International Journal of Medical and Pharmaceutical Research
Website: https://ijmpr.in/ | Print ISSN: 2958-3675 | Online ISSN: 2958-3683
NLM ID: 9918523075206676
Volume: 4 Issue:6 (Nov-Dec 2023); Page No:225-229

Original Article

IJMPR

Comparison of C-Reactive Protein Levels in Preeclampsia Pregnant Women with Normal Trimester III Pregnant Women

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ABSTRACT

Background: The increase in maternal mortality rates (MMR) is an occurrence that needs attention in Indonesia. According to Dinas Kesehatan Jawa Timur, 2019 the MMR in 2020 reached 98,39 per 100.000 live births, with approximately 26,9% or 152 individuals attributed to hypertension during pregnancy. Hypertension is diagnosed with systolic blood pressure reaches more than 140 mmHg and diastolic blood pressure is 90 mmHg. This condition becomes more concerning if hypertension develops after 20 weeks of pregnancy and is accompanied by proteinuria or other organ damage, known as preeclampsia. One of the strongest theory is the presence of uteroplacental ischemia and maternal infection, leading to an increase in pro-inflammatory cytokines (TNF-alpha and IL-6). Thus, it can be concluded that there is an increase in the inflammatory response at low levels. The presence of IL-6 induced the formation of C-Reactive Protein (CRP), a primary biomarker for inflammation if its value is > 0.3 mg/dl, requiring specific attention and appropriate management.
Methods: This study aims to determine the comparison of CRP levels in preeclamptic pregnant women with normal third-trimester pregnant women at Bhakti Dharma Husada Hospital in 2023. The research took place from October 2023 to November 2023. Patient characteristics were obtained through secondary data from patient medical records, and CRP data were obtained from laboratory test.
Results: The research, involving 20 pregnant women, found a significant difference using non-parametric Mann-Whitney test between the preeclampsia group and the normal third-trimester pregnant group (P<0,05).
Conclusions: This indicates that the occurrence of preeclampsia has an impact on increasing CRP.

Key Words: *c-reactive protein, pregnancy, preeclampsia*

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INTRODUCTION

Pregnancy is something desired by most women who have entered the married phase. In 2020, the total fertility rate reached an average of 2,3 births per women[1]. Pregnancy is characterized by anatomical and physiological changes in the mother's body that occur over a span of 9 months. However, often in the course of pregnancy, it can become a pathological condition, and it's important to identify this early to avoid complication and reduce maternal mortality rates[2].

In 2019, the MMR in East Java reached 89, 91 per 100.000 live births. However, in 2020, it increased to 98, 39 per 100.000 live births. The rise in MMR was primarily caused by pregnancy-induced hypertension, accounting for 26,9% or 152 cases, followed by hemorrhage at 21,59%, circulatory system disorders at 7,61%, infections at 5,31%, and metabolic disorders at 1,42%. This increase in MMR is attributed to a decline in awareness among mothers and their families to seek prenatal care, evidenced by a 2,9% decrease in first antenatal care visits (ANC1) and an 8,5% decrease in fourth antenatal care (ANC4) in 2020 compared to 2019 [3]. MMR from bleeding and circulatory dysfunction stands at 28%, while infection due to anemia and chronic energy deficiency in the mother also have significant impact[4].

Hypertension characterized by an increase in systolic blood pressure greater than 140 mmHg and diastolic blood pressure equal to or greater than 90 mmHg. It has been found there's been an increase in the number of hypertension cases in Indonesia compared to 2013, rising from 25, 8% to 31,4%. Hypertension has become a primary factor an illness and mortality as it can lead to cardiovascular, cerebrovascular disorders, and end-stage kidney failure [5]. Hypertension is classified into chronic hypertension, which includes hypertension before pregnancy (prior to 20 weeks gestation) and persists beyond 12 weeks post delivery; preeclampsia-eclampsia, characterized by hypertension an acquired proteinuria after 20 weeks of pregnancy; chronic hypertension superimposed with preeclampsia; and gestational hypertension, which involves hypertension during pregnancy without proteinuria that resolves within 12 weeks after delivery [6].

