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41. Knowledge on Heart Smart Diet among Hypertensive Clients in Selected Urban Areas of Mangalore City 221
Abin P Simon, Vimala Prasad, Vinish V

42. Job Satisfaction of Work Life Balance of Women Employed in Unorganised Sector in Kanchipuram District, Tamilnadu 226
Ramya Thiyagarajan, K Tamizhjyothi

43. Knowledge on Effects of Substance Abuse among Adolescents: - A Descriptive Study 232
Vinish V, Vimala Prasad

44. The Effect of Se'i (Smoked Beef) Toward the Improvement of the Bcl-2 Protein Expression on Colon Cells of Balb/c Strain Mice as a Carcinogenesis Indicator 238
Apris A Adu, Ketut Sudiana, Santi Martini, Mas'amah, Husaini

45. Malaria and Nutritional Status among Female Adolescents in West Sulawesi, Indonesia 243
Noor Bahri Noer, Veni Hadju, Ridwan M Thaha, Anwar Daud, Andi Imam Arundhana, Anwar Mallongi

46. The Influence of Leadership Style of Midwife Coordinator Toward The Performance of Village Midwives on Antenatal Care Through the Job Involvement 249
Syamsul Arifin, Fendy Suhariadi, Nyoman Anita Damayanti

47. The Analysis of Strategic Plan on Sambang Lihum Psychiatric Hospital Kalimantan, Indonesia 2016-2021 toward Drug Rehabilitation with Good Clinical Governance Framework 253
Riswan Iriyandy, Husaini, Eko Suhartono, Roselina Panghiyangani, Bahrul Ilmi, Nurul Rahmi

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K Damodaran

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Naveenkumar C, Swathi S, Jayalakshmi G, Chidambaram R, Srikumar R

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Nishtha Singh, Priyanka Kachwaha, Deepak Kumar Singhal

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Musafaah, Fauzie Rahman, Anggun Wulandari, Susi Yani T

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Salmah Arafah, Rosdiana Natzir, Syahrul Rauf, Mochammad hatta, Yudit Patiku, Ariyanti Saleh

expression of Gen Monocyte Chemoatractant Protein 1 (MCP-1) mRnA on Preeclampsia

salmah Arafah [1], Rosdiana natzir [2], syahrul Rauf [3], Mochammad Hatta[4], Yudit Patiku[5], Ariyanti saleh [6]

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ABstRACt

Background and Objective: This study aims to determine the expression of mRNA MCP-1 gene in Preeclampsia Patients.

Materials and Method: The research method used is quantitative research using case-control design with the sample of 20 respondents consisting 10 cases and 10 controls. Case samples were pregnant women with preeclampsia at the time of the study while control samples were normal pregnant women who met inclusion and exclusion criteria. Data were analyzed using Independent T-Test statistics.

Results : The results showed that 95% CI with LL = -6,465 and UL = - 4,852, with p = 0,000 mean that average expression of mRNA MCP-1 gene in blood expressed was higher in preeclampsia group. While 95% CI value with LL = -6,371 and UL = - 4,688, with p value = 0.000 mean that average expression of mRNA MCP-1 gene on exposed placenta is also higher in preeclampsia group.

Conclusion : It is necessary to follow up with prospective cohort design by making the class of pregnant mothers at risk with guidance for preeclampsia and determine of profile mRNA expression MCP-1 gene in both blood and placenta as molecular pathophysiology.

***Keywords**: Preeclampsia, MCP-1, mRNA*

IntRoDUCtIon

Preeclampsia is one of the complications of pregnancy which is the leading cause of death 15 - 20%, in developing countries along with bleeding and infection. In Indonesia, MMR is still high, the analysis result of Indonesia's demographic and health surveys (SDKI) in 1997 shows that maternal mortality rate is 334 deaths per 100,000 births. This number decreased to 307 per 100,000 births in 2003 to 228 deaths in 2007. The target of maternal mortality for 2010 was 125 deaths per 100,000 births.[5]

The maternal mortality rate in South Sulawesi province in 24 districts was obtained in 2012 are 140 people, in 2013 are 108, in 2014 are 138, and in 2015 are 149 people. From the 24 districts of South Sulawesi Province, Gowa regency has a high prevalence of maternal mortality. This is caused by many factors including lung disease, pregnant women's nutritional problems, hypertension, malaria, STI, abortion, heart disease, diabetes, HIV-AIDS, goiter, asthma, bleeding, Infections and Delinquent Childbirth. Based on the data obtained that the distribution of maternal mortality based

