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Correlation of menopausal status, nutritional status, and uric acid level in Indonesian women

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ABSTRAK

Latar Belakang: *Bertambahnya usia dapat menyebabkan perubahan kondisi fisiologis dan psikologis, salah satunya adalah peningkatan kadar asam urat dalam darah atau yang biasa disebut dengan hiperurisemia. Kadar asam urat yang tinggi dalam darah jika tidak ditanggulangi dan dibiarkan dalam rentang waktu yang lama dapat menyebabkan terjadinya berbagai penyakit tidak menular seperti penyakit ginjal kronis, kerusakan sendi dan penyakit kardiovaskular. Prevalensi kejadian hiperurisemia di Indonesia pada tahun 2015 sebesar 18%. Penelitian terkait status menopause dan status gizi pada wanita usia 15-54 tahun di Indonesia masih belum banyak diteliti dengan mengambil beberapa provinsi untuk dijadikan sampel.*
Tujuan: *Menganalisis hubungan antara status menopause dan status gizi dengan kadar asam urat pada wanita usia 15-54 tahun di Indonesia.*
Metode: *Desain pada penelitian ini yaitu cross sectional dengan subjek wanita berusia 15-54 tahun pada 10 provinsi di Indonesia dengan total jumlah responden sebanyak 606 responden. Teknik sampling untuk penentuan provinsi dan kota menggunakan purposive sampling dan penentuan kecamatan atau kelurahan menggunakan random sampling. Kadar asam urat diperoleh dari pengukuran darah kapiler dan status gizi diperoleh dari pengukuran antropometri yang dilakukan oleh tenaga kesehatan terampil. Status menopause diperoleh dari wawancara oleh enumerator terlatih yang menanyakan terkait riwayat menstruasi dalam satu tahun. Pengelompokkan status menopause dibagi menjadi belum menopause, pra menopause dan menopause.*
Hasil: *Sebanyak 42,9% dari total responden mangalami obesitas, sebagian besar berada pada kelompok usia 41-54 tahun. Subjek yang menderita hiperurisemia sebanyak 21.1% dan yang telah memasuki masa menopause dalam penelitian ini sebanyak 11.4%. Adanya hubungan yang signifikan antara status menopause dengan kadar asam urat (p=0,031) dan adanya hubungan yang signifikan antara status gizi dengan kadar asam urat (p<0,001;r=0,193).*
Kesimpulan: *Kadar asam urat pada wanita yang obesitas dan menopause cenderung akan meningkat jika dibandingkan dengan wanita yang berstatus gizi normal dan belum menopause.*

KATA KUNCI*: hiperurisemia; kadar asam urat; status gizi; status menopause; wanita*

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ABSTRACT

Background: *Increasing age can cause changes in physiological and psychological conditions, one of which is an increase in uric acid levels in the blood, commonly referred to as hyperuricemia. High uric acid levels in the blood, if not addressed and left for a long time, can lead to various non-communicable diseases such as chronic kidney disease, joint damage, and cardiovascular disease. The prevalence of hyperuricemia in Indonesia in 2015 was 18%. Research related to menopausal status and nutritional status in women aged 15-54 years in Indonesia has not been widely studied by taking several provinces as samples.*

Objectives: *To analyze the relationship between menopausal status and nutritional status with uric acid levels in women aged 15-54 years in Indonesia..*

Methods: *The design of this study was cross-sectional, with female subjects aged 15-54 years in 10 provinces in Indonesia and a total number of 606 respondents. Sampling techniques for determining provinces and cities using purposive sampling and determining sub-districts or villages using random sampling. Uric acid levels were obtained from capillary blood measurements, and nutritional status was obtained from anthropometric measurements conducted by skilled health workers. Menopausal status was obtained from interviews by trained enumerators who asked about menstrual history in one year. The classification of menopausal status was divided into not yet menopausal, pre-menopausal, and menopausal..*

