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Interleukin-1β (IL-1β) Levels in Preeclampsia Pregnant Women in Bugis, Makassar, Mandar and Toraja Tribes

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ABSTRACT

Aim: This study aims to determine the comparison of interleukin-1β levels in preeclampsia pregnant women in large tribes in South and West Celebes.

Method: This study used a cross-sectional design with case-control carried out in March to June 2020 in general hospital and Health centerTotoliMajene, general hospital Lasinrang, and Health center Matirobulu Pinrang, Elim Hospital, and Health center Rantepao Tana Toraja, Health center Bara Barayah and Jumpandang Baru in Makassar City. Respondents in this study were pregnant women> 20 weeks divided into 2 groups: 44 pregnant women with preeclampsia and 44 pregnant women with normotension that met the criteria. The supporting data collected includes age, parity, body mass index (BMI) during pregnancy. Interleukin 1β levels were determined using the Human Interleukin 1β Elisa Kit with the ELISA method.

Results: Differences in mean IL-1β levels in the preeclampsia group in four tribes (Bugis, Makassar, Mandar, and Toraja) with a significant value of p-value 0.002 (p <0.05) as well as in the normotension group also had differences in IL-1β levels with a p-value of 0.003 (p <0.05). Whereas the difference in IL-1β levels of preeclampsia and normotensive in each tribe results in a significant difference in Makassar (0.040) and Toraja (0.005) while the other 2 terms do not have significant IL-1β levels.

Conclusion: There are differences in IL-1β levels between preeclampsia and normotension, and IL-1β levels can be influenced by tribal variations.

Key Words: I Cytokines, Interleukin-1β, Preeclampsia, Pregnancy, Tribes

INTRODUCTION

Based on the data from the Indonesian Health Demographic Survey (IDHS), it was explained that there was an increase in MMR from 228 to 359 maternal deaths per 100,000 live births, mostly due to bleeding, hypertension in pregnancy (HDK), and infection. However, the proportion of HDK including preeclampsia-eclampsia has increased by 25% as the main cause of death in mothers to date.[1]

The South Sulawesi Health Office in 2018 reported that the incidence of preeclampsia had increased from 163 to 639 cases spread across several districts, including Toraja and Makassar. Whereas for the West Sulawesi region in 2015 there were 52 cases of maternal death, of which 13% were caused by hypertension in pregnancy, including preeclampsia, which are spread throughout the districts including Majene Regency. The Majene Regional General Hospital reported that throughout 2018, 144 patients diagnosed with preeclampsia had treated them.[2, 3]

Preeclampsia is a multifactorial disorder in pregnancy whose main cause is still unclear, even some experts say that preeclampsia is a theoretical disease.[4] Preeclampsia has typical symptoms such as an increase in systolic blood pressure ≥ 140 mmHg and diastolic ≥ 90 mmHg and proteinuria ≥ 0.3/24 hours that occur after 20 weeks of gestation.[5]

Preeclampsia in pregnancy is considered as excessive inflammation because during pregnancy many cytokines are secreted by immune cells and lymphocytes in trophoblasts and decidua which among them regulate immunity, inflam-

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mation, and hematopoesis. It was found that in preeclampsia pregnancy, the serum level of inflammatory cytokines, one of which IL-1β, was higher.[3,4] Researchers, Redman et al. revealed a theoretical concept that the incidence of preeclampsia is a disorder that occurs in two phases, in which the first phase of decreased placental perfusion leads to failure of blood vessel remodelling resulting in placental hypoxia/ischemia and placental malperfusion which ultimately produces toxic substances such as free radicals that cause oxidative stress .[8] Oxidative stress is a component that mediates the first and second stages of preeclampsia. [9] This oxidative stress induces the release of placental cytotoxic substances into the maternal blood vessels and causes a systemic inflammatory response as well as endothelial dysfunction as a result, in the second stage, maternal symptoms manifesting preeclampsia such as hypertension, proteinuria and edema appear. [10]

Hypoxia and oxidative stress will stimulate increased IL-1β production through one of the signalling pathways for activation of nuclear factor kappa B (NF-κB). IL-1β is produced by monocytes/macrophages and endothelial cells. IL-1β is an important mediator in the systemic inflammatory immune response in preeclampsia. Increased IL-1β levels can stimulate endothelial dysfunction by increasing the release of vasoconstrictor substances such as endothelin and decreasing vasodilator substances such as nitric oxide by endothelial cells, causing systemic vascular damage manifesting into preeclampsia syndromes such as hypertension, proteinuria and edema.[1,5]

Interleukin-1 (IL-1β) affects increasing the regeneration of thrombin, platelet-activating factors, increasing the permeability of endothelial cells, increasing the activity of nitric oxide synthetase and increasing the levels of several prostaglandins. In preeclampsia, there are several acute responses caused by an increase in IL 1β which affects the permeability of endothelial cells which is influenced by oxygen free radicals which can trigger the incidence of preeclampsia.[6,7] In epidemiological research, preeclampsia is often linked to genetic factors where there are disorders of several genes that are influenced by genetic and environmental factors, resulting in immune maladaptation which mediates oxidative stress and eventually chronology of endothelial dysfunction leads to the incidence of preeclampsia.[5, 13.]

