancer tumor locations in Indonesian patients.

Material And Methods

A cross-sectional design study was done and the data was collected from Siloam Hospital Lippo Village radiology and pathology anatomy department within

the 2014-2018 period. Breast cancer patients included have done biopsy evaluated by a pathology anatomist and breast cancer primary tumor locations were gathered from imaging results using chest X-Ray and mammography from the radiologist. The inclusion criteria are female sex diagnosed with breast cancer between 2014 -2018, unilateral breast cancer with documented primary site and exclusive laterally, had done pathology & imaging test. The exclusion criteria is incomplete data. Staging of breast cancer based on American Joint Committee on Cancer 7th edition (late stages are III and IV). The exclusion criteria are bilateral tumor locations, history of recurrence, history of tumor therapy, history of any breast tumor surgery and no result of biopsy. The results were presented using descriptive statistics.

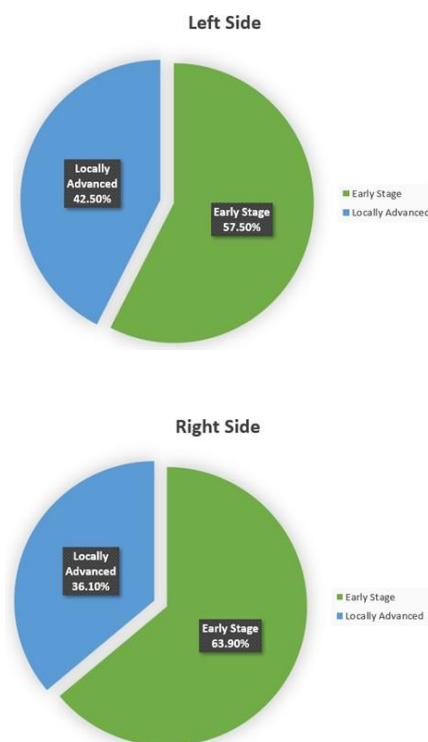
Result

A total of 74 breast cancer patients from various ages and stages were enrolled in this study. There were 51.35% patients which tumors were on the left side with the mean age of 49.45 (SD=11.19) (29-78) years old and 48.65% patients had tumor on the right side with the mean age of 48.44 (SD=9.82) (25-74) years old. Based on stages, 57.5% of patients whose tumors were on the left side and 63.9% on the right breast were in the early stage. The rest were locally advanced. Based on the histopathological types, 84.2% patients left breast tumors and 72.2% patients with right breast tumors had invasive carcinoma of no special type. Furthermore, 10.5% patients with tumors on the left breast and 13.9% on the right breast had mixed type. The least one, 8.3% patients with tumors on the right breast were classified as invasive lobular carcinoma. The rests were ductal carcinoma in situ. 50% tumors on the left breast are in the superolateral quadrant, followed by 31.6% in superomedial, 13.2% in inferomedial, and the rests in inferolateral. On the right breast, 61.1% tumors were in the superolateral quadrant, followed by 16.7% in inferolateral, 13.9% in superomedial, and the rest in inferomedial.

Table 1. Clinicopathologic Characteristics of Breast Cancer Patients

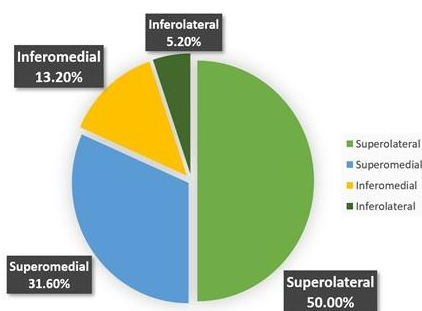
Characteristic		Location				
		Total	Left BCs		Right BCs	
		N	N	%	N	%
Histology	DCIS	74	38	51,35	36	48,65
	IDC NST	7	2	5,3	5	13,9
	ILC	58	32	84,2	26	72,2
	Mix	0	0	0	0	0
Quadrant	Superolateral	9	4	10,5	5	13,9
	Inferolateral					
	Inferomedial					
	Superomedial					
Stage	Early (I - II)	41	19	50,0	22	61,10
	LABC (III - IV)	8	2	5,20	6	16,70
		8	5	13,20	3	8,30
		17	12	31,6	5	13,9
						0,136
		45	22	57,50	23	63,90
		29	16	42,50	13	36,10
						0,766

BC: breast cancer, DCIS: ductal carcinoma in situ, IDC NST: invasive ductal carcinoma of no special type, ILC: invasive lobular carcinoma, LABC: locally advanced breast carcinoma.

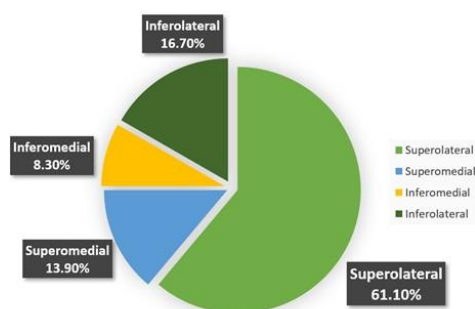


Pie Chart 1. Breast tumor location and stages

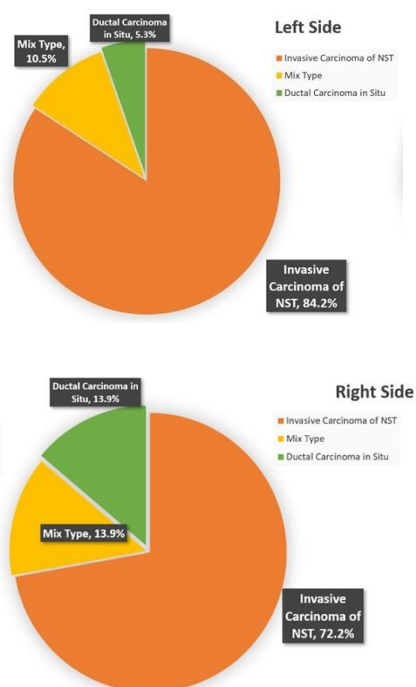
Left Side



Right Side



Pie Chart 2. Breast tumor location and quadrant of primary tumor location



Pie Chart 3. Breast tumor location and histopathology types

Discussion

This study shows that there are variations in the distribution of primary breast cancer tumor locations in Indonesian patients. Based on age, there were 51.35% of patients had tumors on the left side with a mean age of 49.45 (SD = 11.19) (29-78) years and 48.65% of patients had tumors on the right side with mean age 48.44 (SD = 9.82) (25-74) years.

In various other studies, breast cancer was noted to consistently have a tendency to occur on the left breast compared to the right breast. Because the left breast size is slightly larger than the right breast due to hemodynamic asymmetry, initially breast size was thought to be a factor in the laterality of left breast cancer. However, it was later found that the minimal increase in size did not explain the magnitude of the increased risk of left breast cancer compared to the right breast, which in turn found no association between breast size and breast cancer risk. Thus, breast parenchymal mass, or mammary gland cell mass, is more likely to be a predictor of breast cancer risk than breast size.¹

Laterality of breast cancer is thought to be one of the determinants of breast cancer prognosis. In this study, the highest number of tumors was found in the left breast (51.35%) compared to the right breast (48.65%). These results are in line with studies carried out in America and Cairo, which also described that the diagnosis of left breast tumor was a generally consistent finding regardless of age, race, ethnicity, sex, stage and histological category, although differences in the number were affected by race and ethnicity.^{1,2}

From the results of the study, it was found that the most breast tumors were in the superolateral quadrant, 50% in the left breast and 61.1% in the right breast. This result is in line with the results of other studies in China and America, which said superolateral quadrant of the breast is the most common location for occurrence of tumors.^{2,3} The superolateral quadrant has the densest tissue due to the presence of fibrogland and adipose tissue,

which are then the most common sites for primary tumors.⁴

Based on the histopathological type, 84.2% of left breast tumor patients and 72.2% of right breast tumor patients had invasive ductal carcinoma of no special type. This is in line with studies in America, that found invasive ductal carcinoma of no special type which accounted for 71% of invasive cancers, were more likely to be diagnosed in the left breast cancer than the right.² However, in some studies it is explained that left breast cancer can have non-invasive or invasive histological categories.¹

The limitation of this study is small numbers of patients who participated, further studies are needed with a larger number of patients with a longer data collection period in order to minimize the possibility of bias and increase the variety of information that can be found.

Increased alertness is expected as the impact from this study, regarding the mass of breast tumors for health workers, especially the general practitioner as the first line in screening and the discovery of cases in the periphery community with low education in the Indonesian people. General practitioner is expected to put precautions more on tumor mass, especially on the the superolateral quadrant of the left breast, can be aware of the location of the primary tumor.

For the oncology and radiology department, it is expected that the results of this study can be a source of information on choosing the right consideration of chemotherapy in the case of breast cancer located on the left. Since it was found that the risk of high dose radiation has side effects on the exposure to the left side heart radiation.

Further suggestions for the next studies needed are the relationship between breast cancer and factors such as trauma, lactation dysfunction in the left breast and breastfeeding patterns, because the minimum information and the possibility influencing the laterality of breast cancer.¹ Furthermore, Indonesia consists of various ethnic groups, races and local cultures. In this study, the data collection is only from 1 hospital in Tangerang, data collection from every region in Indonesia might generate more representative data for the people of Indonesia.

Conclusion

Patients with tumors located on the left breast are more numerous than those on the right. Patients with early stage have more tumor in the right breast meanwhile, patients with advanced stage have more tumor in the left breast. The most tumors were located in the superolateral and the most histopathologic type is invasive carcinoma of no special type.