Preeclampsia is a pregnancy disorder that often occurs around 20 weeks of gestation and commonly near term or a few weeks before delivery, accompanied by proteinuria. Pregnant women with gestational hypertension without proteinuria can be categorized as having preeclampsia if they exhibit thrombocytopenia, liver dysfunction marked by elevated liver enzymes, kidney insufficiency, visual disturbances, and pulmonary edema. If the systolic blood pressure rises to 160 mmHg or higher with diastolic blood pressure of 110 mmHg pr higher, with or without proteinuria, it should be categorized as severe preeclampsia [7]. Preeclampsia can worsen into eclampsia, a life-threatening complication if not detected early[8]. Eclampsia is seizures that occur due to hypertension, often appearing 48-72 hours after childbirth. Eclampsia can lead to hypoxia, trauma, and aspiration pneumonia[7].

The etiology of preeclampsia is not yet definitively known. However, there are two strongest theory, uteroplacental ischemia and maternal infection. Uteroplacental ischemia begins with a disruption in blood supply from the uterus to the placenta, leading to the release of toxin into circulation, triggering hypertension and proteinuria. Maternal infection is also considered a theory for preeclampsia, where *Bacillus eclampsiae* is thought to cause eclampsia, though it remains highly controversial as preeclampsia or eclampsia doesn't exhibit typical symptoms of infectious disease. There's an increase in soluble vascular endothelial growth factor receptor-1 (sVEGFR-1), also known as soluble fms-like tyrosine kinase-1 (sFlt-1), and endoglin. Additionally, there's an elevation in pro-inflammatory cytokines such as tumor necrosis factor alpha (TNF-alpha) and interleukin-6 (IL-6) [9].

C-reactive protein (CRP) is a protein produced by the liver. Normal human bodies have low levels of CRP, while individuals with inflammation, whether acute or chronic, tend to have higher levels of CRP. CRP is recognized as a key biomarker for the occurrence of inflammation [10]. Initially, CRP can be found in a patient's serum as a sign of acute inflammation induced by IL-6. Prolonged elevation of CRP levels indicates chronic inflammation or infection that has occurred in the body. The interpretation of CRP levels varies and signifies different conditions. For instance, if the level is < 0,3 mg/dl, it's considered normal; 0.3-1.0 mg/dl could be normal or indicate a minor increase; 1.0-10.0 mg/dl signifies a moderate increase; >10.0 mg/dl indicates a significant increase, and > 50.0 mg/dl denotes a severe increase. These diverse elevation can be indicate various pathological conditions that require appropriate management [11].

METHODS

The type of study employed is an observational analysis using a case control study design. The research will involve pregnant women in the third-trimester with gestational age of 20 weeks or more, who are receiving outpatient or inpatient care, categorized into case (preeclampsia) and control (non-preeclampsia) groups at BDH hospital from August to November 2023. Sample determination is based on the Lemeshow formula, which calculated the sample size as 18, with a 10% dropout criterion (1,8), resulting a required sample size of 19,8 (rounded to 20 samples). The sampling technique employed in this study is random sampling.

Establishing inclusion and exclusion criteria. Sample must fulfill inclusion criteria: (1) pregnant women with a history of more than 1 pregnancy (multigravida;, (2) pregnant women with a single fetus; (3) pregnant women diagnosed with mild preeclampsia, severe preeclampsia, eclampsia, chronic hypertension superimposed with preeclampsia; (4) complete medical record data. Excluded samples are (1) pregnant women incomplete medical record; (2) pregnant women that not registered at BDH hospital; (3) pregnant women with pre-existing comorbidities before pregnancy.

Ethical clearance approval must have been obtained from BDH hospital. Compile data including name, age, height, weight, systolic blood pressure, diastolic blood pressure obtained from the patient's medical records. The CRP levels in the blood are obtained directly through venous blood vessel. Before the blood sample is taken through the blood vessels, pregnant women will be provided with informed consent and given appropriate explanations regarding the purpose of blood collection, potential complication, and management. The blood collection process is carried out in sterile manner to prevent further complications. Subsequently, venous blood samples are stored and sent for centrifugation (serum extraction).

