

Influence Of Sympathetic Hyperactivity And Levels Of Endothelin-1 In Hypertension To Pregnancy And Small For Gestational Age (SGA)

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Abstract: Pesta Corry Sihotang. Effect of sympathetic hyperactivity, Endothelial Dysfunction Due to Hypertension and Small for gestational age (SGA). In Indonesia, hypertension due to pregnancy (Pregnancy Induced Hypertension) range from 5-10% of all pregnancies. This is a major cause of death, after bleeding. Hypertension due to pregnancy can be Preeclampsia and eclampsia, if not handled appropriately. This study aimed to prove the influence of the sympathetic hyperactivity, endothelial dysfunction on the incidence of PIH and SGA. The study design is nested cohort. Methods and ways of working: 30 pregnant women who were willing to participate in this study examined after signing the agreement / informed consent. Research subjects are grouped into groups of PIH and Normal and followed until delivery. In conclusion there was a significant difference between the incidence hyper-reactor and hypo-reactor second trimester with the incidence of PIH and normotensive with Chi-Square $P < 0.05$ against the incidence of hypertension. While the risk of PIH on hype-reactor group in the second trimester has RR 3.66 (CI 1.04 to 12.9), while the results of the third trimester there is a difference between having hype-reactor and hypo-reactor with RR of 5.83 (CI 1.37 to 24.6). Results ET-1 shows the differences in levels of endothelin in the third trimester with PIH and normotensive patients, namely ($R = 0.38$ $p = 0.038$ and $R = 0.49$, $p = 0.005$). Furthermore, in the third trimester relationship with the incidence of PIH $R = 0.74$ or 0.01 p in the end there are differences between the mean levels of ET-1 in the third trimester between PIH and normotensive group ($p < 0.05$). Recommendations CPT (Cord Pressure Test) is a tool that can be used to predict the incidence of hypertension in pregnancy, especially in the second trimester, while the results of Elisa can predict the incidence of hypertension in pregnancy.

Index Terms: PIH, CPT, ET-1, SGA

1 INTRODUCTION

National development is the development of insightful health. The vision of healthy Indonesia 2010 is the image of Indonesia in the future to be achieved through the development of the health of the community, the nation and the country that is characterized by its inhabitants to live in healthy living behaviours, has the ability to reach out to quality health services in a fair and equitable health degrees and has extended throughout the territory of the Republic of Indonesia (RI Department of health, 1999). According to the World Health Organization (WHO) estimated 600,000 women die each year from complications related to pregnancy, delivery and parturition. Maternal mortality in 2005 in some countries of ASEAN, Vietnam recorded 95/100,000 live births, Malaysia 30/100,000 live births, and Singapore 9/100,000 live births. Indonesia has the highest maternal mortality rates in ASEAN 291/100,000 live births. It's expected in 2010 maternal mortality is down to 125/100,000 live births. In Indonesia there are three main causes of maternal mortality they are hemorrhage, infection and preeclampsia. One of the most common cause of death is Preeclampsia caused by pregnancy or commonly referred to Pregnancy-Induced Hypertension (PIH) occurs approximately 5 to 10% in pregnant women, because pregnant woman experiencing many changes in the composition of both hormonal, cardiovascular system, urinary tract system. Based on the health profile of South Sulawesi, maternal mortality rate is currently obtained from a limited survey. Maternal mortality rate in 2005 amounted to 163/100,000 live births, with the cause of the bleeding 88 person (53.58%), the PIH (Preeclampsia-eclampsia) 23 people (15.95%)