Results: *A total of 42.9% of the total respondents were obese, mostly in the age group of 41-54 years. Subjects who suffered from hyperuricemia were 21.1%, and those who had entered menopause in this study were 11.4%. There is a significant relationship between menopausal status and uric acid levels ($p=0.031$), and there is a significant relationship between nutritional status and uric acid levels ($p<0.001$; $r=0.193$).*

Conclusions: *Uric acid levels in obese and menopausal women tend to increase when compared to women with normal nutritional status and not yet menopausal.*

KEYWORD*:* *hyperuricemia; menopausal status; nutritional status; uric acid levels; women*

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INTRODUCTION

One indicator of a country's development success can be seen in the degree of public health. Indicators for assessing public health include population mortality, morbidity, and life expectancy. The higher the life expectancy, the more successful health development is (1). Increasing age can affect a person's psychological and physiological conditions (2). Increasing age is at risk of experiencing various complaints and health problems, one of which is hyperuricemia, which is a condition where there is an increase in blood uric acid levels above normal (3). In an epidemiological study, a person is said to have hyperuricemia if uric acid levels in men are more than 7.0 mg/dL and in women more than 6.0 mg/dL (4). Increased uric acid levels can occur in men over 30 years and women after menopause due to decreased production of the hormone estrogen (5). The world's population with hyperuricemia or gout doubled from 1990 to 2010 (6). In several Southeast Asian countries, the proportion of hyperuricemia in Indonesia is 18%, in the Philippines 25%, and in Thailand 11% (7). In Indonesia, hyperuricemia or gout is second only to osteoarthritis, estimated at 1.6-13.6% of the population (100.000 people); this proportion will likely continue to increase as people age (8). In women, there is an increase in uric acid when entering menopause; this is related to the hormone estrogen. The role of this hormone is to help remove uric acid through urine. Men do not have high estrogen hormones, so this causes uric acid to be difficult to remove from the body. Patients with hyperuricemia are found more in women who have entered menopause; this is due to a decrease in estrogen production. The presence of estrogen is very important because it

can help regulate uric acid secretion and protect women from the risk of hyperuricemia (9).

Risk factors that affect uric acid levels can be classified into two factors, namely factors that cannot be controlled (age, gender, and genetics) and factors that can be controlled (food consumption, alcohol consumption, physical activity, and nutritional status) (8). Hyperuricemia is closely related to nutritional status (10). Body Mass Index (BMI) is one of the simple ways to assess a person's nutritional status (11). Nutritional status can be influenced by diet, lifestyle, and socioeconomic factors (12). Excess body mass index can cause an increase in leptin levels in the body. Leptin is a compound that regulates the concentration of uric acid in the blood. Leptin also functions as an appetite controller and regulates the fat-burning process in the body. In obese adults, leptin levels increase, which can cause leptin resistance. If resistance occurs in the kidneys, it can result in urinary resistance, resulting in impaired uric acid excretion through urine, increasing uric acid levels in the blood (13). There has been no research related to the relationship between menopausal status and nutritional status with uric acid levels in the age range of 15-54 years conducted in 10 provinces in Indonesia. This study is expected to provide the proportion of hyperuricemia incidence and the relationship between menopausal status and nutritional status with uric acid levels in women aged 15-54 years in Indonesia.

MATERIALS AND METHODS

The research design used in this study was a cross-sectional study involving women aged 15-54 years. This study was conducted in September 2023-December 2023 in 10 provinces in Indonesia. Submission of the ethical code in this study through the Ethics Commission for Research Involving Human Subjects of IPB University with No: 907/IT3.KEPMSM-IPB/SK/2023. The subjects of this study were obtained from some participants who met the inclusion criteria in the study in collaboration with SEAFEST Center IPB. The inclusion criteria in this study are women aged 15-54 years who can communicate well. Exclusion criteria include suffering from gout and kidney disease. Based on calculations using the Lameshow formula, the minimum number of subjects that must be met in this study is 250 people. Subjects were taken by selecting ten provinces with the largest population in Indonesia based on BPS data in 2021 (14). Assuming that the minimum proportion that must be achieved is 70%, the sampling area can be considered representative of the entire population. So, ten provinces (North Sumatra, Riau, South Sumatra, Lampung, Banten, DKI Jakarta, West Java, Central Java, East Java, and South Sulawesi) were selected with a total of 195.664.900 residents or 71.5% of the total population of Indonesia. The sampling technique for determining provinces and cities used purposive sampling, and subdistricts or villages used random sampling. Based on the calculation of the Slovin formula (n = N/1 + Ne2) with a margin of error of 3%, a sample size of 1036 people was obtained with the addition of 10, so the sample size was 1200 people including men and women aged 15-54 years with age groups namely: adolescents (15-18 years), early adults (19-28 years), middle adults (29-40 years) and late adults (41-54 years).