Before the Univariate analysis technique is used to determine the frequency of each variable under study. Bivariate analysis technique involves two different variables suspected to be related by using normality test and the Mann-Whitney test with a confidence level of 95% (α=0.05) to draw a meaningful conclusion regarding these variables, specifically the increase in CRP levels in preeclampsia.

RESULTS

In this study, there were 20 samples consisting of 10 normal pregnant women (control) and 10 pregnant women with preeclampsia (cases). The result of these research were analyzed using descriptive statistical tests, data normality test, and non-parametric statistical tests.

In table 1, it was found that there are significant difference in the mean age, diastolic blood pressure, systolic blood pressure, weight, height, and body mass index (BMI). In the case group (pregnant women with preeclampsia), the average were higher (age = 32,6; systolic blood pressure = 156,1; diastolic blood pressure = 99,2; weight = 81,3;

height = 158,7; BMI = 32,4) compared to the control group (normal pregnant women in the third trimester), where the averages were lower (age = 27,2; systolic blood pressure = 101,7; diastolic blood pressure = 62,9; weight = 49; height = 158,7; BMI = 32,4).

The average age of pregnant women with preeclampsia is higher compare to those normal pregnancies. This study align with research stating that the group of older pregnant women, there is a greater risk of developing preeclampsia compared to younger pregnant women [12]. The chi-square statistical test conducted in Palembang city indicates a p value of 0.002 ($p<0.05$), demonstrating a significant association between age and the occurrence of preeclampsia [13].

DISCUSSION

The mean systolic blood pressure of preeclamptic women is higher than the normal pregnant women. Highest prevalence of preeclampsia patient admitted to the hospital is due to an increase in systolic blood pressure exceeding 160 mmHg, and the majority of discharged patient have systolic blood pressure between 140-159 mmHg [14]. The study also conducted on 55 respondents with preeclampsia systolic blood pressure (≥ 140 mmHg) found that approximately 9,1% occurred during the 4^{th}, 5^{th}, 6^{th}, and 8^{th} month of pregnancy [15].

The mean diastolic blood pressure of preeclamptic women is higher than the normal pregnant women. The previous study mentioned that out of 55 respondents, 9 of them (16,4%) experience on increase diastolic blood pressure (≥ 90 mmHg) during the 4^{th} to 8^{th} month of pregnancy [15].

Weight has correlation with the occurrence of preeclampsia. This statement is supported by literature review that analyzed 10 journals, where approximately 80% of respondents who experience preeclampsia were attributed to weight gain during pregnancy [16]. This finding is further supported by study involving 40 respondents [17].

Pregnant women with obesity have 2.68 times higher risk of developing preeclampsia. This study involve 40 respondents, with 21 experiencing obesity [18]. Additionally, research on the association between BMI and the occurrence of preeclampsia, using a descriptive-analytical method with a retrospective design, showed result that supported the earlier research. By employing the rank Spearman test, they obtained p value of 0.000 ($p<0.05$), indicating a significant association between BMI and preeclampsia [13].

Table 1. Demographic Characteristics of the Study Population

Kelompok	Nilai	Usia	TD Sistolik	TD Diastolik	BB	TB	IMT
Normal	Min	23	90	59	38.0	144.0	17.33
	Max	33	127	79	69.0	161.0	28.72
	Median	27.5	100.5	60	46	152	20.495
	Mean	27.2	101.7	62.9	49	151.2	21.424
Preeklampsia	Min	27	140	90	70	152	27.4
	Max	39	191	110	91	172	38.4
	Median	32.5	153.5	100	82.5	156	31.8
	Mean	32.6	156.1	99.2	81.3	158.7	32.4

The *Saphiro-Wilk* normality test states that a distribution is considered normal if the p value less than 0.05. In table 2, the significance value for the control group is < 0.001, and for the case group, it's 0.005. Consequently the obtained data is categorized as a having a non-normal distribution.