Infections 11 people (6, 11%), and the other 30 people (23.93 percent). Based on data obtained from Medical records of RSIA Siti Fatimah Makassar from January 1 to December 31 2005 and 2006 there are 130 pregnant women with hypertension. Hypertension that will be discussed in this research is hypertension because of pregnancy or *Pregnancy Induced Hypertension* (PIH) that mostly occur in 20th week, which is more common in *primigravida*. Pregnant women with hypertension showed elevation of risk occurrence of complications, among other diseases of the blood vessels of the brain and organ failure. While they contain high-risk fetuses are exposed the complications or fetal growth obstacles often referred to with the small for gestational age (SGA). According to the report of the 2000 Group of hypertension in pregnancy, there is several classification of hypertension in pregnant women. One of them is chronic hypertension, i.e. systolic blood pressure greater than or equal to 140 mmHg. This disease occurs before pregnancy or diagnosed before 20 weeks of pregnancy or settled after a six-week postpartum. If systolic exceeds 200 blood pressure mmHg, the mortality rate of pregnant women was 22 percent. The treatment of hypertension, in addition to lowering maternal mortality and morbidity rates, will also lower the numbers prelatures, reducing barriers to the growth of the fetus, insemination and lowering perinatal mortality rate. To help in decreasing the maternal mortality rate particularly in hypertension several researchers conduct sympathetic hyperactivity examination by soaking the hands in the ice container called CPT/Cold Pressure Test. occurrence of PIH in pregnant women may be known as early as possible by using a tool called CPT (Cold Pressure Test), which is a tool that can be used to detect the early onset increased blood pressure by soaking the patient's left hand up to the elbow with the water temperature 3 up to 5 degrees Celsius for 30 seconds, to know the blood pressure response to cold temperatures. The results of these measurements can be seen from the increasing of blood pressure called hyper reactor > 15 mmHg and hypo reactor > 15 mmHg, as a prediction of the

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occurrence of hypertension (Ministry of Health et.al, *Cold Pressure Test as a Predictor of Hypertension*, 1998). Increased ET-1 can also be used to detect the occurrence of hypertension in pregnant women. Woisetchlager research result, from 10 of the 123 pregnant women with pregnancy between 16-20 weeks (8%) had severe Hypertension (PIH) and treatment (CPT) or test the emphasis is cool. Systolic and diastolic blood pressure increased significantly (systolic blood pressure, $P = 0.02$; diastolic blood pressure, $P = 0.03$). This indicates increased vasoconstriction response physiology so that researchers will try to test the cold emphasis on pregnant women. From the above assessment will invite the question whether Hypertension (PIH) with measurement parameters hype-reactor and hypo-reactor on CPT and examination of blood plasma ET-1 with Enzyme Link Immune Sorbent Assay (ELISA) can be properly enforced in relation to the occurrence of hypertension (PIH) and Small for Gestational Age (SGA) with the aim of reducing maternal and infant mortality rates. According to Irfan et al (2005), in the Journal Medica Hasanudin University get that blood pressure increases due to submersion at 30 seconds to determine whether or not there's sympathetic Hyperactivity dystrophy (Hype-reactor and Hypo-reactor) means (t test; t pared $< 0,05$). The relative risk of incidence of low birth weight babies in the Group results of the CPT + or Hype-reactor was 2,275 times compared to the group that his hypo-reactor CPT results. Researchers want to continue this research with a planned inspection of the CPT and ET-1 in series in the first trimester, second and third trimester, in order to obtain results that may prove the existence of an influence on each trimester for pregnant women among the *Cold Pressure Test* and examination of ET-1 against Gen. PIH and small for Gestational Age to be scrutinized by *Prospective Cohort*. Based on explanation-the description, then the author is interested in conducting research with the title "The *influence of Sympathetic Hyperactivity*, ET-1 to the Genesis of hypertension (PIH) and small For Gestational Age (SGA).2 Procedure for Paper Submission

2.1 Literature Review

Hypertension due to pregnancy or *Pregnancy Induced Hypertension* (PIH) has many definitions that are adapted to the conditions in this study talk about the definition of PIH with no Proteinuria that is; The occurrence of a blood pressure of 140/90 mmHg or more and/or an increase in diastolic pressure of 20 mmHg or more after the 20th week of pregnancy on at least two separate occasions more than 24 hours apart in a woman known to be previously normotensive. (Broughton Pipkin, 1998 in his book the Tex book for Midwife) This means that the incidence of an increase in blood pressure $> 140/90$ mmHg and 20 mmHg diastolic increases with age after 20 week of pregnancy checked 2 times within 24 hours of a woman who had a normal blood pressure. According to the WHO in his book the *IMPAC 2000*, Ps36 *Pregnancy Induced Hypertention* (PIH) is if the increase in blood pressure occurred after 20 Mg during labor and or 48 hours after the post copy and if Genesis before 20 Mg Hypertensi Chronicle called the gestational age. Said PIH if an increase in systolic blood pressure > 140 mmHg/ > 90 mmHg and/or diastolic blood pressure increase > 20 mmHg after 20 weeks of gestation and examination done least 2 times in 24 hours in women who previously had normal blood pressure. (Sweet, R.B. 1998). From some of the above it can be concluded that

