Uric Acid Levels in Pregnant Women

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ABSTRACT

Background: Preeclampsia in pregnant women can be detected by measuring uric acid levels in the blood. This can occur due to changes in the hemodynamic system and decreased glomerular filtration rate during pregnancy. Purposes: This study aims to determine the description of uric acid levels in pregnant women at Community Health Centers I, South Denpasar. Methods: This study uses a descriptive observational method from April to May 2022, with 31 respondents obtained by non-probability sampling technique. Uric acid levels were measured by the Point of Care Testing (POCT) method. Results: The results showed 23 pregnant women (74.2%) with normal uric acid levels and eight pregnant women (25.8%) with high uric acid levels. Conclusion: High uric acid levels are most suffered by pregnant women aged 30 years (16.1%), most commonly found in the third trimester of pregnancy (16.1%), most pregnant women with a body mass index (BMI) more and obesity (9.7%), and pregnant women with normal blood pressure (22.6%).

Keywords: preeclampsia, pregnant women, uric acid levels

INTRODUCTION

Maternal Health and Mortality Rate (MMR) is one of the clear indicators in describing the welfare of society in a country (1). In the province of Bali in 2020, the maternal mortality rate was 83.8 per 100,000 live births, compared to 2018 at 54.03 per 100,000 live births and the highest case was in Badung district with 12 deaths (2). Several factors caused maternal deaths, namely: bleeding in as many as 1,330 patients, hypertension (preeclampsia and eclampsia) in pregnancy as many as 1,110 cases, and circulatory system disorders of as many as 230 cases (1).

Preeclampsia is a specific condition at the gestational age of more than 20 weeks which is characterized by placental dysfunction and maternal response to systemic inflammation with endothelial activation and coagulation (3). Factors that cause preeclampsia include pregnant women > 35 years, obesity, hypertension, diabetes mellitus, women who are pregnant for the first time (Gravida), previous history of preeclampsia, multiple pregnancies, heart disease, and kidney disease (4). Preeclampsia can be detected by measuring uric acid levels in the blood, which occurs due to changes in the hemodynamic system in pregnant women; decreased blood flow to the kidneys, as well as the glomerular filtration rate, can be reduced by up to 50%, and there is an increase in sensitivity to vasopressor substances and decreased renin-angiotensin activity, thereby causing a decrease in uric acid excretion due to
increased reabsorption in the proximal renal tubules (5).

Uric acid is one of the most sensitive indicators of severity in pregnancy with hypertensive disorders and is very helpful in monitoring the disease process. Increased serum uric acid levels in pregnant women with risk factors for preeclampsia will occur 2-4 weeks before clinical symptoms appear (6). Preeclampsia can have short and long-term effects on the mother and fetus. For mothers, preeclampsia can increase the risk of hypertension, cardiovascular disease, and stroke. The fetus can result in fetal death in the womb, premature birth, placental abruption, and intrauterine growth restriction (IUGR) (7).

In general, there is an increase in uric acid levels in pregnant women in the second to the third trimester of pregnancy, and this is by the research of Talaulikar and Hassan (2012), which showed a general increase in uric acid levels in pregnancy progressed from the second trimester to the third trimester. Based on research conducted by Patricia and Christiana (2013) showed a decrease in uric acid levels during the first trimester between pregnant women and controls. In Febrisya's research (2019), the results were obtained from 32 samples of pregnant women, with as many as seven respondents (21.9%) with high uric acid levels and 25 responses (78.1%) with normal uric acid levels. This study aimed to determine serum uric acid levels in pregnant women at Community Health Centers (CHC) I Denpasar.

METHODS
The type of research used in this research is descriptive observational. The study was carried out from March to May 2022. The population in the study were all pregnant women who had an examination at CHC I, Denpasar Selatan. The sampling used is a nonprobability sampling technique with a purposive sampling method. The research material is the capillary blood of pregnant women using the POCT examination method. This research uses a POCT tool with the Nesco brand. The measuring range of Nesco uric acid is 3-20 mg/dL. The data processing technique is carried out using the obtained data that will be collected, grouped, processed, and presented in tabular form and given a narration.