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on where the death of most mothers in the RSU that are 115 people.[3]

One of the factors causing preeclampsia is the role of increased concentrations of proinflammatory cytokines and the effect on preeclampsia, this cytokine is TNF-α. TNF-α levels will increase and this results in systemic inflammation. This inflammatory process is possible to have a connection with the incidence of preeclampsia. Increased TNF- α will cause increased expression of MCP-1 in endothelial cells and this results in a change in the balance between vasodilator and vasoconstrictor materials resulting in general vasospasm and decreased perfusion of some organs. Decreased perfusion of some organs due to imbalance between vasodilator material and vasoconstrictor material resulted in the emergence of preeclampsia in pregnant women.[9]

The increase of MCP-1 chemokine in maternal circulation plays a central role in increasing the systemic inflammatory response characterized by extensive endothelial dysfunction which is the characteristic of maternal syndrome in preeclampsia.[8]

TNF-α and IL-1β increase the production of MCP-1 in the decidua in the first trimester. This demonstrates the mechanism by which excess macrophages in the decidua can damage endovascular trophoblastic invasion, placental defects primarily in preeclampsia.[2] This study aims to determine the expression of mRNA MCP-1 gene in Preeclampsia and normotensive.

MAteRIALs AnD MetHoD

The study population was all normal pregnant women and preeclampsia at BLUD RSUD H. Padjonga Daeng Ngalle Takalar from October 2016 until June 2017 with No.47/445/RSUD-HPDN/PM/IX/2017. The sample in this research is pregnant women who meet inclusion criteria of primigravida and multigravida mother with third trimester pregnancy age. The subjects of the study were purposive sampling consisting of 20 samples of patients with two groups of 10 samples of normal pregnant women and 10 samples of preeclampsia pregnant women. In this study, interviews were conducted to obtain information about the characteristics and general circumstances of the subjects such as name, age, number of children, history of previous illness and health service history (ANC) by looking at KIA book / midwife notebook, then diagnosed by using blood pressure criteria ≥ 140 / 90mmHg as case and blood pressure less than 140 / 90mmHg as control. Urine samples were then taken for proteinuria and edema testing. Furthermore, samples of blood respondents were taken for examination of mRNA expression MCP-1 gene. The blood specimens of the study subjects were taken when the mother visited the ANC Room of the Hospital of H. Padjonga Daeng Ngalle Takalar Takalar then traced until the mother gave birth and taken the placenta tissue then examined. In Immunology and Molecular Biology Laboratory of Hasanuddin University of Makassar University Indonesia using molecular technique i.e. Real-Time Polymerase Chain Reaction (RT-PCR). Data analysis was performed using Independent T-Test using SPSS version 22 statistic program.

ResULts

After calculation all data from research then data was elaborated in term of table as follow, table1.

t able 1. Respondents Characteristics

Variables	Normotensive		Preeclampsia	
	n	%	n	%
Age				
<20 and > 35	2	20	5	50
20-35	8	80	5	50
Parities				
1-3	10	100	7	70
>3	0	0	3	30

Table 1 shows that the age of respondents in the normotensive group is <20 and> 35 years of age as many as 2 respondents, while the age of 20-35 years is 8 respondents. While the age of respondents in the preeclampsia group is <20 and> 35 years old as many as 5 respondents, while the age of 20-35 years as many as 5 respondents. While based on parity shows that the highest percentage is respondents with 1-3 persons in the group preeclampsia group that is as much as 70% while respondents with parity> 3 people in the case group as much as 30%. While in the group of normotensive parity of 1-3 people is as much as 10 or 100%.

t able 2. expression of mRnA Gene MCP-1 in Blood

Expression of mRNA gene MCP-1 in blood	n	Mean	SD	95%CI	P
Normotensive	10	5,738	0,617	(-6,465);(-4,852)	0,000
Preeclampsia	10	11,398	1,045		

Table 2. showed that the mean of mRNA expression MCP-1 blood in the normotensive group was 5.738 Ct with a standard deviation of 0.617 Ct while in preeclampsia 11.398 Ct with a standard deviation of 1.045 Ct. Based on statistical analysis. 95% CI with LL = -6,465 and UL = - 4,852 with p = 0,000 mean that the average expression of mRNA expression MCP-1 in blood was higher in preeclampsia group.