definis hypertension in pregnancy are hypertensive, appear in pregnancy, then declined after the post copy. If hypertension occurs after the age of 20 Mg pregnancy and PIH are called if the occurred before 20 Mg is called Chronic Hypertension. The cause of the occurrence of hypertension because of pregnancy, there are several theories which explain the theory that describes the approximate cause of these abnormalities or commonly called *The Diseases of Theory*. As for the theory is the role of Thromboxane and Prostacyclin, namely Vascular Endothelial damage occurs so that the decrease in production of Prostacyclin (PG 12) which in normal pregnancy increases fibrinolysis activity which was later replaced by Thrombin and Plasmin. Platelet activity cause the release of Thromboxane (TA2 Serotin and so vasospasm and endothelial damage) The incidence is high in pregnancy on hypertension young primigravida, rising at old primigravida. In pregnant women less than 25 years of greater incidence 3 fold, in pregnant women over 35 years latent hypertension can occur. According to the high incidence rate of parity on prigravida young and old while the elderly primigravida higher risks for severe preeclampsia. Hereditary factors if there is a history of preeclampsia in the mother/grandmother sufferer increased 25% risk factor whereas factor genes thought to be existence of recessive trait that specified genotype of mother and fetus. Causes of PIH until now not yet known for sure. But it is estimated the existence of genetic factors. Women tend to suffer abnormalities if the biological mother is experiencing a similar thing. In pregnant women, the walls of the spiral arteries injected trophoblastic and revamped into a winding channel that carries the blood to the site of intervillous, this occurred in week 22th of pregnancy that can trigger the onset of decreased peripheral endurance. Uteri blood vessel became resistant to vasomotor substances. The influence of hypertension in pregnancy on a pregnant woman is the presence of symptoms of headache and blurred vision. The pregnant woman or the women who just give birth often suffer from seizures and unconsciousness. If it continues hypertension can be change become mild preeclampsia and severe preeclampsia even be eclampsia (convulsions). Low birth weight in the first pregnancy had twice the risk of developing hypertension in the second pregnancy. While the risk of hypertension in pregnancy second frequency by 20-50%. Hypertension on pregnancy without proteinuria if less than 37 weeks of pregnancy handled by outpatient, blood pressure monitor, and proteinuria fetal condition, if the blood pressure still increasing handled it as preeclampsia. If the fetus condition worsens or fetal growth occurs stunted, cared for and termination of pregnancy. Management on mild preeclampsia, if the pregnancy is less than 37 weeks and there are no signs of improvement, 2 times a week do assessment, monitoring blood pressure, proteinuria, reflexes, the condition of the fetus, more rest, regular diet and do not need drugs. If there are signs of fetal growth stunted consider the termination of pregnancy. Endothelial function in maintaining blood flow and the capacity of endothelial antithrombotic therefore release humoral factors that control the contraction and relaxation of vascular smooth muscle thrombogenesis and fibrinolysis and platelet activation and inhibition. With the ability to regulate hemostasis, endothelial contribute to the control of blood pressure, blood flow and blood vessel potency (Abdurazzak, G. 2000). Endothelial dysfunction is a condition in which obtained a balance between factors vasodilation and vasoconstriction. Healthy

endothelial cells capable of maintaining vascular integrity prevent platelet adhesion and affect vascular muscle tone. Hyperactivity of the sympathetic nerve is excessive increase occurred in the sympathetic nerves that can lead to vasoconstriction. To determine the presence of vasoconstriction of the blood vessels used cold pressure test, this test is a simple test that can measure the presence of sympathetic hyperactivity by providing an external stimulus such as cold temperatures or ice 5⁰ C. The meaning of SGA infants is when the baby weighs less than 10% from the actual weight with age pregnancy. The average growth of the baby in the womb is influenced by various factors.