In table 3, which compare the levels of CRP (C-Reactive Protein) in normal pregnant women and pregnant women with preeclampsia, there is a significant difference with the mean values in preeclampsia patients being higher than in normal pregnant women. Previous research that involving 60 pregnant women divided into 30 control and 30 case groups, resulted in a chi-square test with p value of 0.001, OR = 7.56, CI 95%= 2.41-23.75 indicating that a high CRP level could cause a 7.5 times higher likelihood of preeclampsia [19]. However, another research found that the mean obtained was 8.26±6.9 mg/l in the case group, which was higher compared to the control group (6.22±4.29), but without statistical significance (p=0.08) [20]. This result also supported by another researcher that said in 9 pregnant women with preeclampsia, 4 pregnant women has showed an increase CRP levels[21].

Table 2. CRP Normality test

	Preeclampsia	**Non-Preeclampsia**
Statistic	.766	.637
Sig.	.005	<.001

In table 3, presents the result of the Mann-Whitney test on two groups of pregnant women, where the Asymp. Sig. (2-tailed) value is grater than the significance level (α=0.05), specifically 0.003. Consequently, this study concludes that there is a significant difference between the samples of normal pregnant women and the group of pregnant women with preeclampsia.

Table 3. *Mann-Whitney* test

	Results
Mann – Whitney	13.000
Asymp. Sig. (2-tailed)	0.003

ACKNOWLEDGEMENTS

Based on the conducted research, it was concluded that there is a significant difference in the comparison of CRP levels in the blood of pregnant women with preeclampsia and normal pregnant women in the third trimester. Pregnant women with preeclampsia have a higher mean level compared to normal pregnant women in the third trimester (14,2 : 6,8). This supports the theoretical basis stating that the occurrence of preeclampsia leads to an increase in one of the inflammatory markers, namely c-reactive protein (CRP).

REFERENCES

1. Worldometer. (2022). *Indonesia Population (2019) -Worldometer*.Www.worldometers.info. https://www.worldometers.info/world-population/indonesia-population
2. Susanti, E., Firdayanti, & Haruna, N. (2019). ManajemenAsuhanKebidanan Antenatal pada Ny "S" denganHiperemesis Gravidarum Tingkat II di RS TNI Angkatan Laut Jala Ammari pada Tanggal 27 Mei-18 Juli 2018. *Jurnal Midwifery*, *1*(2), 79–91.
3. Dinas Kesehatan Provinsi Jawa Timur. (2020). *Profil Kesehatan Provinsi Jawa Timur*. Dinas Kesehatan Provinsi Jawa Timur.
4. HenderaHenderi, Salmon Charles Siahaan, Irwin PriyatnaKusumah, Heru Cahjono, Ferdinand AprianToTannus, Nimas Pristiwanto D S, & Octavia, H. (2021). Correlation of Vitamin D with Ferritin in Pregnant Mothers Chronic Energy Deficiency of the Second Trimester. *BerkalaKedokteran*, *17*(2), 143–143. https://doi.org/10.20527/jbk.v17i2.11675
5. Kementerian Kesehatan Republik Indonesia. (2018). *Potret Sehat Indonesia dariRiskesdas 2018*. Kementerian Kesehatan Republik Indonesia. https://www.kemkes.go.id/article/view/18110200003/potret-sehat-indonesia-dari-riskesdas-2018.html
6. Kementerian PPN/Bappenas. (2022). *SDGs Indonesia*. Kementrian PPN/Bappenas. https://sdgs.bappenas.go.id/dashboard/
7. Espinoza, J., Vidaeff, A., Pettker, C., &Simhan, H. (2020). *ACOG PRACTICE BULLETIN Clinical Management Guidelines for Obstetrician-Gynecologists NUMBER 222*.
8. World Health Organization. (2023, February 22). *Maternal Mortality*. Who.int; World Health Organization: WHO. https://www.who.int/news-room/fact-sheets/detail/maternal-mortality
9. Jung, E., Romero, R., Yeo, L., Gomez-Lopez, N., Chaemsaithong, P., Jaovisidha, A., Gotsch, F., & Erez, O. (2022). The etiology of preeclampsia. *American Journal of Obstetrics and Gynecology*, *226*(2), S844–S866. https://doi.org/10.1016/j.ajog.2021.11.1356
10. MidlinePlus. (2022, September 28). *C-Reactive Protein (CRP) Test: MedlinePlus Medical Test*. Medlineplus.gov. https://medlineplus.gov/lab-tests/c-reactive-protein-crp-test
11. Nehring, S. M., Goyal, A., & C. Patel, B. (2023, January 1). *C Reactive Protein*. PubMed. https://pubmed.ncbi.nlm.nih.gov/28722873
12. Rauf, R., Harismayanti, Retni, A., Studi, P., Keperawatan, I., Muhammadiyah, U., Alamat, G., Mansoer, H., No, P., Desa, T., Telaga Biru, K., Gorontalo, K., & Gorontalo. (2023). Analisis Faktor ResikoTerjadiPreeklampsia Pada Ibu Hamil di PuskesmasTolangohulaKabupatenGorontalo Provinsi Gorontalo. *JurnalIlmu Kesehatan Dan Gizi (JIG)*, *1*(2), 46–58. https://prin.or.id/index.php/jig/article/download/963/1033
13. Handayani, S., &Nurjanah, S. (2021). HubunganIndeks Massa TubuhDenganKejadianPreeklampsia Pada Ibu Hamil di RSUD TrikolaSalakan. *JurnalKebidanan*, *XIII*(02), 128–242.