METHOD

Research sites

The study was conducted in January - June 2020 and has received an ethical permit recommendation with protocol number UH19121020. This research was conducted in several hospitals and health centers in the provinces of South and West Sulawesi, namely hospital Lasinrang and health center Mattirobulu Pinrang, health center Bara barayah and health center Jumpandang Baru Makassar City, general hospital and health center Totoli Majene, Elim Hospital and health center Rantepao Tana Toraja. This research is a prospective study with cross sectional method with case control, the study was conducted in several hospitals and health centers with a sample of 44 preeclampsia pregnant women and 44 pregnant women with normotension, a total sample of 88 samples that met the inclusion criteria, namely: Pregnant women> 20 weeks diagnosed preeclampsia with blood pressure ≥ 140/90 and proteinurin ≥ positive 1 (+), Gestational age> 20 weeks - 42 weeks, Patients with clear HPHT, Willing to be a respondent

Exclusion Criteria have no experience systemic disease, have no experience premature rupture of membrane, nonlysis blood samples.

Data Collection Techniques

Data related to the demographics and obstetric history collected age, parity, and body mass index Meanwhile, for blood sampling, researchers were assisted by laboratory staff at research hospitals and health centers. The collected samples were then centrifuged and stored in a refrigerator at -20^{0}C. after all, samples had been collected IL-1β cytokine levels were examined using the Human Interleukin IL-1β Kit by the ELISA method at the Research Center Laboratory (HUM-RC) of Hasanuddin Medical University. Statistical analysis using the SPSS statistical application 23 p-value calculated with p-value <0.05 is considered significant, in this study using the chi-square test, Kruskall Wallis and Man Whitney.

MATERIALS AND METHODS

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RESULTS

Data shows that age and parity in the preeclampsia and normotension groups in all ethnic groups have similar characteristics. While the body mass index (BMI) characteristics of the two groups there were significant differences. (table.1)

Characteristics of respondents

Table 1: Characteristics of research respondents

Characteristics	Preeclampsia (n = 44)	Normotensive (n = 44)	p-value
Age n (%)			
Low risk	7 (46.7)	8 (53.3)	0.500 *
High risk	37 (50.7)	36 (49.3)	
BMI n (%)			
Less	0 (0)	1 (100)	
Normal	8 (30.8)	18 (69.2)	0.005 *
Over	21 (48.8)	22 (51.2)	
Obesity	15 (83.3)	1 (100)	
Parity n (%)			
Primigravida	14 (51.9)	13 (48.1)	0.500 *
Multigravida	30 (49.2)	31 (50.8)	

*Chi-square

The results of the mean IL-1β levels of the four ethnicities that experienced preeclampsia had a significant difference and the Makassar tribe had the highest average IL-1β level of 1399.76 pg/ml. (table.2)

Levels of IL-1β in normotensive pregnant women also have a significant average difference between tribes and ethnic groups which have the lowest IL-1β levels is Toraja with a value of 669.98 pg/ml. (Table 3).

Table 2: IL-1β levels in pregnant women in the Bugis, Makassar, Mandar and Toraja tribes who have preeclampsia (n = 44)

Suku	IL-1β levels (Pg/ml) Mean ± SD	p-value *	Sig. **
Bugis	1046.63 ± 134.20	0.002	0.985
Makassar	1943.06 ± 507.09		0.419
Mandar	1206.96 ± 357.25		0.048
Toraja	1119.31 ± 243.36		0.297

** kruskall-wallis test; ** Shapiro-Wilk normality test*

Table 3: Levels of IL-1β in pregnant women in the Bugis, Makassar, Mandar and Toraja tribes that are normotensive (n = 44)

Suku	IL-1β levels (Pg/ml) Mean ± SD	p-value *	Sig. **
Bugis	1043.41 ± 102.89	**0.003**	0.392
Makassar	1399.76 ± 514.12		0.008
Mandar	1049.14 ± 100.76		0.084
Toraja	669.98 ± 333.73		0.397

** kruskall-wallis test; ** Shapiro-Wilk normality test*

The mean in the group of preeclampsia and normotension mothers in each tribe showed that IL-1β levels were significant in Makassar and Toraja tribes, while in Bugis and Mandar did not have significant differences. However, other results indicate that IL-1β levels are higher in the preeclampsia group than in the group of pregnant women with normotension in all tribes in this study. (table.4)

Table 4: Differences in IL-1β levels between preeclampsia pregnant women and normotensive pregnant women in the Bugis, Makassar, Mandar, and Toraja tribes (n = 88).