2.2 Methodology

A research design that will be used is observation with research approaches "NEASTED COHORT" longitudinal/time basis approach period. This research takes the sample at one of Gowa Makassar in BPS began in early April 2005 to April 2006 conducted at private practice Midwife (CPM) of Tirana Gowa Makassar. And while the research starts from July 2005 to April 2006. The population was overall observation is of concern. With reference to the above points can be defined that expectant mothers aged less than 20 weeks and followed up until delivery. The samples in this research are pregnant women who saw a pregnancy to BPS Tirana Gowa which meets the criteria and is willing to participate in the study until birth. The characteristics of the sample can give the right picture about the characteristics of the population investigated. So sampling techniques used in this research is a simple random sample is taken from, where the population is randomly composed of selected elements of the population, namely pregnant women by as much as 30 people which is the sample, then after observation, who meets the criteria as much as 30 samples included hypertension and meets the criteria of inclusion in this research are:

- a. Pregnant women < 20 weeks gestation who is willing to sign an informed consent to inspection of the Plasma Endothelin and Sympatis Hyperaktivitas.
- b. There is no pregnancy complications and other diseases
- c. This research is observational aims to notice any effect of the Hyperaktivitas Sympatis, ET-1 against Gen. PIH and SGA

Preparation of Tools/materials used:

- a. Sphygmomanometer OMRON and Stethoscope
- b. Cold Pressure Test Apparatus
- c. ELISA kit and gloves
- d. Serum and EDTA Tubes
- e. Syringe 10 cc
- f. The chunk of ice

Samples were taken by total sampling in pregnant women Trimester I, II, III in research place that has been determined. Work Procedures

- a. After signing the agreement, the respondent conducted an examination Sympathetic Hyperactivity, i.e., respondents in a sitting position. Blood pressure was measured and then asked them to soak hands up a bit above the elbow in a container containing water ice with a temperature of 3-5 ° c. After the respondent's hands soaked do the blood pressure measurements after finished soaking 30 seconds. Systolic blood pressure and diastolic blood pressure compared to going to the break.

- b. Proceed with the taking of blood samples from as many as 5 cc venous cubitis then inserted into the tubing vakuteaner 2.5 cc respectively.
- c. The respondents then remained followed an examination from 1st trimester until the subject gave birth.

To control the whole operational aspect of research ranging from stage to stage of sampling data management performed the steps as follows:

- a. Standardizing the way data retrieval of CPT by its own researchers and research assistants (in BPS Tirana Gowa). Standardize how blood examination ET-1 was conducted in the laboratory of Prodia Makassar.
- b. Standardization of determination or not hypertensi hypertensi determined after giving birth to 9 months later
- c. Infusion and verify data to authenticate the computer.

2.3 Result

Characteristics of respondents taken in this research include Maternal Age, Gestational Age, Gravidity, history of hypertension, and weight. Based on the general picture of the number of 30 respondents obtained a description of the most common in the age of 20-30 years (70%), according to the gravidity were primiparous (40%), according to gestational age are at a mean gestational age of 12-20 mg (43%), according to a history of hypertension of mother average 33.3%, while the weight gain during pregnancy is 9 months the average increase in weight > 14 kg about 63%. CPT results variable on subsequent Trimester I, II, III showed an increase from time to time and the results of ET-1 is seen by PIH and Normal blood pressure tested by Chi Square. Furthermore, we will see if there is a difference between the incident hypo reactor and hype reactor each trimester and calculate the relative risk / RR hereinafter see the effect of CPT, ET-1 against hypertension in pregnancy with Logistic Regression which ultimately saw the baby weight after birth is small for gestational age / SGA. From the results of the research there is a noticeable difference between the 1st trimester to 3rd trimester for ET1, since $\alpha > p 0.05$ for PIH and Non-PIH also shows that there is a real difference between the 1st trimester to 3rd trimester ($\alpha < p 0.05$). There is a noticeable difference between the 1st trimester to 3rd trimester for ET1, since $\alpha > p 0.05$, for the hype reactor and for which no hype reactor also shows there is a real difference between the 1st trimester to 3rd trimester ($\alpha < p 0.05$). There is a real difference between the 1st trimester to 3rd trimester to ET1 on SGA and non SGA, because $p < \alpha 0.05$, for the SGA and to non-SGA also showed significant difference between first trimester to 3rd trimester ($p < \alpha 0.05$).