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<https://doi.org/10.1245/s10434-006-9231-5>

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Signature ,



(dr. Erna Kristiani, Sp. PA)

The Relationship between High Fiber Diet and Severity of Premenstrual Syndrome Symptoms in Medical Students of Pelita Harapan University

Ignatius Kelvin¹, Dwi Savitri Rivami²

^{1,2} Faculty of Medicine, Pelita Harapan University

Abstract

Citation: Kelvin Ignatius, Rivami Dwi Savitri. The Relationship between High Fiber Diet and Severity of Premenstrual Syndrome Symptoms in Medical Students of Pelita Harapan University Medicus. 2021 October; 9(3): 91-97

Keywords: Premenstrual syndrome; High fiber diet; Adolescents; Menstrual cycle; Hormone

***Correspondance:** Ignatius Kelvin. Faculty of Medicine, Pelita Harapan University, Karawaci, Tangerang, Banten, Indonesia

E-mail : ignatiuskelvin9@gmail.com

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Introduction: 47.8% of women worldwide experience symptoms of premenstrual syndrome and 20% of women experience symptoms that are severe enough to interfere with daily activities. This occurs during the last 14 days of the menstrual cycle or luteal phase, and it is caused by hormonal fluctuations.

Aim: This study is going to be conducted to determine the relationship between high fiber diet and the severity of premenstrual syndrome in adolescents.

Method: This study used a comparative analytic categorical study with two unpaired categories with a cross-sectional study design. The research sample is female students at the Faculty of Medicine, University of Pelita Harapan who met the inclusion criteria of at least 74 samples by judgmental sampling. Data were collected using a questionnaire in the form of a Premenstrual Symptom Scale, Estimated Food Record and Perceived Stress Scale with the chi-square method, and data analysis using SPSS 24.0.

Results: There were 85 samples that matched the inclusion and exclusion criteria of this study. The majority of the sample came from the 2018 class (64.7%), 20 years old (61.2%), experiencing moderate stress (61.2%), and have normal body mass index (72.9%). Researcher found a p value of 0.309 ($p > 0.05$), which means that there is no significant relationship between a high-fiber diet and the severity of premenstrual syndrome symptoms.

Introduction

Diet is a habit made by an individual or a certain group of people regarding what food choices they eat in their daily lives.¹ A proper diet requires the consumption of vitamins, minerals, carbohydrates, proteins, and fats to achieve balanced nutrition.¹ Dietary choices play an important role in human health.¹ An adequate and balanced diet is necessary to maintain a healthy body and mind and prevent disease.² A study of health-related diet and lifestyle shows that a poor diet is not only interfere with

physical growth but also affect emotional development.²

Premenstrual syndrome is a clinical symptom that occurs significantly, including somatic and psychological symptoms. This occurs during the last 14 days of the menstrual cycle and causes substantial and functional impairment.³ Premenstrual syndrome occurs in 47.8% of women of childbearing age worldwide and in 20% of women occurs so severely that it can interfere with their daily activities.⁴ The symptoms of premenstrual syndrome include weight gain, pain in the abdomen and back, excessive anxiety,

fatigue and various other symptoms.⁴ A study conducted on 300 female university students in Sharjah, United Arab Emirates (UAE) for 4 months in 2016 showed that diet affects symptoms of premenstrual syndrome.⁵ Foods with high calories, fat, sugar, and salt have been shown to have an effect on aggravating symptoms of premenstrual syndrome. On the other hand, fruits that contain lots of fiber have been shown to relieve symptoms of premenstrual syndrome.⁵ However, a study conducted on 11,429 women aged 25-42 years stated that carbohydrates and fiber did not affect the symptoms of premenstrual syndrome, only women who smoked had an index Excess body mass (BMI), and excessive consumption of maltose have a high risk of severe premenstrual syndrome symptoms.⁶

Factors that play an important role in premenstrual etiology, when compared with asymptomatic women, women with symptoms of premenstrual syndrome were shown to consume more refined sugar, refined carbohydrates, sodium, and dairy products and less B vitamins, iron, zinc, and zinc. manganese.

Vegetarian women who consumed less total fat and more fiber than omnivorous women were shown to have fewer symptoms of premenstrual syndrome. This suggests that an increase in dietary fiber and a decrease in fat intake significantly affects estrogen levels in a woman's body.

Consumption of refined sugar can interfere with levels of chromium, manganese, zinc, and B vitamins in the body, this is due to substances needed by the body to process glucose.⁷ In addition, sugar consumption also increases a person's risk of experiencing hypoglycemia, irritability, craving for something sweet, and headaches. Consumption of high sugar with sodium

intake can interfere with the kidney's job of clearing excess water and sodium.⁷

Other dietary habits such as excessive consumption of alcohol and caffeine as well as irregular eating patterns that cause a person to experience malnutrition can interfere with liver function. Disrupted liver function causes an increase in circulating estrogen.⁷

When compared with people in general, people who follow a high-fiber diet tend to have a lower body mass index (BMI), lower total cholesterol and low-density lipid (LDL) cholesterol, lower blood pressure, and lower blood pressure. increase insulin sensitivity. Some of these things cause someone who runs a high-fiber diet to avoid obesity and dyslipidemia.⁸

Given the conflicting research results regarding the relationship between diet and the severity of premenstrual syndrome symptoms, the authors wanted to find out whether diet really has an influence on PMS symptoms. It is hoped that with this research, more of the population will be educated about how they choose a diet that is suitable for PMS.

Objective

This study aims to determine the relationship between a high-fiber diet and the severity of premenstrual syndrome symptoms.

Subject and Methods Samples

The research sample is adolescents of reproductive age at the Faculty of Medicine, Pelita Harapan University who met the inclusion criteria and agreed to sign an informed consent. The data obtained from research respondents were 85 respondents. Data collection is carried

out using google form in the period January to March 2021.

Study Design

A cross sectional study was conducted in Faculty of Medicine, Pelita Harapan University from January to March 2021. The data obtained was processed using the chi square test in accordance with this research method, namely a cross-sectional study with unpaired categorical analytical methods. The minimum number of research samples is 74 respondents.

Data Collection Method

Data was collected using several questionnaire methods. The sociodemographic information such as name, age, Body Mass Index (BMI), batch and caffeine consumption were collected using a self-administered questionnaire. Perceived stress data was collected using the Perceived Stress Scale-10 questionnaire (PSS-10), and the severity of premenstrual syndrome symptoms was collected using Premenstrual Syndrome Scale questionnaire (PMSS). The answers regarding Body Mass Index (BMI) are classified into <17.0 = severe underweight, $17.0 - 18.49$ = mild underweight, $18.5 - 25.0$ = Normal, $25.1 - 27.0$ = Mildly overweight, >27.0 = overweight.^{9,10} The Perceived Stress Scale-10 questionnaire answers are classified into mild stress (0- 13), moderate stress (14-26), severe stress (27-40).^{11,12} The PMSS questionnaire consist of 44 questions symptoms that happened during menstruation. Each assessment criterion on the PMSS questionnaire is filled in by considering the conditions that occurred during the week before menstruation and divided into $1 - 44$ = no symptom, $45 - 103$ = mild symptoms, $104 - 163$ = moderate symptoms, $164 - 220$ = severe symptoms.^{13,14} Estimated Food Record

was used to determine UPH Faculty of Medicine students dietary habit, it was divided into 2 categories based on WHO recommendation which is healthy diet (> 400 grams of vegetables and fruit a day or at least one serving of fiber a day), unhealthy diet (<400 grams of vegetables and fruit a day or no consumption of vegetables and fruit in a day).^{1,15} The exclusion criteria for this study are experiencing severe stress, consumed caffeine (coffee) in the last 24 hours, and overweight.

Statistical Analysis

All of the collected data were analyzed using Microsoft Excel 2019 and Statistic Package for Social Sciences 24th version (IBM SPSS 24). The relationship between high fiber diet and premenstrual syndrome symptoms in medical students of Pelita Harapan University were analyzed using Chi square test. Other variables such as caffeine, stress, and nutritional status are also analyzed using Chi square tests. The result said to be significant if the p-value below 0.05 ($p \leq 0.05$) in two tailed hypothesis testing.

Results

Demographical Data and Respondent Characteristics

Table 1 . Respondent Characteristics (N=85)

Variable	Frequency (n)	Percentage (%)
Age (years)		
19	29	34,1
20	52	61,2
21	4	4,7
Batch		
2018	55	64,7
2019	29	34,1
2020	1	1,2
Stress		
Mild Stress	33	38,8
Moderate Stress	52	61,2
Body Mass Index		
Severe Underweight	6	7,1
Mild Underweight	14	16,5
Normal	62	72,9
Mildly Underweight	3	3,5

In this study, the data obtained from research respondents namely preclinical students of the Faculty of Medicine, Pelita Harapan University, were 85 respondents. The respondents have met the inclusion criteria. Respondent characteristics can be seen in **table 1**. The majority of respondents in this study were 20 years old as many as 52 people (61.2%), respondents from the 2018 batch were 55 people (64.7%), and experiencing moderate stress as many as 52 people (61.2%). Most respondents had normal Body Mass Index (BMI) as many as 62 people (72.9%).

Eating Habits of Medical Students of Pelita Harapan University

Table 2. Eating Habits of Medical Students of Pelita Harapan University (N=85)

Variable	Frequency (n)	Percentage (%)
Frequency of Eating Fiber in a day		
Do Not Consume		
1	29	34,1
2	52	61,2
3	4	4,7
4	1	1,2
Dietary Habit		
Fiber Consumption	55	64,7
No Fiber Consumption	30	34,1
WHO Recommendation		
Fulfil	0	0
Do Not Fulfil	85	100
Fiber Portions		
Do Not Consume	30	35,3
½ Portion	3	3,5
1 Portion	18	21,2
1½ Portions	4	4,7
2 Portions	22	25,9
3 Portions	7	8,2
4 Portions	1	1,2
Jenis Serat		
Fruit Juice	23	23,9
Fruit Salad	3	3,2
Fresh Fruit	4	4,1
Beans, Peas	4	4,1
Vegetables Salad	4	4,1
Fruit Cake	2	2,1
Mixed Vegetables with Peanut Sauce	1	1,1
Stir-fried Vegetables	22	22,9
Vegetables Soup	21	21,9
Vegetarian Noodles	1	1,1
Steamed Taro	1	1,1
Kale cooked with Shri Paste	4	4,1
Cornbread	1	1,1
Fried Breadfruit	1	1,1
Chinese Cabbage	4	4,1

Table 2. Shows a picture of dietary habit of students of the Faculty of Medicine, University Pelita Harapan, where none of them meet the recommendations for a fiber diet from the WHO, namely 5 servings of vegetables and fruit a day. The closest dietary fiber pattern is 4 servings of vegetables and fruit made by 1 (1.2%) participants. For the types of vegetables and fruit, fruit juice was the most frequently consumed fiber, which was consumed 23 (23.9%) times by participants.