RESULTS
The following are the research results carried out at CHC I, South Denpasar on 31 pregnant women. From this study, the results of the examination of uric acid levels obtained research data as many as eight people (26%) of pregnant women had high uric acid levels, and 23 people (74%) had normal uric acid.

Table 1. Characteristics of Respondents

| Characteristics          | Uric Acid Level |     |     |
|-------------------------|-----------------|-----|-----|
|                         | High            |     |     |
|                         | Normal          |     |     |
| Age                     |                 |     |     |
| ≥ 30 years old          | 5               | 16.1| 3   | 9.7 |
| < 30 years old          | 3               | 9.7 | 20  | 64.5|
| Gestational age         |                 |     |     |
| Trimester I             | -               | -   | 7   | 22.6|
| Trimester II            | 3               | 9.7 | 15  | 48.4|
| Trimester III           | 5               | 16.1| 1   | 3.2 |
| Body mass index         |                 |     |     |
| Not enough              | 2               | 6.5 | 21  | 67.7|
| Normal                  | 3               | 9.7 | 1   | 3.2 |
| More                    | 3               | 9.7 | 0   | 0   |
| Obesity                 |                 |     |     |
| Blood pressure          |                 |     |     |
| High                    | 1               | 3.2 | 1   | 3.2 |
| Normal                  | 7               | 22.6| 18  | 58.1|
| Low                     | 0               | 0   | 4   | 12.9|
DISCUSSION

Uric acid is the result of the metabolism of purine substances in the form of crystals. Purine substances can be found in our food, whether from animals or plants. Eating foods that contain purine substances can cause these purine substances to enter the body. Excessive purine substances in the body will cause the kidneys to no longer be able to excrete them, and this is what triggers the build-up of purine substances in the body which then turns into uric acid (8).

The results of the examination of uric acid levels on 31 respondents of pregnant women at Puskesmas I South Denpasar obtained research data as many as eight people (26%) pregnant women had high uric acid levels, and 23 people (74%) had normal uric acid levels with low uric acid levels. The lowest uric acid level is 3.0 mg/dl, and the highest is 6.6 mg/dl. The results of this study are different from the research conducted by Kesumasari (2017) (9) which stated that of 33 pregnant women, 19 pregnant women (57.58%) with high uric acid levels. This can be caused by differences in the use of laboratory examination methods; in this study, the uricase peroxidase method was used, while in this study, the POCT method was used.

During pregnancy in pregnant women there will be hemodynamic changes, decreased blood flow to the kidneys, decreased glomerular filtration and uric acid clearance will also decrease, so that it can cause an increase in uric acid levels. Theoretically, uric acid levels during pregnancy are determined by the intake of purines in the diet and the metabolic production of uric acid by the mother and fetus, as well as excretion by the kidneys and the gastrointestinal tract. Disorders of one or more of these factors can change uric acid levels into preeclampsia. Decreased uric acid clearance due to decreased glomerular filtration rate, increased reabsorption, and decreased secretion are the origins of increased uric acid levels in pregnant women with preeclampsia (10). This statement is in accordance with the results of research by Sumanti (2013) (11), namely from 44 pregnant women with preeclampsia, 41 pregnant women (93%) experienced an increase in uric acid levels. Uric acid levels will be high in mild preeclampsia and severe preeclampsia, in severe preeclampsia there are pathological changes in the function of a number of organs and systems caused by vasospasm and ischemia. Increased levels of uric acid in severe preeclampsia can increase the risk of pregnancy that is harmful to the mother and fetus, such as anemia, urinary tract infections (UTI), premature birth and miscarriage (12).