Hype reactor + PIH Cross tabulation

		PIH		Total
		PIH	Normal Blood Pressure	
Hype reactor	Count	7	4	11
	% within Hype reactor	63,6%	was 36.4%	100.0%
	% within PIH	100.0%	100.0%	36.7%
Hype reactor	% of Total	23.3%	13.3%	36.7%
	Count	0	19	19
	% within Non Hype reactor	0%	100.0%	100.0%
Non Hype reactor	% within PIH	0%	82.6%	63,3%
	% of Total	0%	63,3%	63,3%

	Count	7	23	30
	% within Hype reactor	23.3%	76.7%	100.0%
Total	% within PIH	100.0%	100.0%	100.0%
	% of Total	23.3%	76.7%	100.0%

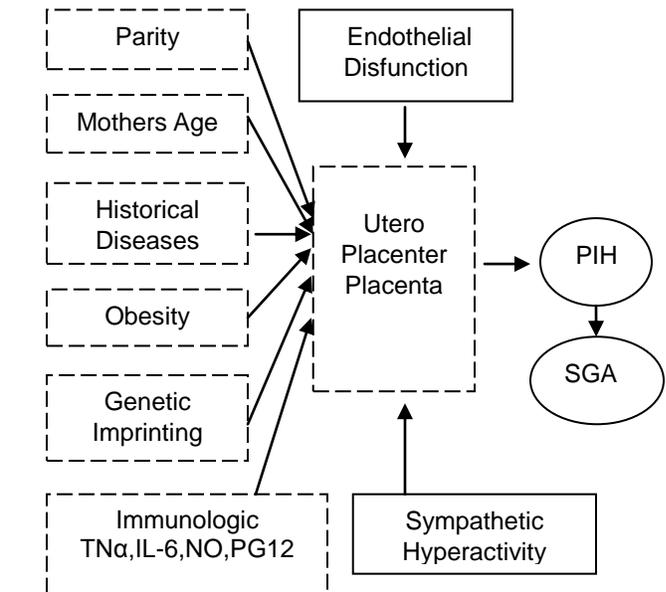
Chi-Square Test

	Value	Df	Asymp. SIG. (2-sided)	Exact Sig. (2-sided)	Exact Sig. (1-sided)
Pearson Chi-Square	15,771 (b)	1	.000		
Continuity Correction (a)	12,414	1	.000		
Likelihood Ratio	18,176	1	.000		
Fisher's Exact Test				.000	.000
Linear-by-linear Association	15,245	1	.000		
N of Valid Cases	30				

From the results of the study found the average value of the mean between PIH and normotensive against maternal age is 25.5714 and the standard deviation is 6.15447, next to maternal gestational age at PIH is 18.8571 and the mean standard deviation is 1.06904 and the normotensive is 19.4783, standard deviation is 2.64351. The average value of the mean between PIH and normotensive against HB is 10.2286 and sd 0.40574, for PIH and 10.3870 for normotensive and sd is 0.16106, next to maternal gestational age on the mean PIH is 3028.5714 and sd is 209.26662 and in normotensive is 19.4783, sd is 87.24168. The average value of the mean between PIH and normotensive against ET-1 first trimester is 0.73929 and 0.259074 sd for PIH, for normotensive is 0.71871, for ET-1 in the second half of PIH is 0.81100 and sd is 0, 370 116 and normotensive is 0.70686, sd is 0.192320, next to ET-1 in the third semester of PIH is 1.11373 and 0.086047 and sd are normotensive is 0.77105, sd is 0.189165. Characteristics of PIH and normotensive age on average at the age of 20-35 years, it is still a healthy reproductive age, the next most mean parity was the first child. This is in line with research conducted by several researchers who claim that hypertension in pregnancy increased 3 times over the first child, this is due to the rejection of sperm from men, especially if the husband is the second husband. CPT Results of trimester showed an increase of resting blood pressure compared with the 30-minute immersion. This is in line with research conducted Cliniko Hospital Universitario Santiago, that soaking with CPT can predict the occurrence of hypertension. This study wants to see an increase in the differences and the influence of the CPT and the results of ET-1 in pregnant women trimester I, II, III on the incidence of hypertension in pregnancy. In this study found no significant differences in the characteristics of maternal age, gestational age parity, as well as the history of the disease that can affect the results of the analysis of the differences between PIH and normotensive groups. In this study found no difference between the incidence Hype reactor and Hypo reactor in the first trimester with HDK and non HDK > 0.05. When examined, there were 7 people who hypertension of 30 respondents this case there were 42.5% and 57.5% Hype reactor the Hypo reactor. In the second trimester shows the difference between the incident of hypo reactor with 3 people and 4 people in hype reactor. If the observed results are increased in the second trimester to the relative value of Risk (RR) of 3.66 (CI 955 1.04-12,9) means may be a prediction for the third trimester of 3.66 times. While the results of the third trimester