Characteristics of Premenstrual Syndrome Severity

Table 3. Characteristics of Premenstrual Syndrome Severity (N=85)

Age	PMS Severity			Total (%)
	Mild	Moderate	Severe	
19	16 (55,2%)	9 (31,0%)	4 (13,8%)	29 (100%)
20	27 (51,9%)	24 (46,2%)	1 (1,9%)	52 (100%)
21	3 (75,0%)	0 (0,0%)	1 (25,0%)	4 (100%)
TOTAL	46 (54,1%)	33 (38,8%)	6 (7,1%)	85 (100%)

Based on table 3, the majority of respondents experiencing mild premenstrual syndrome symptoms, that happened to 46 (54.1%) respondents. Researchers categorized the severity of moderate and severe premenstrual syndrome into one category, namely severe severity, where 39 (45.9%) respondents experienced severe premenstrual syndromesymptoms.

The relationship between diet and the severity of premenstrual syndrome symptoms

Table 4. The relationship between diet and the severity of premenstrual syndrome symptoms

Eating Habits	PMS Severity		Total N(%)	P Value	OR (95%CI)
	Low	High			
Fiber	32 (58,2%)	23 (41,8%)	55 (100%)	0,309	1,590 (0,650-3,893)
No Fiber Consumption	14 (46,7%)	16 (53,3%)	30 (100%)		
Total (N,%)	46 (54,1%)	39 (45,9%)	85 (100%)		

In this study, statistical analysis assessed using the Chi squared test to obtain a pvalue obtained of 0.309 (>0.05). This shows that there is no significant relationship between a high-fiber diet and the severity of premenstrual syndrome symptoms in UPH Faculty of Medicine students.

Discussion

In this study, researchers compared the consumption of a high-fiber diet, in this case the consumption of vegetables and fruit of more than five servings a day according to WHO recommendations or consuming fiber at least once a day, and the consumption of a low-fiber diet which consume vegetables and fruit of less than five servings in a day or eating patterns without vegetables and fruit in one day.¹⁶ Researchers also saw a picture of the dietary habit and menstrual patterns of UPH Faculty of Medicine students.

The dietary habit of UPH Faculty of Medicine students as shown in table 5.2 shows that the consumption of vegetables and fruits of UPH Faculty of Medicine students is not in line with the fiber recommendation from WHO. WHO recommends 400 grams of vegetables and fruit or the equivalent of five servings of good food to be consumed in a day or at least once a day in every serving of food consumed.¹⁶ This is in line with the findings made by the Ministry of Health in a 2013 basic health research study which stated that 93.5% of the population aged >10 years consume vegetables and fruits below the recommended level.¹⁷ Even though vegetables and fruit are an important part of achieving balanced nutrition, the Ministry of Health recommends consuming 3-4 servings of vegetables and 2-3 servings of fruit a

day.¹⁷ In addition, through the community movement (GERMAS) in 2017, the Ministry of Health recommended to consume vegetables and fruit every day so that balanced nutrition can be realized in the community.⁴⁷ According to Agus in 2011, there was a reduction in the consumption of vegetables and fruits in almost all of Indonesia.¹⁸ This is due to changes in food consumption patterns in Indonesia. Another reason is that urban communities experience lifestyle changes to become more mobile and busier so they tend to consume fast food.¹⁸ The fast food diet causes a shift in eating patterns from high carbohydrates, fiber and low fat to low carbohydrates and fiber, high fat diets. and protein.¹⁸ In addition, as many as 30 (35.3%) respondents did not consume vegetables and fruit in their diet.

In this study, researchers compared the association of a high-fiber diet with the severity of premenstrual syndrome symptoms. Because none of the respondents met the requirements for a high-fiber diet as recommended by WHO, the researchers divided diet into two new categories, namely diets with fiber consumption and diets without fiber consumption. The fiber referred to in this case is vegetables and fruit in accordance with WHO recommendations where the requirement for a healthy diet is the consumption of vegetables, fruit, nuts, and legumes in a day.

The results of the analysis test using chi squared obtained a p value of 0.309 ($p > 0.05$). A p-value greater than 0.05 indicates that there is no significant relationship between a high-fiber diet and the severity of premenstrual syndrome symptoms in UPH Faculty of Medicine students. This study is in line with research conducted by Houghton, et al in 2017 on 116,429 women aged 25-42 years in Boston, United States.⁶ This study states that consumption of carbohydrates and fiber does not have a significant relationship with a person's risk of experiencing symptoms of premenstrual syndrome.⁶ Body mass index is said to have a greater influence on a person's risk of experiencing symptoms of premenstrual syndrome.⁶

However, another study conducted by Hamad, et al in 2019 on 300 students in Sharjah, UAE in a cross-sectional section stated that consumption of fruits can reduce the risk of developing premenstrual syndrome symptoms in women.⁵

In a study conducted by Hamad, et al in 2019, there were several other variables that were also investigated in this case smoking habits and eating patterns high in sugar/fat/calories/ and salt.⁵ Smoking habits have been proven to increase a person's risk of suffering from premenstrual syndrome symptoms. In addition, a diet high in sugar/fat/calories and salt also has a significant relationship with the risk of developing premenstrual syndrome symptoms in women.⁵ This is contrary to the research revealed by Houghton, et al in 2017. However, in this study it was said that there was a significant increase in total energy and all macronutrients before menstruation when compared to after menstruation. This makes it difficult to determine whether the increase in calories exacerbates premenstrual syndrome or as a result of hormonal changes occurring.⁵

Conclusion

Based on the results and discussion of the research on the relationship

between a high-fiber diet and the severity of premenstrual syndrome symptoms in UPH Faculty of Medicine students, it can be concluded that there is no significant relationship between a high-fiber diet and the severity of premenstrual syndrome symptoms in UPH Faculty of Medicine students.

Limitation

There is some limitation in this study. In this case, the first is the limitations of the data collection method carried out by the researcher, the researcher uses the judgmental sampling method so that the sampling is not random and cannot be said to represent the entire population. In addition, the use of the questionnaire method that was distributed online caused respondents to answer the questionnaire subjectively and some did not understand the question clearly, causing bias. Researchers have tried to avoid bias by contacting respondents directly one by one and explaining questions that are considered difficult but due to time and place limitations caused by the pandemic, researchers have difficulty getting responses from respondents and there are limitations in explaining online questionnaires.

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Relationship Between Breakfast Intake with Mood and Short-Term Memory Among Medical Students of Pelita Harapan University : A Cross Sectional Study

Yang Yang Endro Arjuna¹, Dwi Savitri Rivami².

^{1,2}*Faculty of Medicine, Pelita Harapan University*

Abstract

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Correspondance: Yang Yang Endro Arjuna, Faculty of Medicine, Pelita Harapan University, Jl. Jenderal Sudirman No.20, Tangerang, Indonesia.

E-mail : yangyangear@gmail.com

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Introduction: Epidemiological studies stated people rarely eat breakfast even though breakfast have an important role in human physicality, mood and short-term memory. Mood is the tone of feelings a person feels, while short-term memory is part of the cognitive system used to store memories for a short time.

Aims: This research was conducted to determine the relationship between breakfast with mood and short-term memory among Medical Students of Pelita Harapan University.

Methods: This study used a cross-sectional study carried out on 133 students who were obtained based on the method of calculating, unpaired categorical comparative analytic samples. The sample population was taken by judgmental sampling on active students of the Faculty of Medicine, University of Pelita Harapan in 2020 according to the inclusion and exclusion criteria. Data were collected using a self-administered questionnaire, Positive and Negative Affect Schedule, Digit Span Test Forward Span. The statistical test used was Chi square and Fisher Exact, with data processing using Microsoft Excel 2019 and SPSS 24.0.

Result: There were 133 samples based on inclusion and exclusion criteria. The majority of sample was female (54.1%), batch 2018 (37.6%), 20 years old (36.8%), used to breakfast (62.4%), had a positive mood (96.2%), optimal short-term memory (64.7%). The result showed no significant between breakfast intake with mood (OR 2.585; 95%CI (0.417- 16.034); p=0.364) and significant relationship between breakfast intake with short term memory (OR 2.773; 95%CI (1.325-5.801); p=0.011).

Conclusions: There was no significant relationship between breakfast intake with mood, and a significant relationship between breakfast intake and mood was found. Further studies with larger samples are need to minimize biases in future studies.