Ethnic	Preeclampsia status	IL-1β levels		p-value*
		Mean rank	Sum of rank (Pg/ml)	
Makassar	Preeclampsia	14.36	158.00	0.040
	Normotension	8.64	95.00	
Bugis	Preeclampsia	11.64	128.00	0.949
	Normotension	111.36	125.00	
Mandar	Preeclampsia	12.55	138.00	0.478
	Normotension	10.36	115.00	
Toraja	Preeclampsia	15.27	168.00	0.005
	Normotension	7.73	85.00	

** Mann-Whitney test*

DISCUSSION

Based on the statistical test in Table I, it is found that age and parity have no relationship with the incidence of preeclampsia with a p-value of 0.500, <0.05, while the body mass index (BMI) shows that obesity is more in the group of mothers with preeclampsia which is significantly related with the incidence of preeclampsia with a p-value of 0.005, <0.05. Age is related to the increase and decrease in bodily functions so that it can affect one's health status explained that the safe age for a pregnant woman at the age of 20-35 years after that will have a high risk for complications such as preeclampsia.[14]Similarly, parity was found to be unrelated to the incidence of preeclampsia in contrast to the results of other studies which explained that parties are an important factor that needs to be monitored in the prevention of preeclampsia. However, this study is inversely proportional to the results of previous studies, possibly due to the awareness of mothers in the number of antenatal care visits to routine health facilities as prevention of risk factors for mothers.

While the body mass index characteristics of the two groups are known to have a close relationship in the case of preeclampsia. According to previous research, obesity is a risk factor for preeclampsia. It was also stated that mothers who are obese have the potential to increase the risk of preeclampsia for every 5-7kg / m2 weight gain through the mechanism of hyperleptinemia, metabolic syndrome, the subsequent inflammatory reaction, an increase in oxidative stress which causes endothelial cells not to function properly and leads to on the typical symptoms of preeclampsia.[15]

The results of the average IL-1β level test in preeclamptic and normotensive mothers in the Bugis, Makassar, Mandar, and Toraja tribes using Kruskal Wallis proved that there were differences in IL-1β levels in each tribe. Preeclampsia is often referred to as a multifactorial disease, one of which is related to genetic factors where there are disorders of several genes that are influenced by environmental factors, resulting in immune maladaptation which mediates oxidative stress and ultimately endothelial dysfunction that leads to typical symptoms of preeclampsia. increased blood pressure, urine protein and edema.[5, 13] In a study conducted by Anderson Steward, 2014, it was reported that minority groups compared to whites had a higher risk of developing preeclampsia, in line with this study in other studies Wong, et al. 2008 conducted retrospectively in Asia, Hawaii, Samo, Guamanian, and the Philippines were more likely to be preeclampsia than the Chinese population.[16]

In another study, it was explained that the variation in ethnicity affected the level of cytokine release due to gene polymorphisms.[17] From the research conducted, it was found that the levels of IL-1β in preeclampsia were different in each region, the differences in geographic, cultural and cultural characteristics of each tribe studied could be a contributing factor so that there were differences in levels significantly and higher than the levels at normotension. Differences in IL-1β levels in preeclamptic women and normotension in each tribe. Other findings in this study also showed that there were differences in IL-1β levels in pregnant women with preeclampsia and normotension known to be more elevated during preeclampsia compared to normotension. inline with research Taylor et al., 2016 that preeclampsia in pregnancy is considered excessive inflammation because during pregnancy many cytokines are secreted by immune cells and lymphocytes in the trophoblast and decidua which include regulating immunity, inflammation, haematopoiesis. Different from research by *Gupta and Chari, 2015* conducted on 75 pregnant women with preeclampsia and normotension to predict the value of cytokines pregnant women concluded that the IL-1β levels in the two groups were not found to be different. On the contrary, there was a decrease in IL-1β levels in pregnant women with preeclampsia.[19] whereas in other studies it was concluded that in preeclampsia pregnancy, the serum level of inflammatory cytokines, one of which IL-1β, was higher. Likewise, other studies suggest that the proinflammatory cytokine IL-1 β increases in the circulation of mothers with preeclampsia when compared to normotensive pregnant women.[20]

CONCLUSION

The levels of proinflammatory cytokine IL-1β were increased in preeclamptic pregnant women and had varying levels in each tribe.

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