Uric acid levels in pregnant women by age

Age is one of the factors that can affect uric acid levels. This is related to the function of organs in the body, such as the kidneys in excreting uric acid (13). Uric acid levels increase starting from the age of > 30 years. This is because at the age of more than 30 years, the aging process begins. The older a person gets, the risk of suffering from gout will be even greater, because aging can cause reduced kidney function. So this results in increased uric acid levels (14). This is in line with Febrisya's research (2019) (15) regarding the description of uric acid levels in pregnant women at the Siti Khadijah Islamic Hospital in Palembang City, where the results of uric acid levels in the risky age category were 5 pregnant women (16.1%)
with high uric acid. and as many as 2 pregnant women (9.7%) in the age category not at risk of having normal uric acid levels.

Uric acid levels in pregnant women are more at risk of increasing at the age of 30 years. This is because at the age of 30 years is the final period of reproductive fertility so that pregnancies at this age are at risk for preeclampsia (14). This is in accordance with Rizki’s research (2014) (16), of 67 pregnant women, as many as 40 pregnant women (59.7%) with age at risk of experiencing preeclampsia and as many as 27 people (40.3%) pregnant women with age not at risk of experiencing preeclampsia.

**Uric acid levels in pregnant women based on gestational age**
The increased concentration of uric acid in the later stages of pregnancy is also a secondary consequence of increased fetal production, reduced albumin binding and increased tubular reabsorption with decreased renal clearance of uric acid. Increased levels of uric acid in the third trimester of pregnancy can be caused by abnormal changes during pregnancy, namely a decrease in the glomerular filtration rate that occurs at the beginning of the second trimester which can cause uric acid levels to increase and will continue to increase until the next trimester (17). Based on research conducted by Bawah (2018) (18) uric acid levels in this study statistically showed an increase in results from the second trimester to the third trimester of pregnancy. Research that has been conducted also found that pregnant women in the third trimester experienced an increase in uric acid levels which were higher than those in the third trimester (19).

The results of this study showed that all pregnant women with first trimester pregnancy as many as 7 people (22.6%) had normal uric acid levels. Uric acid levels in normal pregnancy will decrease in the first trimester of pregnancy, this situation can be caused by hemodilution due to an increase in plasma volume, while an increase in uric acid levels in the next trimester is caused by increased reabsorption and decreased renal excretion (17). In early pregnancy uric acid levels will decrease to 3 mg / dl, this is related to the uricosuric effect of estrogen and from increased blood flow to the kidneys. Uric acid levels increase when entering the third trimester of pregnancy reaching 4-6 mg/dl (20). This is in accordance with Ismi’s research (2013) (21), regarding the description of blood uric acid levels in pregnant women, where all pregnant women with the first trimester of pregnancy were 2 pregnant women (8%) with normal uric acid levels, in the second trimester of pregnancy, as many as 6 pregnant women (24%) with normal uric acid levels and pregnant women in the third trimester of pregnancy as many as 10 pregnant women (40%) with high uric acid levels.

**Uric acid levels in pregnant women based on BMI**
Someone who is overweight will increase the risk of having excessive uric acid levels in the body, this is because in obese people there is an increase in leptin levels, leptin levels are substances that function to regulate the concentration of uric acid in the blood, which triggers the production of acid levels. Excess uric acid, besides being overweight can cause stress on the joints so that uric acid is difficult to remove from the body, so obesity is a risk factor for gout.
This result is in accordance with Hidayah’s research (2017) (22) from research that has been carried out, it is found that there is a relationship between body mass index and high uric acid levels, Ulandari’s research (2021) (23) also found a significant relationship between BMI and uric acid levels in the adult population in Banjar Kullu, Tampaksiring District, Gianyar Regency.

Obese pregnancies are also at risk for increased uric acid levels caused by lifestyle factors such as poor diet and lack of physical activity, causing obesity. However, it can be avoided by doing physical activity, reducing purine-containing foods and healthy living behavior to avoid gout. Healthy lifestyle behavior in addition to controlling purine intake is to do regular exercise in addition to consuming water (at least 10-12 glasses per day) and high fiber consumption such as oats, broccoli, apples, oranges, pears, strawberries, blueberries, cucumbers, celery, carrots, acacia fiber and barley (13).