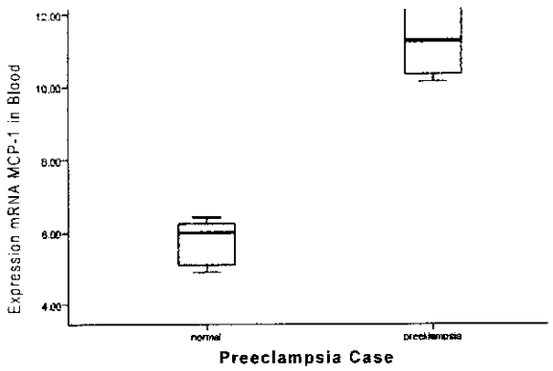

Figure 1. the MCP-1 mRnA expression in Blood

t able 3. expression of mRnA Gene MCP-1 in Placenta

Expression of mRNA gen MCP-1 Placenta	n	Mean	SD	95% CI	P
Normotensive	10	6,565	0,655	(-6,371)-(-4,688)	0,000
Preeclampsia	10	12,094	1,083		

Indicates that, the mean mRNA expression of placental MCP-1 in the normotensive group was 6.565 Ct with a standard deviation of 0.655 Ct while in preeclampsia was 12.094 Ct with a standard deviation of 1.083 Ct. Based on statistical analysis, 95% CI with LL = -6,371 and UL = - 4,688, with p = 0.000 mean that average of mRNA expression of MCP-1 in placenta expressed higher in preeclampsia group.

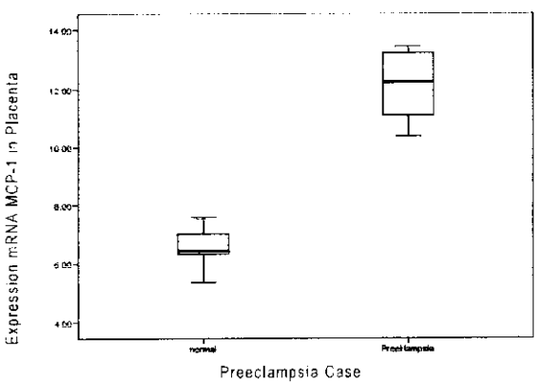

Figure 2. the MCP-1 mRnA expression in Placenta

DIsCUssIon

Age is an essential part of reproduction status. The Age has relation to the increase or decrease of body's function by which it influences the status of someone's health. The best and the most secure age for pregnancy and bearing is between 20-35 of age whereas the woman's first pregnancy of young age as well as the pregnant woman at the age of >35 would be in very high risk in preeclampsia.

The Pregnant woman without hypertension who is in the hazard of preeclampsia is the one at the age of >35. The age group of that has a vital correlation with preeclampsia, so does the age variable to high blood pressure.

The result of research reveals that the respondents who have had preeclampsia at risking parity >3 are 3 (30%) of 10 respondents. Furthermore, those at not risking parity (1-3 times) are 7 respondents (70%). The respondents without dominant preeclampsia at not risking parity (1-3 times) are 10 respondents (100%).

The first parity is related to the lack of experience and knowledge of the mother in the care of pregnancy. The parity 2-3 is the safest one. The Parity one and high parity (more than 3) are the hazardous parity at most. The Mother with great parity (more than 4) has been in a reduction at the system function of reproduction. The other reason, the mother at certain time is so stuck in keeping house that the one would be exhausted and is less- attention of nutrient adequacy.[1]

According to[8] preeclampsia / eclampsia constitute 80% of all cases of hypertension in pregnancy and affects between 3-8% of patients, primarily primigravida/ primipara in second trimester pregnancy. This is consistent with Rozhikan's[6] study, suggesting that the parity factor (the first child) is at risk for severe preeclampsia 4,751 times compared with the second or third pregnant women (multigravida). This is in line with theory[7], which says that in primigravida the frequency of preeclampsia is higher when compared with multigravida.