The types of data collected in this study are primary and secondary. Primary data included menopausal status and uric acid levels, while secondary data included subject characteristics and nutritional status obtained from SEAFAST Center IPB research. Urinary acid levels were measured by taking capillary blood, and nutritional status data was obtained by anthropometric measurements using digital scales and microtomes conducted by skilled health workers. Menopausal status data was obtained through interviews conducted by trained enumerators who asked about the subject's menstrual history within a year. Data processing through editing, coding, entry, cleaning, categorization, and analysis. Data processing using Microsoft Excel 2019 and analyzed using the Statistical Program for Social Sciences (SPSS) version 22. The Spearman test was used to see the relationship between menopausal status and nutritional status with uric acid levels. If the p-value <0.05, there is a significant relationship between the variables tested.

RESULTS AND DISCUSSIONS

Subject characteristics, including age, province, education, occupation, and family history of gout or kidney, are presented in **Table**

1. The total subjects in this study were 606 people aged 15-54 years spread across ten provinces in Indonesia. Based on **Table 1**, most subjects were in the age range of 41-54 years (26.1), and more than a quarter of all total subjects in this study were in the late adult age group. Most of the subjects came from West Java province (23.1%), and the majority had a high school / vocational high school education (50.3%) with a dominant occupation as a housewife (43.6%). The distribution of data in **Table 1** shows that 28.88% of the subjects had relatives who suffered from gout or kidney disease (**Table 1**). Menopause occurs due to decreased levels of the reproductive hormone estrogen. Menopause is a scientific phase that every woman will experience. Table 2 shows that 11.4% of the subjects in this study have experienced menopause.

Table 1. Characteristics of participants

Subjects Characteristic	n=606	%
Age		
15-18 years	145	23.9
19-28 years	154	25.4
29-40 tahun	149	24.6
41-54 years	158	26.1
Province		
North Sumatra	56	9.2
Riau	21	3.4
South Sumatra	11	1.8
Lampung	26	4.2
Banten	24	3.9
DKI Jakarta	61	10.0
West Java	140	23.1
Central Java	112	18.4
East Java	126	20.7
South Sulawesi	29	4.7
Education		
Not in school	3	0.5
Elementary school	78	12.9
Junior high school	135	22.3
Senior high school	305	50.3
College	85	14.0
Occupation		
Civil servants / police / army	14	2.3
Private employees	40	6.6
Enterpreneur	46	7.6
Farmers, laborers	28	4.6
Housewife	264	43.6
More (students, college students)	214	35.3
Family history of gout / kidney disease		
Yes	175	28.8
No	431	71.1

The categorization of menopausal status in this study was obtained from the results of interviews by trained enumerators by asking about the history of the menstrual cycle in a year, said to be menopausal if the subject did not experience menstruation for more than 12 months, pre-menopause if the menstrual cycle was not smooth every month or in a year only experienced menstruation 2-3 times and not yet menopausal if the menstrual cycle was smooth every month (15).

Assessment of nutritional status can provide an overview of whether or not a person's nutritional status is good (16). Nutritional status is a state of the body that describes the body's condition based on food consumption and the use of nutrients consumed daily. Assessment of a person's nutritional status can be done by anthropometric measurements, one of which is by measuring body mass index (17). Enumerators and trained health workers measured body mass index measurements in this study. **Table 2**, 42.9% of the total respondents were obese, mostly in the 41-54 years age group. Based on RISKESDAS in 2023, the incidence of obesity in Indonesia is 15.3% (18).