The results of this study also found 2 respondents with high uric acid levels in the normal BMI category. This can occur due to increased production of uric acid and decreased excretion of uric acid. The production of uric acid in the body can be influenced by the intake of foods containing purines, such as offal, spinach, butter, durian, meat, seafood, jengkol, petai, tape, and coconut milk. BMI status does not reflect purine intake, but only reflects fat intake, carbohydrate intake and uric acid clearance status (13).

Uric acid levels in pregnant women based on blood pressure
Elevated uric acid levels are associated with increased blood pressure or hypertension. Hypertension can cause blood vessels to constrict and blood flow in the kidneys to decrease so that uric acid levels in the blood increase (24). The decrease in renal perfusion will stimulate the renin-angiotensin mechanism. Renin is released in the glomerulus, then cleaves angiotensin I from angiotensinogen. Angiotensin I is then converted to angiotensin II through the intermediary of a converting enzyme, namely the converting enzyme found in various tissues. Angiotensin II has a strong vasoconstrictor effect that can cause an increase in blood pressure or hypertension (25).

Hypertension is the most common problem in pregnancy. Hypertension is 5-10% of complications in pregnancy and is one of the most common causes of death in addition to bleeding and infection, and also contributes a lot to maternal morbidity and mortality (25). A study conducted by Sultana (2013), which compared the average uric acid levels in subjects with normal blood pressure and preeclampsia, showed that preeclampsia was associated with hyperuricemia. According to Hawkins (2012) (26), hyperuricemia in pregnant women with high blood pressure is one of the early identifications that can cause pregnant women to be exposed to complications in the mother and fetus that can cause death.

Hypertension in pregnancy will cause blood flow to the kidneys and glomerular filtration rate to decrease. Decreased glomerular filtration rate in the kidneys can cause absorption of protein to decrease gradually, causing high uric acid levels (27). In pregnancy, low blood pressure can also occur due to physical and hormonal changes during pregnancy such as increased blood flow to the fetus and
insufficient intravascular fluid. This can be caused by anemia, dehydration, nutritional deficiencies, heart problems. Low blood pressure in pregnant women can be avoided by exercising regularly, eating a balanced nutritious diet, drinking lots of water, and sleeping lying on the left side to increase blood flow to the heart.

CONCLUSION
High uric acid levels in pregnant women by age category are primarily women aged 30 years. Based on gestational age, most are in the third trimester of pregnancy. BMI category is mainly found in women pregnant with more BMI and Obesity, and based on blood pressure, most were found at normal blood pressure.

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CONFLICT OF INTEREST
The authors have no conflicts of interest to declare. All co-authors have seen and agree with the contents of the manuscript. We certify that the submission is original work and is not under review at any other publication.

REFERENCES
1. Kementerian Kesehatan Republik Indonesia. Profil Kesehatan Indonesia Tahun 2020, 2021.
2. Dinas Kesehatan Provinsi Bali. Profil Kesehatan Dinas Kesehatan Provinsi Bali. 2020.
3. POGI. Pelatihan Klinik Asuhan Persalinan Normal. Jakarta: JNPK-KR Depkes RI; 2016.
4. Cunningham F, K. L, S. B, J H, D R. Spong Obstetri. 23 Vol 2. William, editor. Jakarta; 2013.
5. Sahin AS, Yüce T, Kalafat E, Seval M, Soylemez F. Association of first trimester serum uric acid levels gestational diabetes mellitus development. Turk J Obs Gynecol 2. 2016;13(2):71–4.
6. Sumanti N, Alamsyah M, Rostini T, Goenawan Partowidigo M, Bogor C. Kadar Asam Urat Serum sebagai Biomarker Preeklamasi. Maj Kedokt Bandung. 2013;45(2):98–104.
7. Fox R, Kitt J, Leeson P, Aye CYL, Lewandowski AJ. Preeclampsia: Risk factors, diagnosis, management, and the cardiovascular impact on the offspring. J Clin Med. 2019;8(10):1–22.
8. Junaidi I. Rematik dan Asam Urat. Revisi. Jakarta: PT Bhuana Ilmu Populer; 2012.
9. Kesumasari MW. Gambaran kadar asam urat pada ibu hamil trimester II dan III di Puskesmas I Denpasar Selatan. Politeknik Kesehatan Kemenkes Denpasar; 2017.
10. Bellome G. Serum uric acid and preeclampsia:an update. Expert Rev Cardiovasc Ther. 2013;5(3):635–50.
11. Sumanti N, Noormartany, Alamsyah M. Kadar Asam Urat Serum sebagai Biomarker Preeklamasi. Mkb. 2013;45(2):98–104.
12. Aker, S. S., T. Yüce , E. Kalafat, M. Seval FS. Association of first trimester serum uric acid levels gestational diabetes mellitus development. Turk J Obs Gynecol. 2016;13(2):71–4.
13. Harrison. Prinsip-prinsip Ilmu Penyakit Dalam. Bahasa Ind.
Hartono A, editor. Jakarta: EGC; 2012.