All women have a risk of preeclampsia during pregnancy, maternity, and childbirth. Preeclampsia does not only occur in primigravida / primipara, in Grande multipara also has the risk to experience eclampsia. For example, it occurs in pregnant women and maternity

more than three times. Excessive stretching of the uterus causes excessive ischemia which can lead to preeclampsia.[6]

The results of the study based on bivariate test of mRNA expression MCP-1 showed significant results in preeclampsia. Statistical results showed that expression of placental MCP-1 mRNA expressed higher than blood in the preeclampsia and normotensive groups. This is in line with the results of a study conducted by[2] which describes a statistically significant increase in macrophages (CD68-positive cells) in decidua in patients with preeclampsia. To explain the regulation of monocyte infiltration, the expression of monocyte chemo-attractant protein-1 (MCP-1) can be assessed in the first trimester of the leucocyte decidua cell independently. Comparison of response concentrations revealed that 0.01 ng / ml TNF-α or IL-1β increased the production of MCP-1 by more than 15-fold. This study shows that TNF-α and IL-1β increase the production of MCP-1 in the decidua in the first trimester. This study demonstrates the mechanism by which macrophages excess in the decidua can damage endovascular trophoblastic invasion, placental impairment primarily in preeclampsia.[2]

The interstitial cytotrophoblast enters the decidua floor, then circles and penetrates the spiral arteries and arterioles, and becomes the endovascular cytotrophoblast that alters the smooth muscle layers and endothelial vessels. This process changes the small blood vessels, high vascular resistance to large diameter blood vessels, low blood vessel resistance to meet the demands of fetal placenta unit growth by increasing maternal blood flow. The invasion of endovascular trophoblastic is the occurrence of failure of major placental defects in preeclampsia and fetal intrauterine growth. This leads to inadequate conversion of the uterine artery and reduces the amount of blood in uteroplacental development. This can affect 3 to 10% of all pregnancies; preeclampsia is a major cause of maternal and fetal mortality and morbidity worldwide.[1]

ConCLUsIon

mRNA expression MCP-1 gene in blood and Placenta was expressed higher in the preeclampsia group than in the normotensi group at the BLUD Hospital H. Padjonga Daeng Ngalle Takalar.

Conflict of Interest: No conflict of interest was declared.

ethical Clearance- Approved by Medical Faculty committee, Hasanuddin University, Makassar.

Acknowledgement: Researchers would like to thank the BLUD RSUD H. Padjonga Daeng Ngalle of Takalar District for their assistance by making the hospital as a place of research in taking cases of preeclampsia. Thank you to say to the research and development of human resources BLUD RSUD H. Padjonga Daeng Ngalle Takalar District who has given the research permission and thanks also to the midwives who have helped the research.

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ResULts

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table 2. expression of mRnA Gene MCP-1 in Blood

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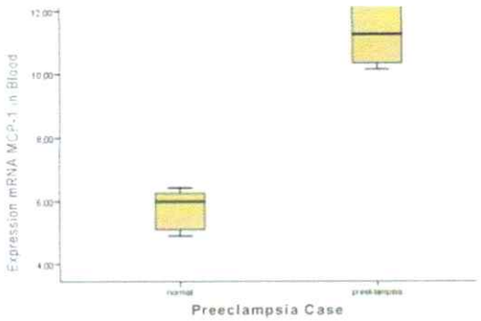

Figure 1. the MCP-1 mRnA expression in Blood

t able 3. expression of mRnA Gene MCP-1 in Placenta

Expression of mRNA gen MCP-1 Placenta	n	Mean	SD	95% CI	P
Normotensive	10	6,565	0,655	(-6,371)-(-4,688)	0,000
Preeclampsia	10	12,094	1,083		

Indicates that, the mean mRNA expression of placental MCP-1 in the normotensive group was 6.565 Ct with a standard deviation of 0.655 Ct while in preeclampsia was 12.094 Ct with a standard deviation of 1.083 Ct. Based on statistical analysis, 95% CI with LL = -6.371 and UL = - 4.688, with p = 0.000 mean that average of mRNA expression of MCP-1 in placenta expressed higher in preeclampsia group.