Introduction

Breakfast is defined as the first meal of the day before 10:00 am and does not include drinking water.¹ Breakfast is also required at least 8 hours between the meal and the last meal that was consumed at night.² In fact, the awareness of eating breakfast is still minimally realized by some groups. A systematic review study by Monzani in the year of 2019, found that 30% of 286.804 respondents aged 2-18

years did not eat breakfast.³ This research is also supported by other studies made by Sutanto in 2015 in Jakarta found that almost 59% of 945 respondents aged 6-12 years did not eat breakfast as well.⁴ Breakfast must be recognized as a mandatory thing for all groups, because there are so many benefits that can be obtained from breakfast.^{3,5} Breakfast can reduce the risk of obesity, metabolic syndrome, improve function cognitive,

make a positive mood, improve the quality of life, and so on.^{3,5}

Mood is a feeling that someone feels during a certain period of time or on the other hand it can be defined as a tone of pleasant or unpleasant feelings that accompany a thought and lasted for a long time.⁶ Short term memory is a cognitive system that is used to store various sensory events, movements, cognitive information such as numbers, words, names, or other things in a short period of time.⁷ There are so many factors that can cause changes in mood and short-term memory, such as: sleep patterns, physical activity, lifestyle, food, stress, and so on.⁸⁻¹¹

In the central nervous system, there are several pathways that regulate mood. The regulation is formed by several hypotheses, including: monoamine, neurotrophic, and neuroendocrine pathways.¹² Monoamine pathways says that serotonin, norepinephrine and dopamine present in the cortex and limbic system play a role in maintaining mood.¹² Neurotrophic pathways says that Brain Derived Neurotrophic Factor plays a role in nerve growth.¹² Disturbance or mutation in BDNF interfere mood, intellectual, attention function, and many more.¹² Neuroendocrine pathways says that high level of cortisol and dysregulation of thyroid function also interfere daily mood.^{12,13} Other studies prove that breakfast plays an important role in the regulation of neurotransmitters and neuromodulators in the nervous system.¹⁴ When blood sugar decreases, there is an expenditure of cortisol hormone which can induce the release of inflammatory cytokines that inhibits the function of neurotransmitters in humans so that it can decrease the level of serotonin hormone which trigger depression.¹⁵ On the other hand, breakfast can inhibit the excretion of

cortisol, therefore serotonin levels can increase and are closely related to a better mood.¹⁵ In conclusion, breakfast plays an important role in maintaining a positive mood.^{14,15}

Our memory system is divided into three different parts: sensory memory, short-term memory, and long-term memory.¹⁶ These three systems are mutually sustainable. According to Atkinson and Shiffrin, sensory memory received stimuli from the external environment through sight, hearing, smell, touch, and taste.¹⁶ Human have the capacity to forget all the memory given by the sensory stimulus but human also have the capacity to store the memory given by the sensory stimulus as a short-term memory.¹⁶ Once in the short-term memory, the information can be forwarded to be stored in the long-term memory capacity or it can be replaced with a new information.¹⁶ The learning and memory functions in humans are arranged in a complex system in the human brain. Hippocampus and amygdala play an important role in maintaining human memory, on other hand amygdala maintain human emotional as well.¹⁷ Memory functions not only depends by an intact amygdala or hippocampus but it also depends on the lines connecting the hippocampus with the surrounding area as well as the amygdala with the surrounding area plays an important role.¹⁷ Lesion or diseases of the brain that involve these structures and circuits may cause memory disruption.¹⁷ Breakfast increases the level of sugar in the blood which is used by the brain neurotransmitter to produce a good neuronal activity that leads to a positive effect of short-term memory.¹⁷ On the other hand, gastrointestinal hormones that are present, triggered by an increase blood glucose level may lead an

improvement of the short-term memory function.¹⁸

Objectives

The present study aimed to know the overview of breakfast intake, mood, and short-term memory among Medical Students of Pelita Harapan University and also to determine the correlation of breakfast intake with mood and short-term memory among Medical Students of Pelita Harapan University.

Methods

Participants

The research sample was obtained from all Faculty Medicine, University of Pelita Harapan active students aged 17-22 years old, both men and women who meet the inclusion criteria. The total of 133 from 221 respondents were collected from December 2020 to February 2021. 88 respondents were excluded because they didn't meet the inclusion criteria.

Study Design

A cross-sectional study was conducted in Faculty Medicine, University of Pelita Harapan from December 2020 to February 2021. A judgmental sampling was used to collect 133 respondents based on method of calculating unpaired categorical comparative analytic samples. This research was approved by the ethic department in Faculty of Medicine, University of Pelita Harapan

Research Instrument

Data were taken using several questionnaires. Socio-demographic data such as name, gender, batch, age, breakfast habits, sleeping pattern, fasting, smoking, drug consumed, previous

diagnosed of mood, memory, and thyroid dysfunction were collected using self-administered questionnaire. Stress was collected using Perceived Stress Scale Questionnaire and physical activity was collected using International Physical Activity Questionnaire Short Form. On the other hand, Mood was collected using Positive and Negative Affect (PANAS) questionnaire and was categorized into positive affect and negative affect based on scoring system. Short-term memory was collected verbally using Digit Span Test Forward Span. Respondent will repeat length of number starting from 2 – 9 digits. If respondent can repeat numbers without making any mistake, then the numbers of digits will be added, but if respondent fails to repeat one long sequence, then respondents are given another opportunity to repeat one long sequence with different figures but same length. The test will be terminated if respondent fails to repeat 2 length sequences consecutively. Respondent who can repeat ≥ 6 numbers are said to be optimal, on the other hand respondent who can't repeat 6 numbers are said to be not optimal. Respondent whom age under 17 or above 22, sleeping pattern less than 7 hours a day, fasting, consuming drug such as antidepressants, anticonvulsants, anti-obesity, hormonal contraception, and other prohibited drugs, actively smoking, history of thyroid, mood, and memory dysfunction, history of moderate to severe stress in one week, and inadequate physical activity should be excluded from the study.

Statistical Analysis

Data analysis were performed using Microsoft Excel 2019 and Statistic Package for the Social Sciences 24th version. Fisher exact test was conducted

to assess the relationship between breakfast intake with mood among Medical Students of Pelita Harapan University and Chi Square test was conducted to assess the relationship between breakfast intake with short-term among Medical Students of Pelita Harapan University. The test is said to be significant when the p value is below 0.05.

Results

Table 1. Respondent Characteristic (N=133)

Respondent Characteristic	Number of Participants	Percentage
Gender		
Male	61	45.9%
Female	72	54.1%
Batch		
2018	50	37.6%
2019	42	31.6%
2020	41	30.8%
Age		
17	3	2.3%
18	34	25.6%
19	41	30.8%
20	49	36.8%
21	4	3.0%
22	2	1.5%
Breakfast Habits		
Used to ($\geq 3x/week$)	83	62.4%
Not Used to ($< 3x/week$)	50	37.6%
Mood		
Positive	128	96.2%
Negative	5	3.8%
Short-term Memory		
Optimal	86	64.7%
Non-Optimal	47	35.3%

Respondent Characteristic

Research and data collection was carried out in December 2020 - February 2021. The total sample that has been obtained is 133 respondents who have met the inclusion criteria. Respondent characteristics can be seen in table 1. Of the 133 respondents whose data had been processed, characteristics data was found as follows: majority respondents are female (54.1%), batch 2018 (37.6%), 20 years old (36.8%), used to breakfast

(62.4%), had a positive mood (96.2%), optimal short-term memory (64.7%).

Statistical Test Results

Relationship between breakfast intake with mood among Medical Students of Pelita Harapan University

Table 2 shows the Fisher exact test analysis regarding the relationship between breakfast with mood among Medical Students of Pelita Harapan university. Fisher Exact test was used because the results did not meet the Chi Square criteria which there was a column with an expected value of less than 5.

Table 2. Fisher Exact Analysis Relationship between Breakfast and Mood (N=133)

Breakfast Habits	Mood		P-value	Odds Ratio (OR)	CI (95%)
	Positive n (%)	Negative n (%)			
Used to	81 (97.6%)	2 (2.4%)	0.364	2.585	0.417-16.034
Not Used to	47 (94.0%)	3 (6.0%)			

Table 3. Chi Square Analysis Relationship between Breakfast and Short-term Memory (N=133)

Breakfast Habits	Short-term Memory		P-value	Odds Ratio (OR)	CI (95%)
	Optimal n (%)	Non-Optimal n (%)			
Used to	61 (73.5%)	22 (26.5%)	0.011	2.773	1.325-5.801
Not Used to	25 (50%)	25 (50%)			

From the results of data analysis using Fisher Exact test, the P-value was 0.364. The P-value is above 0.05, means there is no significant relationship between breakfast intake with mood among Medical Students of Pelita Harapan University.

Relationship between breakfast intake with short-term memory among Medical Students of Pelita Harapan University

Table 3 shows the Chi Square analysis regarding the relationship between breakfast and short-term memory among Medical Students of Pelita Harapan University.

From the results of data analysis using Chi Square test, the P-value is 0.011. P-value is below 0.05, there is a significant relationship between breakfast and short-term memory among Medical Students of Pelita Harapan University. Data analysis showed an odds ratio of 2.773, which means that people who are not used to eat breakfast have a 2.773 times risk of having non-optimal short-term memory.

Discussion

In this study, there was no significant relationship between breakfast and mood, shown from the p value of 0.364 ($p > 0.05$). This research in line with the cross-sectional study conducted by Daung, et al. on 2014 in Malaysia involving 127 respondents where the results of the study found that breakfast was not significantly associated with mood.^[19] These insignificant results can happen because study implemented by Daung, et al. carried out on work days as well as not seeing the work stress load that each employee has, where the moderate or heavy stress can interfere overall mood.^[19] Similar cross-sectional studies implemented by Alrayes, et al. in 2018 involving 170 respondents also found that there was no significant relationship between breakfast and mood.^[20] Alrayes stated that study was conducted at schools that have International Quality Certification and Certificate of Excellence in Educational Performance in Saudi Arabia for 5 consecutive years.^[20] On the other hand, study did not look at the stress history of each respondent. So that Alrayes said it can be the main factor of these

insignificant results.^[20] The same thing happened in this current study. This study was majority carried out on end of semester holidays and student days off, on the other hand this study also pay attention to respondent stress levels using Perceived Stress Scale Questionnaire so that there were very few respondents that have a negative mood and it may be the main cause of this insignificant results.