14. Karuniawati B. Hubungan Usia Dengan Kadar Asam Urat Pada Wanita Dewasa. J Kesehat Mardani Med. 2018;9(2):19–22.

15. Febrisya E valeriska. Gambaran kadar asam urat pada ibu hamil di rumah sakit islam siti khadijah kota Palembang. Politeknik Kesehatan Palembang; 2019.

16. Rizki EM. Hubungan Usia Dengan Kejadian Preeklampsia Pada Ibu Bersalin di RSUD Wonesari Tahun 2013. Sekolah Tinggi Ilmu Kesehatan Aisyiyah Yogyakarta; 2014.

17. Batchu NJ, Tumati SJ. Serum Uric Levels in Pregnancy Induced Hypertension – a Cross Sectional Study. J Evid Based Med Healthc. 2016;3(14):501–2.

18. A. Bawah, Kuffour FAO, Boateng MA, Mustapha M, Amoah P, Ussher FA, et al. Effect of pregnancy on the metabolism of creatinine, urea and uric acid among pregnant women at the volta regional hospital. Int J Med Heal Sci. 2018;7(4):166–71.

19. Johnson, RJ. M, Kanbay, D. Kang, L. Sanchez DF. Uric acid: a clinically useful marker to distinguish preeclampsia from gestational hypertension. Hypertension. 2011;58 (4):548–9.

20. Adhiyanti, Y., R. Pitriani IPD. Panduan Lengkap Keterampilan Dasar Kebidanan I. 2015.

21. Ismi H. Gambaran Kadar Asam Urat Dalam Darah Pada Wanita Hamil. Universitas Muhammadiyah Palangkaraya; 2013.

22. Hidayah Anharul. Hubungan Indeks Massa Tubuh Dengan Kadar Asam Urat Darah Pada Usia 35 Tahun Keatas di Desa Klagen Serut Kecamatan Jiwan Kabupaten Madiun. Sekolah Tinggi Ilmu Kesehatan Bhakti Husada Mulia Madiun; 2017.

23. Ulandari NK. Hubungan Indeks Massa Tubuh Dengan Kadar Asam Urat Pada Penduduk Dewasa Di Banjar Kulu Kecamatan Tampaksiring Kabupaten Gianyar. Politeknik Kesehatan Denpasar; 2021.

24. Laughon SK, J. Catov, R.W. Powers, J.M. Roberts and RG. First trimester uric acid and adverse pregnancy outcomes. Am J Hypertens. Am J Hypertens. 2014;24(4):489–95.

25. Cunningham F, K. L, S. B, J H, D R. Pregnancy Hypertension. Edisi 24. 2012.

26. Hawkins, TL, J. Roberts, G. Mangos, L. Roberts and MB. Plasma Uric Acid Remains a Marker of Poor Outcome in Hypertensive Pregnancy Retrospective Cohort Study. BJOG An Int J Obstet Gynaecol. 2012;119(4):484–92.

27. Diwan J. A Comparative Study of Serum Uric Acid Level in Normal Pregnancy, and Pregnancy Induced Hypertension. Int J Med Public Heal. 2011;1(1):39–42.