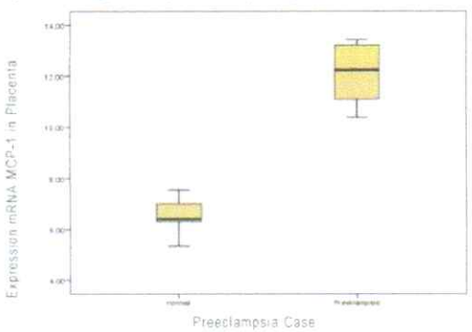

Figure 2. the MCP-1 mRnA expression in Placenta

DIsCUssIon

Age is an essential part of reproduction status. The Age has relation to the increase or decrease of body's function by which it influences the status of someone's health. The best and the most secure age for pregnancy and bearing is between 20-35 of age whereas the woman's first pregnancy of young age as well as the pregnant woman at the age of >35 would be in very high risk in preeclampsia.

The Pregnant woman without hypertension who is in the hazard of preeclampsia is the one at the age of >35. The age group of that has a vital correlation with preeclampsia, so does the age variable to high blood pressure.

The result of research reveals that the respondents who have had preeclampsia at risking parity >3 are 3 (30%) of 10 respondents. Furthermore, those at not risking parity (1-3 times) are 7 respondents (70%). The respondents without dominant preeclampsia at not risking parity (1-3 times) are 10 respondents (100%).

The first parity is related to the lack of experience and knowledge of the mother in the care of pregnancy. The parity 2-3 is the safest one. The Parity one and high parity (more than 3) are the hazardous parity at most. The Mother with great parity (more than 4) has been in a reduction at the system function of reproduction. The other reason, the mother at certain time is so stuck in keeping house that the one would be exhausted and is less- attention of nutrient adequacy.[11]

According to[8] preeclampsia / eclampsia constitute 80% of all cases of hypertension in pregnancy and affects between 3-8% of patients, primarily primigravida/ primipara in second trimester pregnancy. This is consistent with Rozhikan's[9] study, suggesting that the parity factor (the first child) is at risk for severe preeclampsia 4,751 times compared with the second or third pregnant women (multigravida). This is in line with theory[7], which says that in primigravida the frequency of preeclampsia is higher when compared with multigravida.

All women have a risk of preeclampsia during pregnancy, maternity, and childbirth. Preeclampsia does not only occur in primigravida / primipara, in Grande multipara also has the risk to experience eclampsia. For example, it occurs in pregnant women and maternity

more than three times. Excessive stretching of the uterus causes excessive ischemia which can lead to preeclampsia.[7]

The results of the study based on bivariate test of mRNA expression MCP-1 showed significant results in preeclampsia. Statistical results showed that expression of placental MCP-1 mRNA expressed higher than blood in the preeclampsia and normotensive groups. This is in line with the results of a study conducted by[3] which describes a statistically significant increase in macrophages (CD68-positive cells) in decidua in patients with preeclampsia. To explain the regulation of monocyte infiltration, the expression of monocyte chemo-attractant protein-1 (MCP-1) can be assessed in the first trimester of the leucocyte decidua cell independently. Comparison of response concentrations revealed that 0.01 ng · ml TNF-α or IL-1β increased the production of MCP-1 by more than 15-fold. This study shows that TNF-α and IL-1β increase the production of MCP-1 in the decidua in the first trimester. This study demonstrates the mechanism by which macrophages excess in the decidua can damage endovascular trophoblastic invasion, placental impairment primarily in preeclampsia.[2]

The interstitial cytotrophoblast enters the decidua floor, then circles and penetrates the spiral arteries and arterioles, and becomes the endovascular cytotrophoblast that alters the smooth muscle layers and endothelial vessels. This process changes the small blood vessels, high vascular resistance to large diameter blood vessels, low blood vessel resistance to meet the demands of fetal placenta unit growth by increasing maternal blood flow. The invasion of endovascular trophoblastic is the occurrence of failure of major placental defects in preeclampsia and fetal intrauterine growth. This leads to inadequate conversion of the uterine artery and reduces the amount of blood in uteroplacental development. This can affect 3 to 10% of all pregnancies; preeclampsia is a major cause of maternal and fetal mortality and morbidity worldwide.

ConCLUsIon

mRNA expression MCP-1 gene in blood and Placenta was expressed higher in the preeclampsia group than in the normotensi group at the BLUD Hospital H. Padjonga Daeng Ngalle Takalar.

Conflict of Interest: No conflict of interest was declared.

ethical Clearance- Approved by Medical Faculty committee, Hasanuddin University, Makassar.

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