Results of this study are not in line with the cross-sectional studies carried out by Ren et al. in China in 2020, found that people who are not used to have breakfast tend to be at risk for negative mood.^[21] Therefore, there is a relationship between breakfast and mood.^[21] Similar study conducted by Zhu, et al. in 2015 in China also found a relationship between breakfast and mood.^[22] The differences in the results of this study can occur due to differences in the number of respondents. Research conducted by Ren, et al. followed by 1,060 respondents, research conducted by Zhu, et al. followed by 10,174 respondents, while in this current study followed by 133 respondents. On the other hand, differences of mood assessment questionnaires also gave different results.

Results of this study found a significant relationship between breakfast with short-term memory shown from the p value of 0.011 ($p < 0.05$). This study is in line with the cross-sectional study carried out by Awaliyah in 2019 which involved 74 respondents, found that breakfast plays an important role in short-term memory.^[23] On the other hand, this study is also supported by a cross-sectional study implemented by Bakhtiyari, et al. in 2020 which was attended by 60 respondents also stated that breakfast plays an important role in short-term memory.^[24] These same results can occur due to the same method that was used to take each sample. Breakfast habits pattern was seen for the past week also short-term memory sampling used a recall test. This

significant result shows that breakfast plays an important role in gastrointestinal hormones, neurotransmitter, and good neuronal activity that keep an optimal short-term memory.

Conclusion

In conclusion, majority of respondents used to have breakfast, have a positive mood and an optimal short-term memory. On the other hand, there is no significant relationship between breakfast and mood among Medical Students of Pelita Harapan University and there is a significant relationship between breakfast and short-term memory among Medical Students of Pelita Harapan University.

Limitation

Study of relationship between breakfast and mood implemented by using self-report questionnaire, where the method has a high risk of bias. Among other things, respondents over-reported or under-reported. The use of English based questionnaire is expected to represent mood of respondent in better way, but it creates confusion for some respondent. On the other hand, study of relationship between breakfast and short-term memory implemented by using video call method due to the COVID-19 pandemic and it depends on each internet network. This caused some respondents to ask repetition of digit span test due to unstable internet connection. Also in this study, there were some difficulties to find respondents due to the COVID-19 pandemic.

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The Relationship Between Sedentary Lifestyle and Body Mass Index Among Junior High School Students at Jayapura Christian School

Engelberta Pardamean¹, Elvira Wonda², Veli Sungono³

¹ Department of Psychiatry, Faculty of Medicine, University of Pelita Harapan

² Faculty of Medicine, University of Pelita Harapan

³ Department of Public Health, Faculty of Medicine, University of Pelita Harapan

Abstract

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***Correspondance:** Engelberta Pardamean. Department of Psychiatry, Faculty of Medicine, University of Pelita Harapan.
E-mail: engelberta.pardamean@yahoo.com
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Introduction: As a result of today's technology advancements, many people, including youngsters, are spending more time watching television, playing video games, or using social media on computers or phones. Sedentary lifestyle refers to behaviors like these. Students' activities became passive as a result of studying online at home. As a result, the chance of acquiring more weight and eventually being obese increases. That is the basic issue addressed in the study. The majority of youngsters spend their time on video games, television, or social networking. One of the signs of a sedentary lifestyle is a lack of physical activity. In youngsters, a lack of physical activity might raise the chance of being overweight or obese.

Objective: The purpose of this study is to look into the link between a sedentary lifestyle and a high BMI among Jayapura Christian School Junior High School students.

Methods: This is a cross-sectional study including Jayapura Christian School Junior High School students. Purposive sampling is a strategy for collecting data. The Adolescent Sedentary Activity Questionnaire (ASAQ) was used to collect data and determine Sedentary Lifestyle. In addition, BMI categories were utilized to determine whether someone was normal, overweight, or obese.

Results: The majority of the respondents have an overweight or obese BMI (n=35; 67.3 percent) and a normal BMI (n=17; 32.7 percent), as well as a heavy sedentary lifestyle (n=45; 86.5 percent) and a moderate or light (n=7; 13.5 percent) lifestyle. Using the chi-square statistical test, the results of the two variables analysis, sedentary lifestyle and body mass index category, yielded a p-value of 0.003 and an odds ratio of 17.37 (95 percent CI:2.262–440.1). When compared to students who have a mild or moderate sedentary lifestyle, students with a severe sedentary lifestyle have odds 17.37 times higher chance of having a BMI above normal.

Conclusions: There is a substantial link between a sedentary lifestyle and a BMI over the usual limit among Jayapura Christian School Junior High School students.

Introduction

Sedentary lifestyle is one of many risk factors that can lead to an increase in body weight above what is considered

normal (obesity or overweight), which is a risk factor for cardiovascular illnesses. Low levels of physical activity, in addition to a sedentary lifestyle, are a risk factor for obesity, diabetes, hypertension, and other

diseases. Sedentary lifestyle is estimated to cause 2 million deaths worldwide, making it one of the top ten causes of mortality.^{1,2}

The additional of today's technological advancement among society have made many individuals, including children, spending more times watching television, playing video games, or even use social media with the help of either computers or phones. Behaviors like these are called sedentary lifestyle.

As a result of today's technological advancements in society, many people, including youngsters, are spending more time watching television, playing video games, or even using social media on computers or phones. Sedentary behaviors are referred to as sedentary lifestyles^{3,4,5}, which refers to any activity performed outside of bedtime that does not require a lot of energy. Sedentary lifestyles include activities done while studying online in a sitting or sleeping position, as well as passive activities done at home or elsewhere such as playing computer games, using social media, or watching television, which all increase the risk of gaining weight and eventually becoming obese.^{6,7} The purpose of this study is to look into the link between a sedentary lifestyle and a high BMI among Jayapura Christian School Junior High School students.

Material And Methods

This is a cross-sectional study of 52 students from Jayapura Christian School Junior High School. Between January and May 2021, data was gathered using the Adolescent Sedentary Activity Questionnaire (ASAQ) to determine the Sedentary Lifestyle Category and Body Mass Index categories to determine normal, overweight, and obese. Teenagers between the ages of 12 and 16 are the target demographic. Purposive sampling was used to collect samples for this study.

Result

This study involved 52 students of Jayapura Christian Junior Highschool, consist of 48.1% male and 51.9% female with range age 12-16 years old. Table 1 has shown the Body mass index measurement has show most of the respondent are overweight and obese (n=35 or 67.3%) and normal (n=17 32.7%). The questionnaire result has show that most of the respondent have heavy sedentary life style (n=45; 86.5%) and moderate + light only 7 respondents or 13.5%.

Table 1. Characteristic of Respondents

Variabel	N	%
Gender		
Male	25	48.1
Female	27	51.9
Age		
12	6	11.5
13	9	17.3
14	6	11.5
15	8	15.4
16	23	44.3
BMI		
Normal	17	32.7
Overweight+Obese	35	67.3
Sedentary Life Style		
Heavy	45	86.5
Moderate+Light	7	13.5

Table 2. Type of Activity with Sedentary Lifestyle Category

Type of activity	Mild		Moderate		Severe	
	n	%	n	%	n	%
Watching TV/Video	19	36.5	15	28.9	18	34.6
Playing Games	32	61.5	12	23.1	8	15.4
Study	9	17.3	18	34.6	25	48.1
Doing Hobbies	3	5.8	10	19.2	39	75

On the basis of table 2. The most common type of activity that people engage in throughout a week is worshipping 44 people, hobbies (driving, reading, playing musical instruments, and using cell phones) 39 people, and studying up to 25 people.

Meanwhile, the most frequent moderate sedentary lifestyle activity was using a computer/laptop to play games, which involved up to 32 individuals, and watching TV/video, which involved 19 people.

Table 3. Association of Sedentary Lifestyle and Body Mass index

Sedentary Life style	Overweight+ Obese		Normal		P Value	OR 95% CI
	n	%	n	%		
Severe	34	75.6	11	24.4	0.00 352	17.37
Mild+Moderate	1	14.3	6	85.7		2.26-440

*Analysis by using chi-square analysis

According to the results of Table 3, data from 52 respondents indicate that 34 people (75.6 percent) have a severe sedentary lifestyle and are overweight or obese, while 11 people (24.4 percent) have a normal weight. Meanwhile, only 1 person (14.3 percent) with a mild or moderate sedentary lifestyle was overweight or obese, while 6 persons (85.7 percent) were normal weight. The Chi-square analysis revealed a p-value of 0.003, indicating a significant association between a sedentary lifestyle, body mass index, and the occurrence of weight gain over normal among Jayapura Christian School Junior High School students. According to the table above, the OR value is 17.37, indicating that students who follow a severe sedentary lifestyle have odds of 17.37-fold increased chance of being overweight or obese compared to students who follow a mild or moderate sedentary lifestyle.

Discussion

According to the findings and discussion above, there is a significant association between sedentary lifestyle,

body mass index, and the occurrence of weight increase over normal among Junior HighSchool students at Jayapura Christian School, with a p value of 0.003.

The results can be derived that the most common severe sedentary lifestyle activity performed during the week is worship (84.6 percent), as evidenced by the fact that they participated in two worship activities, namely public worship and youth worship, for a total of four to five hours each week.

Meanwhile, the most severe sedentary behavior performed on a weekly basis is playing games (15.3 percent) on a laptop or computer, as indicated in the interview that they prefer smartphones to laptops or desktops. Apart from the activities mentioned previously, other activities such as driving, reading, playing musical instruments, using a cellphone, and studying may result in weight gain above the normal level among Junior High School students at Jayapura Christian School due to the amount of time spent sitting or lying down while performing activities, resulting in a decrease in energy expenditure. This can result in the accumulation of body fat, which results in overweight and obesity. Previously, similar research was conducted in 2019 among primary school pupils in Makassar. The findings indicate a link between a sedentary lifestyle and obesity.

This research has certain limitations. Because this study used a cross-sectional design, the causal relationship between sedentary lifestyle and BMI is unclear, and there is a difficulty with temporality. Selection bias and measurement bias are limited when purposive sampling is used.