Uric acid is the end result of purine metabolism that occurs in the body (19). The normal value of uric acid levels in the blood is 2.4-6.0 mg/dl in women and 3.5-7.0 mg/dl in men (20). The subject's uric acid levels were obtained from capillary blood draws performed by skilled health personnel. **Table 2** shows that almost a quarter of the total subjects experienced hyperuricemia (21.1%). When compared with RISKESDAS data in 2018, it was found that patients with joint disease in Indonesia were 7.3%, which women more suffered at 8.5% (21). According to data from SKI 2023, 0,14% of women aged ≥ 15 years had chronic kidney disease based on a doctor's diagnosis (22). This chronic kidney disease can be caused by hyperuricemia that is left for a long time.

Table 3 shows the results of the analysis of the relationship between menopausal status and uric acid levels. The results of statistical tests using the Spearman correlation test show a significant relationship with a positive correlation direction (p=0.031). Menopausal status and uric acid levels have a unidirectional relationship, meaning that the closer to menopause, the higher the subject's uric acid levels.

Table 2. Distribution of menopausal status, nutritional status, and uric acid level subject

Subjects Characteristic	n=606	%
Menopausal status		
Not menopause	494	81.5
Pre menopause	43	7.1
Menopause	69	11.4
Nutritional status		
Undernutrition	38	6.3
Normal	234	38.6
Overweight	74	12.2
Obesity	260	42.9
Uric acid levels		
Normal	478	78.9
Hyperuricemia	128	21.1

In this study, it was found that hyperuricemia sufferers were mostly found in women who had not entered menopause (**Figure 1**). This can happen because it can be influenced by other factors such as physical activity, purine intake, consumption of drugs, and consumption of alcoholic beverages. Research conducted by Karuniawati states that age is associated with increased uric acid levels; women who have entered menopause have the opportunity to experience hyperuricemia compared to women who have not entered menopause (23). As age increases, uric acid levels in men decrease, while in women it increases. This is because advanced adult women will experience a menopausal phase characterized by a decrease in the performance of the hormone estrogen, which works in the process of regulating uric acid in the body (24). The increasing age increases the risk of degenerative disease (25). Research conducted by Maksimov et al. also states that there is a relationship between menopause and the incidence of hyperuricemia (26). Several factors, such as food consumption patterns, physical activity, and body

weight can determine health conditions in adulthood. Uric acid levels tend to be lower only in childhood and women before menopause (27). The presence of estrogen is very important because it can help regulate uric acid secretion and protect women from the risk of hyperuricemia

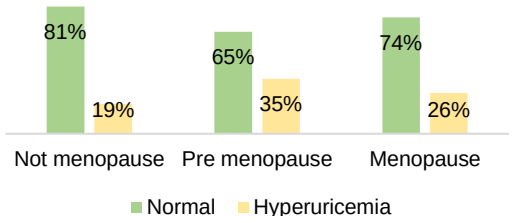

Figure 1. Diagram of the incidence of hyperuricemia based on menopausal status.

(9). Body mass index is one method of assessing nutritional status. Body mass index measurement can provide an overview of a person's nutritional status. Nutritional status describes the body's condition based on a person's diet and physical activity. Nutritional status is highly dependent on consumption, the amount and type of food consumed and must be in accordance with nutritional needs to achieve maximum health status (17).

The results of the Spearman correlation test in **Table 4** show a significant relationship between nutritional status and uric acid levels (p<0.001; r=0.193). Nutritional status with uric acid levels has a unidirectional relationship; the higher the nutritional status, the higher the uric acid levels of the subject.