14. Nurmainah, N., Hadad, F. M., & Andrie, M. (2021). Profil Proteinuria dan Tekanan Darah pada PasienPreeklampsia Berat yang menggunakanAntihipertensi. *Indonesian Journal of Clinical Pharmacy*, *10*(2), 79. https://doi.org/10.15416/ijcp.2021.10.2.79
15. Susanti, S., Susanti, S., &BIstara, D. N. (2019). Pengaruh Range of Motion (ROM) terhadapKekuatanOtot pada Pasien Stroke. *Jurnal Kesehatan Vokasional*, *4*(2), 112. https://doi.org/10.22146/jkesvo.44497
16. Wibowo, N., Irwinda, R., Frisdiantiny, E., Karkata, M. K., & Mose, J. C. (2016). *Diagnosis dan TatalaksanaPreeklampsia*. PerkumpulanObstetri dan Ginekologi Indonesia.
17. Handayani, S., Solama, W., Hipson, M., Aisyiyah, J., 43, P., Yang, F.-F., Dengan, B., Preeklamsi, K., Ibu, P., Handayani, H., Kebidanan, S., Tinggi, I., Aisyiyah, & Palembang. (2023). Faktor yang BerhubungandenganKejadianPreeklampsi Pada Ibu Hamil. *JurnalAisyiyah Palembang*, *8*(1), 43–57.
18. Kasriatun, K., Kartasurya, M. I., &Nugraheni, S. A. (2019). Faktor Risiko Internal dan EksternalPreeklampsia di Wilayah Kabupaten Pati Provinsi Jawa Tengah. *JurnalManajemen Kesehatan Indonesia*, *7*(1), 30–38. https://doi.org/10.14710/jmki.7.1.2019.30-38
19. Angelina, M., Surya, I. G. P., & Agung Suwardewa, T. G. (2019). High sensitivity C-Reactive Protein dan leukosit serum yang tinggimerupakanfaktorrisikoterjadinyapreeklampsia. *Medicina*, *50*(1), 123–128. https://doi.org/10.15562/medicina.v50i1.201
20. Manjula, D., Usharani, N., & Purushottam, K. (2023). A prospective analytical comparative assessment of the association CRP and uric acid with severity of preeclampsia. *Journal of Cardiovascular Disease Research*, *14*(3), 759–762.
21. Nasruddin, Z., Lukas, E., Malinta, U., & Chalid, M. T. (2018). The Association of Creactive Protein Levels in Second Trimester of Pregnancy with Preeclampsia. *Indonesian Journal of Obstetrics and Gynecology*, *6*(1), 18. https://doi.org/10.32771/inajog.v6i1.752