Conclusions

Sedentary living behavior is strongly linked to being overweight or obese

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Knowledge, Attitude and Behavior of Methodist 2 Palembang High School Student towards Clean and Healthy Lifestyle (PHBS)

Theodora Christine ¹, Dwi Savitri Rivami ²

^{1,2} Faculty of Medicine, Universitas Pelita Harapan

Abstract

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Correspondance : Theodora Christine. Faculty of Medicine, Universitas Pelita Harapan.

E-mail : theodora0909@yahoo.co.id

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Background: Clean and Healthy Lifestyle or namely PHBS (Perilaku Hidup Bersih dan Sehat) in Indonesia is a program from the Indonesian Ministry of Health that has been implemented since 1996. PHBS in school settings is very important to be realized in order to create a clean and healthy school environment so that the learning and teaching process can run effectively.

Aims: This study aims to describe the knowledge, attitudes and behavior of Methodist 2 High School students towards PHBS. In addition, this study also aims to see the relationship between PHBS knowledge and attitudes towards PHBS behavior in Methodist 2 Palembang High school students

Methods: This study uses a cross-sectional study involving 216 students obtained by calculating unpaired categorical analytic samples. Samples were taken using purposive sampling technique. Data was collected using a questionnaire distributed online via google form. The data obtained were processed using Chi Square through the SPSS 25.

Result: There were 216 respondents who met the inclusion and exclusion criteria of this study. The sample consisting of female (n=124 (57.4%)) and male (n=92 (42.6%)) and distributed evenly from 1st grade to 3rd grade (1st grade n=65 (30.1%), 2nd grade n=75 (34.7%), 3rd grade n=76 (35.2%)). Using average value as cut off point (12.7), most of the students of Methodist 2 Palembang high school had a sufficient knowledge of PHBS (n=132 (61%)) and the rest of it had insufficient knowledge of PHBS (n=84 (38.9%)). With median value (57.6) as the cut-off point, it showed that most of the students had a sufficient PHBS attitude (n=118 (54.6%)) and the rest of it had insufficient attitude of PHBS (n=98 (45.5%)). With average value (13.2) as cut off point, most of the students had insufficient PHBS behavior (n=102 (52.8%)) and the rest of it had sufficient behavior of PHBS (n=102 (42.7%)). The results of the analysis found that there was no significant relationship between knowledge and PHBS behavior among Methodist 2 Palembang high school students (p value = 0.744) and there was a significant relationship between PHBS attitudes towards PHBS behavior among Methodist 2 Palembang high school students (p value = <0.001)

Introduction

Clean and Healthy Lifestyle or more commonly known as PHBS (*Perilaku Hidup Bersih dan Sehat*) in Indonesian is one of the Ministry of Health of the Republic of Indonesia programs that has been implemented since 1996.^{1,2} PHBS defined by the Indonesia Health Ministry as a collection of behaviors that are practiced on the basis of personal

awareness as a result of learning, which makes a person, family, group or community able to help themselves independently in the health sector and play an active role in realizing public health.¹ Healthy living behavior stated by Hitchcock, et al. in 2004 covering physical and emotional health care, not smoking, and not using narcotics.³ in 2001 Nies, et al. also stated that a good healthy lifestyle

includes adequate sleep (7-8 hours a day), eating nutritious foods, not drinking alcohol, and doing regular physical activity.⁴

PBHS has five arrangements, namely PBHS in households, schools, workplaces, health facilities and public places.^{1,2} PHBS arrangements in schools have eight indicators, namely: washing hands with clean water and soap before and after eating, consuming healthy snacks, using healthy latrines, exercising regularly, eliminating mosquito larvae, not smoking in the school area, throwing garbage in its place, and not consuming narcotics, alcohol, psychotropics and other addictive substances.^{2,5}

PHBS in the school setting aims to empower all school members (students, teachers and the school community) to implement a healthy lifestyle in order to create a clean and healthy school environment.^{1,6} Schools with a clean and healthy environment strongly support the learning and teaching process.^{1,2,6}

There are several factors that can affect the implementation of PHBS in schools, which are:⁷

1. The role of teachers in providing education regarding PHBS
2. Attitudes owned by schools in health care
3. School facilities that support the implementation of PHBS

According to Bloom's explanation in 1975 quoted in Notoadmojo in 2003, knowledge is a result of knowing and this occurs after someone has sensed a certain object. A person in carrying out an action is very dependent on the knowledge or cognitive domain.⁸ Knowledge has six levels of cognitive domain which are: knowledge,

comprehension, application, analysis, synthesis and evaluation.⁸⁻¹¹

Attitude is a closed response that a person gives to a stimulus or object. The meaning of a closed response is that the reaction has not been realized into an open behavior or in other words, attitude is a predisposition of a behavior.⁸

Behavior is all activities carried out by humans, where these activities can be observed directly or indirectly by outsiders.^{8,10,11}

In 2018 Riset Kesehatan Dasar (RISKESDAS) or basic health research in Indonesia stated that some of the PHBS indicators did not show a positive increase from the 2013 RISKESDAS results. The indicators were: smoking prevalence aged 10-18 years, lack of physical activity at the age of 10 years.¹² Another survey done by the Depok Public Health Office during 2013 and 2014 found a decrease in the percentage for implementing PHBS in school settings.^{13,14} The decrease in percentage occurred in indicators: consuming healthy snacks from 67.96% to 54%, throwing garbage in its place from 75.08% to 47.5% and several other indicators such as washing hands with clean water, using clean latrines, eradicating mosquito larvae.^{13,14} In 2017 Prautami conducted a study on high school students in a school in Palembang regarding PHBS behavior (smoking behavior), and found as many as 63.3% of high school students who smoke.¹⁵ In addition to smoking, in Palembang itself there are also problems in terms of drug use behavior. The National Narcotics Agency or Badan Narkotika Nasional (BNN) of South Sumatra in 2019 stated that there were more than 96,000 cases of drug use, where most of the users were teenagers.

Objectives

This study is conducted with the aim of knowing the description and relationship between the knowledge, attitudes, and behavior of Methodist 2 High School students regarding PHBS.

Subjects and Methods

Participants

This study involved all students from all levels at SMA Methodist 2 Palembang. There were 216 respondents out of 242 who met the inclusion criteria and exclusion criteria. A total of 26 respondents were excluded because they did not answer the questionnaire completely.

Study design

This study used a cross-sectional study design and this study was conducted from January 2021 to February 2021. The sampling in this study used a purposive sampling technique and by calculating the unpaired categorical analytical study formula, the minimum required sample was 216 samples. This research was approved by the ethics committee of the Faculty of Medicine, Pelita Harapan University.

Research Instrument

Data were collected using several questionnaires that were distributed to respondents using a google form. The questionnaires contain questions and statements regarding knowledge, attitudes and behavior towards PHBS. In addition, there are also questionnaires containing socio-demographic data of the respondents (name, gender and grade) and questionnaires regarding PHBS facilities.

Statistical Analysis

Data analysis was carried out using Microsoft Excel and IBM SPSS Statistics 25. The data obtained were processed using Chi square to determine the relationship between knowledge and attitudes towards PHBS behavior in Methodist 2 Palembang High School students. It is said to be significant if the p value is <0.05 .

Results

Respondent Characteristic

Table 1. Respondent Characteristic (N=216)

Respondent Characteristic	Number of Participant	Percentage (%)
Gender		
Male	92	42.6%
Female	124	57.4%
Grade		
1 st grade	65	30.1%
2 nd grade	75	34.7%
3 rd grade	76	35.2%

Research on the knowledge, attitudes and behavior of clean and healthy living involved all students from all levels in Methodist 2 Palembang Highschool. There were 216 respondents who met the inclusion and exclusion criteria. Most of the respondents were women (57.4%) and the respondents were evenly distributed from 1st grade to 3rd grade.

Knowledge, Attitude and Behavior towards PHBS

Table 2. Knowledge, Attitude and Behavior towards PHBS

	Number of Participant	Percentage (%)
Knowledge*		
Cutoff with median value (7)		
Insufficient (< 7)	0	0%
Sufficient (≥ 7)	216	100%
Cut off with average value (12,7)		
Insufficient (<12.7)	84	38.9%
Sufficient (≥12.7)	132	61.1%

Attitude**		
Insufficient (<57.6)	98	45.5%
Sufficient (≥57.6)	118	54.6%
Behavior***		
Cutoff with median value (8)		
Insufficient (< 8)	0	0%
Sufficient (≥ 8)	216	100%
Cutoff with average value (13,2)		
Insufficient (< 8)	114	52.8%
Sufficient (≥ 8)	102	42.7%

* Original cutoff for knowledge was 7 (median value). Score for knowledge (0-14). Average value for knowledge is (12.7)

** Attitudes are categorized into sufficient and insufficient using the average value (57.6)

*** Original cutoff for behavior was 8 (median value). Score for behavior (0-16). Average value for behavior is (13.2)

Initially the assessment of the questionnaire was divided into sufficient and insufficient knowledge of PHBS using the median value (7) as the cut-off point. It was found that all respondents had sufficient knowledge of PHBS (100%). Therefore, the cut value for knowledge is changed to the average value (12.7) so that in the Chi square calculation (the relationship between knowledge and behavior) there will be no cells with a value of 0. With knowledge, using the cut-off point of the average value (12.7) found that more than half of the respondents (61.1%) had sufficient knowledge of PHBS.

For the calculation of attitude assessment using the average value (57.6) as the cut-off point and it was found that the majority had a sufficient attitude towards PHBS (54.6%).

The initial behavioral assessment used the median value (8) as the cut-off point, and it was found that all respondents (100%) had sufficient PHBS behavior. Therefore, the cut-off point for PHBS behavior was changed to the average value (13.2) so that in the Chi square calculation there were no cells with a value of 0. With behavior, using the

mean value cut-off point (13.2) found that the majority of respondents had insufficient PHBS behavior (52.8%).