Table 3. Distribution of menopausal status based on uric acid levels

Menopausal Status	Uric acid levels				*p-value*[1]
	Normal		Hyperuricemia		
	n=606	%	n=606	%	
Not menopause	399	84	95	74	0.031
Pre menopause	28	6	15	12	
Menopause	51	10	18	14	

[1]Significant relationship based on the Chi-Square test (p<0.05)

, it was found that patients with joint disease in Indonesia were 7.3%, which women more suffered at 8.5%. In this study, it was found that hyperuricemia sufferers were mostly found in women with obese nutritional status (**Figure 2**).

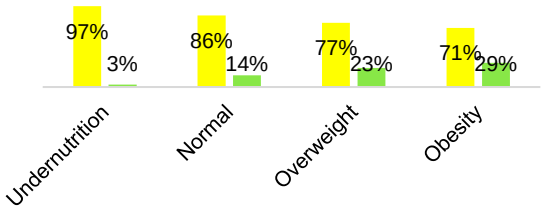

Figure 2. Diagram of the incidence of hyperuricemia based on nutritional status.

Uric acid levels are closely related to body mass index in both men and women (28). Hyperuricemia is also associated with the risk of other metabolic syndrome events, such as hypercholesterolemia and hypertension (29). Obesity is one of the determinants of uric acid levels in the body and is positively associated with gender or age (30). One way to reduce uric acid levels, according to Dessein et al., is to lose weight by not consuming excessive calories and increasing physical activity so that the body mass index is included in the normal category (31). The National Health and Nutrition Examination Survey in 2017-2018 stated that the prevalence of obesity in women (11.5%) was higher than that of men (6.9%) (32).

Table 4. Distribution of nutritional status based on uric acid levels

Nutritional Status	Uric acid levels				*p-value*[1]
	Normal		Hyperuricemia		
	n=606	%	n=606	%	
Undernutrition	37	8	1	1	<0.001
Normal	200	42	34	27	
Overweight	57	12	17	13	
Obesity	184	38	76	59	

[1]significant relationship based on the Spearman correlation test (p<0.05)

The high prevalence of obesity in women can not only be caused by lifestyle, sedentary behavior, and high-calorie food consumption, but menopausal conditions and oral contraceptive consumption can also cause obesity in women (33). Women in the pre-menopausal phase experience a gradual loss of the hormone estrogen, which naturally decreases with age. Reduced estrogen levels, along with increased androgen levels, result in redistribution of fat in the gluteal and femoral regions to the abdominal region, increasing the risk of central obesity. Fluctuating estrogen levels will affect the effectiveness of the hormone in suppressing appetite so that the desire to eat will increase (34,35).

CONCLUSIONS AND RECOMMENDATIONS

The subjects in this study were 606 people, with the highest number of subjects in the age range of 41-54 years. The highest number of subjects came from West Java province (23.1%). The subjects' education level showed that the majority of subjects had a high school / vocational high school education (50.3%), with the most occupations being housewives (43.6%). None of the subjects had a history of gout or kidney disease, but there were 28.88% of subjects who had family suffering from gout/kidney disease.A total of 21.1% of subjects in this study suffered from hyperuricemia. It was found that 11.4% of subjects had menopause, and almost half of the total subjects were obese (42.9%). Subjects suffering from hyperuricemia and obesity were most commonly found in women with an age range of 41-54 years.

Based on the results of bivariate tests between menopausal status and nutritional status with uric acid levels, there was a significant relationship ($p < 0.05$) with a correlation level ($r = 0.092; 0.326$). Hyperuricemia is often associated with obesity in a person, besides uric acid is one of the indicators of metabolic syndrome. However, this study showed a small number of hyperuricemia cases. However, nutritional status dominated by obesity has a number that is not small. Real preventive actions that health workers can provide are providing counseling related to maintaining ideal body weight and providing information related to the relationship between uric acid and the risk of degenerative disease events.

Suggestions for further research are expected to take male samples to be used as subjects so that later, a different test can be carried out regarding what factors are most associated with uric acid levels between men and women. This study also has several variables that have not been studied, which may be risk factors for hyperuricemia, such as visceral fat, protein intake, smoking habits, alcohol consumption, and drugs that can be used as variables in future studies.

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