Facilities of PHBS

Methodist 2 Palembang High School has all the facilities that support the implementation of PHBS. The facilities in question are clean and healthy latrines, clean water and soap are always available at school toilets, smoking bans in schools, activities to eradicate mosquitoes, activities to clean the school environment, good waste disposal sites, scales are in good condition and functioning well in the school health unit.

Statistical Test Result

Table 3. Analysis of the relationship between PHBS knowledge and PHBS behavior (N=216)

Knowledge of PHBS*	PHBS Behavior**		P value	Ratio (OR)	CI (95%)
	Good (≥13,2) n (%)	Poor (<13,2) n (%)			
Sufficient (≥12,7)	64 (48,5%)	68 (51,5%)	0,744	1,139	0,658-1,972
Insufficient (<12,7)	38 (45,2%)	46 (54,8%)			

* Sufficient and insufficient knowledge categories use the average value (12.7)

** Sufficient and insufficient behavior categories use the average value (13.2)

Analysis of the relationship between PHBS knowledge and PHBS behavior using Chi squared obtained a p value of 0.744. The p-value obtained is >0.05 so it can be said that there is no significant relationship between PHBS knowledge and PHBS behavior in Methodist 2 Palembang High School students.

Tabel 4. Analysis of the relationship between PHBS attitude and PHBS behavior (N=216)

PHBS Attitude*	PHBS Behavior**		P value	Ratio (OR)	CI (95%)
	Good (≥13,2) n (%)	Poor (<13,2) n (%)			
Sufficient (≥57,6)	72 (61,0%)	46 (39,0%)	<0,001	3,548	2,103-6,254
Insufficient (<57,6)	30 (30,6%)	68 (69,4%)			

Analysis of the relationship between PHBS attitudes towards PHBS behavior using chi squares obtained a p value of <0.001. Because the p value <0.05, it can be stated that there is a significant relationship between PHBS attitudes towards PHBS behavior in Methodist 2 Palembang High School students. Students with insufficient PHBS attitudes have a 3.5 times risk of showing insufficient PHBS behavior compared to students who have sufficient attitudes of PHBS.

Discussion

Relationship between PHBS knowledge and PHBS behavior in Methodist 2 Palembang high school students

The results of the analysis of the relationship between PHBS knowledge and behavior towards PHBS in Methodist 2 Palembang High School students who used chi squared obtained a p value of 0.744. Because the p value > 0.05, it can be stated that there is no significant relationship between PHBS knowledge and behavior towards PHBS in Methodist 2 Palembang High School students.

This study is not in line with research conducted by Zubaidah in 2014.¹⁴ Zubaidah conducted a study entitled "The Relationship of Demographic Characteristics, Knowledge and Attitudes with PHBS of Depok City Elementary

School Students".¹⁴ Zubaidah's research stated that there was a significant relationship between PHBS knowledge and PHBS behavior.¹⁴ This research is also not in line with research conducted by Prautami in 2017. Prautami conducted a study entitled "The Relationship of Knowledge and Attitudes with Smoking Behavior in Adolescents at PGRI 2 Palembang High School." In his research, he found a significant relationship between PHBS knowledge and PHBS behavior.¹⁵

In this study, it was found that there was no significant relationship between PHBS knowledge and PHBS behavior. The reason for this is because behavior is not only influenced by knowledge, but also by attitudes.¹⁴ In other words, a behavior arises because of stimuli from inside and outside the body (knowledge/cognitive), but the behavior itself is also determined by the feelings towards the stimulus (attitude/affective).^{8,14,16}

In addition, the insignificant results in this study can also be influenced by the sample selection method. The sample selection method in this study is purposive sampling where the sampling is determined or adjusted to the research objectives so that the sample does not represent the general population. Meanwhile, in the research conducted by Zubaidah and Prautami, both of them used a sample selection method that could better represent the general population, namely simple random sampling.

Relationship between PHBS attitude and PHBS behavior in Methodist 2 Palembang high school students

In this study, it was found that the attitudes of Methodist 2 High School

students towards sufficient and insufficient PHBS were almost the same (sufficient attitude 54.6%, insufficient attitude (45.5%). The results of the analysis of the relationship between PHBS attitudes and behavior towards PHBS in students Methodist 2 Palembang High School which uses chi squared obtained p value of <0.001 . From the p value obtained, it can be said that there is a significant relationship between PHBS attitudes and behavior towards PHBS in Methodist 2 High School students. Based on the odds ratio value, students who have insufficient PHBS attitudes have a 3.5 times greater risk for insufficient PHBS behavior compared to students who have sufficient attitudes of PHBS.

This research is in line with research conducted by Zubaidah in 2014 with the title "Relationship of

Demographic Characteristics, Knowledge and Attitudes with PHBS of Depok City Elementary School Students".¹⁴ In his research, it was found that there was a significant relationship between PHBS attitudes and PHBS behavior. This study also in line with the research conducted by Fauziah in 2004 with the title "Factors Associated with Clean and Healthy Life Behavior in 2 Elementary Schools (With and Without the PHBS Program) at Pakjo Palembang Village." In his research, it was found that there was a significant relationship between PHBS attitudes towards PHBS behavior. The research conducted by Fauziah divided the categories of attitudes into negative and positive, the categories of behavior became poor and good, then from the research it was found that 21.9% of students who had positive attitudes with poor behavior and 78.1% of students with positive attitudes had good PHBS behavior.¹⁷

A similar study was also conducted by Prautami in 2017. Prautami conducted research related to one of the indicators of PHBS, namely smoking. The research entitled "The Relationship of Knowledge and Attitudes with Smoking Behavior in Adolescents at SMA PGRI 2 Palembang." The results of the study showed that there was a significant relationship between smoking attitudes and smoking behavior.¹⁵

This research is in line with several studies that have been conducted previously. Attitude itself is a predisposing factor in the occurrence of a behavior according to Green's theory in 1980 which was presented by Zubaidah in 2014.¹⁴ One of the three behavioral domains is affective where affective is focused on a feeling, emotion or can also be referred to as the level of acceptance or rejection. This affective itself is also often referred to as attitude. Zubaidah in 2014 also emphasized that the attitude involves thoughts, attention and other psychological matters or in other words the attitude is a collection of symptoms that respond to a stimulus or object.¹⁴

Conclusion

The conclusion of this study is:

1. Most students have sufficient PHBS knowledge (61.1%) and the rest have insufficient knowledge of PHBS (38.9%)
2. The majority of the students of SMA Methodist 2 Palembang (54.6%) have a sufficient attitude towards PHBS
3. More than half of the students (52.8%) have insufficient PHBS behavior and the rest have sufficient behavior of PHBS (42.7%)
4. There is no significant relationship between knowledge and PHBS behavior in Methodist 2 Palembang

High School students

5. There is a significant relationship between attitudes towards PHBS behavior in Methodist 2 Palembang High School students

Limitation

This study was conducted using a self-report questionnaire which could lead to a risk of bias. The bias could be due to the respondent in filling the questionnaires.

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Reversible Bilateral Basal Ganglia and Brainstem Lesions in Neuropsychiatric Systemic Lupus Erythematosus: A Case Report

Rocksy Fransisca V Situmeang^{1,2}, Reza Stevano², Ekawaty Yasinta Yohana Larope^{2,3}, Ratna Sutanto^{2,4}

¹ Department of Neurology, Siloam Hospitals Lippo Village

² Faculty of Medicine, Pelita Harapan University

³ Department of Pediatrics, Siloam Hospitals Lippo Village

⁴ Department of Radiology, Siloam Hospitals Lippo Village

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***Correspondance:** Rocksy Fransisca V Situmeang. Department of Neurology, Siloam Hospitals Lippo Village, Faculty of Medicine, Pelita Harapan University

E-mail : rocksy.situmeang@lecturer.uph.edu

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The pathophysiology behind neuropsychiatric SLE (NPSLE) remains poorly understood and its clinical and radiological manifestations are highly varied. In this report, we present a complex case of an adolescent female patient with a three-week history of systemic symptoms (fever, nausea, vomiting, weight-loss, polyarticular joint pain), progressive motor weakness, tremor, and altered mental status. Physical examination was significant for oromandibular and cervical dystonia rigidity, and general weakness with imposed right-sided hemiparesis. A head MRI demonstrated bilateral hyperintense lesions of the basal ganglia and brainstem, SSwithout restricted diffusion. The patient was diagnosed with NPSLE, lupus nephritis, electrolyte imbalance, severe hypoalbuminemia, lupus cardiomyopathy, autoimmune hemolytic anemia, pulmonary tuberculosis, and sepsis. The patient was given treatment in the ICU with pulse dose corticosteroids, intravenous antibiotics, intravenous immunoglobulins (IVIg), and supportive treatment with correction of hematologic and electrolyte abnormalities. Her condition improved rapidly. Full alertness was regained, and symptoms of oromandibular dystonia, tremor, and weakness diminished significantly. A follow-up MRI three weeks later revealed complete disappearance of lesions, which we attribute to resolution of the inflammatory process in the brain.

Introduction

Nervous system involvement in systemic lupus erythematosus (SLE), or neuropsychiatric SLE (NPSLE), constitutes a serious complication affecting up to 40% of all SLE patients.¹ According to nomenclature set by the American College of Rheumatology (ACR), NPSLE can be categorized into 19 distinct manifestations, 12 involving the central nervous system (CNS) and 7 involving the peripheral.² The clinical and radiological manifestations of NPSLE are widely varied, from mild cognitive dysfunction to potentially fatal

cerebrovascular accidents, with serious implications to both prognosis and quality of life.³ Multiple diagnostic modalities, such as serology and neuroimaging, are often required to support the diagnosis and exclude the presence of other conditions. Previous studies have shown that approximately 50% of NPSLE patients present with abnormal MRI features, in which vascular lesions were the most common finding, accounting for nearly 70% of MRI abnormalities, while inflammatory lesions compose just 6.5% of abnormalities.^{4,5} We present an adolescent NPSLE patient with an atypical feature of bilateral near-

symmetrical basal ganglia and brainstem lesions, suspected of inflammatory origin, that disappeared completely following the administration of immunoglobulin therapy.

Case

A 16-year-old Melanesian female was referred from Sorong, West Papua, with a three-week history of remittent fever, nausea, vomiting, abdominal pain, poor intake, palpitations, headaches, progressively worsening general weakness with pronounced right-sided involvement, tremor, and polyarticular joint pain. The patient reports a history of weight loss within the past three months, and experienced difficulties in moving her neck and mouth, producing difficulties in communication. She has a history of pulmonary tuberculosis diagnosed one month before and was started on anti-tubercular drug therapy. Two days before admission, she fell unconscious. Previous medical, family, and social history was found to be non-significant. Examinations in the previous hospital reveal the presence of anemia, leukopenia, thrombocytopenia, severe hyponatremia, and an elevated ESR. Tests for the presence of malaria, dengue, and ASTO were found to be negative. Urinalysis was significant for marked albuminuria and hematuria. An ANA profile was ordered, and the patient was found to be positive for anti-SM, anti-dsDNA, anti-NUC, anti-HI, anti-RIB, anti-M2, and anti-DFS70. Findings were suggestive of SLE with lupus nephritis and pulse dose corticosteroids were given and hyponatremia corrected, after which her condition improved in following days. She was then referred to our hospital.

Upon physical examination, she was somnolent, tachycardic, tachypneic, hypotensive and febrile. General examination found conjunctival pallor,

bilateral rhonchi, epigastric tenderness, and bilateral lower extremity pitting edema. On neurological examination, severe oromandibular and cervical dystonia were found that resulted in speech difficulties and the inability to open her mouth and move her neck, while still able to understand and obey commands. General weakness with imposed right-sided hemiparesis was also present. Physiological reflexes were decreased, and no pathological reflexes nor clonus were found, as well as sensoric abnormalities.

Laboratory tests reveal the presence of a normocytic normochromic anemia with features suggestive of autoimmune hemolysis (elevated LDH, and positive coombs' test), thrombocytopenia, hyponatremia, hypocalcemia, as well as elevated D-dimer, procalcitonin, transaminases, direct bilirubin and ureum levels. Complement levels (C3, C4), lupus anticoagulants (LA1, LA2), and anti- β 2GPI IgG and IgM, were also found to be low. An echocardiogram revealed a regional wall motion abnormality with reduced left-ventricular systolic function, mild-moderate mitral and tricuspid regurgitation, and mild pericardial effusion, suggestive of lupus cardiomyopathy. A lumbar puncture was planned, but could not be performed due to hemodynamic compromise. Diagnoses considered include tuberculous meningitis, osmotic degradation syndrome (ODS), and acute disseminated encephalomyelitis (ADEM). A head MRI with contrast was done, and revealed bilateral hyperintense lesions of the basal ganglia, with greater involvement of the left hemisphere, and the posterior aspect of the midbrain-pons, on T2, FLAIR, and DWI sequences, without restricted diffusion or contrast-enhancement. Due to the presence of these lesions, frank signs of systemic SLE, absence of

leptomeningeal enhancement typical of meningitis, and white matter lesions as in ADEM, a final diagnosis of NPSLE was made, along with lupus nephritis, electrolyte imbalance, severe hypoalbuminemia, lupus cardiomyopathy, autoimmune hemolytic anemia, pulmonary tuberculosis, and sepsis.

During hospitalization, the patient was transferred to the ICU for four days due to cardiorespiratory failure and was intubated and ventilated mechanically. She received methylprednisolone, calcium gluconate, digoxin, bisoprolol, lisinopril, furosemide, vitamin D supplementation, albumin, ceftriaxone, meropenem, micafungin, and multiple packed red cell transfusions. Anti-tubercular drugs were temporarily halted due to suspected hepatotoxicity. Considering the lack of neurological improvement and presence of contraindications in administering immunosuppressants, we decided to give 10% IVIg (2 grams per kilogram of body weight over a period of five days) beginning on day-eight of care. She improved markedly, with complete resolution of oromandibular and cervical dystonia, tremor, and significant motor improvement following physical therapy. Antitubercular drugs were reintroduced in stages, starting with isoniazid and ethambutol, and the full regimen was successfully reintroduced with good tolerance. At a follow-up MRI performed three weeks later, both bilateral basal ganglia and pontine lesions disappeared completely.

Discussion

The pathomechanism behind NPSLE remains poorly understood and could be a result of multiple factors. There are two primary theories regarding the process involved in NPSLE: the non-

inflammatory and inflammatory mechanisms. Non-inflammatory mechanisms of NPSLE are attributable to thromboses of both large and small intracranial blood vessels, possibly mediated by autoantibodies, immune complex formation, complement deposition, leukoagglutination, and accelerated atherosclerosis. The inflammatory mechanism involves autoantibody and inflammatory mediator-mediated dysfunction, and may be accompanied by blood-brain-barrier dysfunction and intrathecal immune complex formation.^{6,7}

The clinical and radiological features of NPSLE vary immensely, complicating efforts in establishing the diagnosis, which often requires a combination of multiple modalities such as immuno-serology tests, neuroimaging, and neuropsychiatric evaluation. Previous studies demonstrated that abnormal appearances on MRI are found in approximately 50% of NPSLE patients, in which vascular lesions (composed of a range of small vessel manifestations and large vessel disease) are the most common finding, accounting for nearly 70% of abnormalities.^{4,5} In a different study evaluating MRI features in diffuse NPSLE, abnormalities were observed in 47.2% of patients, among which multiple white matter hyperintensities, seen on T2-weighted or FLAIR, were the most common finding (88% of abnormal results). Grey matter hyperintensities, located in the basal ganglia, cerebellum and brainstem, followed with 28% (86% of which existed concurrently with white matter lesions).⁸ Another study corroborated these results, in which 46% of NPSLE patients were found to have white matter hyperintensities on MRI.⁹

In our case, the lesions were of gray-matter origin, and distributed near-symmetrically in the basal ganglia and

midbrain-pons. The lesions exhibited high intensity signaling on T2, FLAIR, and DWI sequences, without restricted diffusion or contrast enhancement. The symmetrical distribution of lesions, as well as its selectiveness for gray-matter areas, effectively excludes vascular, specifically large vessel disease, as the cause for the patient's condition. Furthermore, the pattern of increased signaling on T2, FLAIR, and DWI, without restricted diffusion, may be suggestive of vasogenic edema or inflammation, while the lack of contrast enhancement denotes a relatively intact blood-brain barrier.¹⁰ Taken together, the constellation of these findings suggests an inflammatory, perhaps vasculitic, process involving the basal ganglia and midbrain-pons. The physical findings observed in the patient, such as tremor, oromandibular and cervical dystonia, and right-sided hemiparesis, are consistent with abnormalities found on imaging. Both tremor and oromandibular dystonia may appear secondary to lesions of the basal ganglia.¹¹ Additionally, the significant improvement in symptoms experienced by the patient following IVIg administration serves as further evidence that an immune-mediated process underlies the patient's condition. A limitation to our case report is that we could not perform a lumbar puncture and CSF analysis due to risks of hemodynamic compromise, hence we could not objectively confirm nor exclude the presence of intracranial inflammation.

Based on imaging, a number of disease entities may be suspected as the cause for the patient's condition, including ADEM, posterior reversible encephalopathy syndrome (PRES), and progressive multifocal leukoencephalopathy (PML). ADEM, PRES, and PML are inflammatory disorders of the CNS, and consistent with

what can be observed in the patient, may appear as hyperintense on T2 and FLAIR, with variable restricted diffusion and contrast enhancement patterns. While most commonly appearing in subcortical white-matter areas, cases of gray-matter lesions, including basal ganglia and brainstem involvement, have been reported.^(12–14) Additionally, all three diseases have been associated with SLE, either as a direct result of an immune process, secondarily as complications of immunosuppressive treatment, or both. Additionally ODS, which could potentially manifest bilateral basal ganglia lesions as a result of extrapontine involvement, has also been considered in the patient, considering her history of severe hyponatremia and correction. However, ODS is unlikely as pontine lesions in ODS tend to be centrally placed with a characteristic “trident-shaped” lesion, while the midbrain-pons lesion found in the patient is located posteriorly.¹⁵

Although rare, similar cases have been reported.^{16–20} Of note, while MRI imaging profiles of the lesions were always nearly identical, the same cannot be said for clinical manifestations experienced by patients, or the attributable cause, in which proposed mechanisms include aseptic meningitis¹⁶, immune-mediated lupus vasculopathy¹⁷, and ADEM.¹⁸ Common to these cases are the presence of unilateral or bilateral basal ganglia hyperintensities on T2W, FLAIR, and DWI, while additional hyperintensities could be found in periventricular areas¹⁷, thalamus, midbrain, pons, and cerebellum.¹⁸ Also common are their improvement and reversibility following therapy with corticosteroids and immunosuppressants, which are consistent with current approaches in the treatment of NPSLE.²¹ Compared to these reports however, our case is unique in that immunosuppressant

medication cannot be given due to contraindications, and IVIg therapy was administered instead. In our patient IVIg also had the added benefit as an adjunctive treatment to sepsis in addition to NPSLE, as previous studies have shown that IVIg is effective in reducing mortality in septic patients.²²

Conclusion

The underlying pathophysiology of NPSLE has not yet been completely elucidated, and as NPSLE consists of an umbrella term reflecting 19 distinct

entities, the clinical and radiological features found in NPSLE remain equivocal and non-specific. We report a unique case of an adolescent NPSLE patient with hyperintense lesions of the basal ganglia and midbrain-pons suggestive of vasogenic edema, with complete resolution of both symptoms and imaging following immunoglobulin therapy. We suspect the lesions may be due to an immune-mediated inflammatory process. However, research is needed to further understand the clinical and prognostic significance of these findings.

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