showed the difference between the incident and Hypo reactor 2 people and 5 people for Hype reactor in order to get the results of Chi square test $p < 0.05$ so that the risk of HDK in the third trimester have 5.83 times. It is proved that there are statistically significant differences and to predict the increase in the incidence of hypertension. If seen statistically there is a relationship between Hype-reactor with hypertension where Hype-reactor 42.5% of this amount tends Hypertension. From the test results of the third trimester Test found that the most significant variables between PIH and normotensive are the results of ET-1 3rd trimester (0,000). Research shows the results of hypertension in pregnancy and 7 persons exposed to hypertension showed 42.5% hype reactor hereinafter after traced up to the delivery of 7 people found that there are 3 small for gestational age infants with meaning to the size of 2450 grams in which physical and neuromuscular maturity has adapted to the 40-week gestation baby weight average below 10%. Where hypertension of 7 mothers who gave birth there were 3 people KMK, this phenomenon can be explained as follows: the occurrence of vasospasm maternal great because of high levels of ET-1 will cause a decrease in utero-placental perfusion, this disruption will result in disruption of placental growth anyway, so the size / smaller placental weight. Secondly, the occurrence of placental ischemia will result in the formation of smaller placentas. Placental ischemia circumstances will trigger the formation of cytotoxic substances against free radicals and endothelial such as pro-inflammatory cytokines. These materials will cause endothelial dysfunction and release of vasoactive substances such as ET-1. The more severe placental ischemia, the more severe endothelial damage, which resulted in increased production of ET-1.

2.4 Research Paradigm



of Chart:
 [Solid Box] Free variables are examined
 [Dashed Box] Free variables not examined
 [Circle] Variables Bound

The dependent variable: Hypertension in pregnancy and SGA
 Independent variable: Sympathetic Hyperactivity, Endothelial Dysfunction
 Confounding: Variable Utero placenter placenta
 Operational Definition

- a. Because pregnancy is increased Hypertensi blood pressure ≥ 140 mmHg, systolik and Diastole ≥ 90 mmHg with gestational age > 20 mg. in case of chronic Hypertensi called < 20 mg. Objective Criteria: Hypertension: systolic blood pressure ≥ 140 mmHg and diastolic blood pressure ≥ 90 mmHg.
- b. Hyperaktivitas Sympatis nerves is an excessive increase occurred in sarh sympatis which can result in the occurrence of vasokonsriksi. Objective Criteria: Hype reactor: that if a rise of systolic blood pressure > 15 mmHg and diastolic > 15 mmHg. Hypo reactor: that if a rise of systolic blood pressure > 15 mmHg and diastolic > 15 mmHg.
- c. Cold Presor Test is a container made of cold temperature resistant Arkilik 3 – 5⁰ to measure hyperactivity.
- d. Dysfungsi Endothel is if there is disruption on the endothelium of blood vessels which results in excessive cytokines. Endotelin-1 levels are measured in units of pg/ml as measured by ELISA technique
 Objective criteria: 1 pico ml value is abnormal, if more than 0.5 – 1 normal value.
- e. Under 20 weeks gestational age is calculated based on the first day of the last day of the period by using the formula of neagle's next awaited gestational age 26 weeks and 40 weeks and wait until the birth.
 Objective criteria: If the hypertension occurs in gestational age 12 – 20 weeks it called chronic Hypertension. If gestational age > 20 mg it called PIH
- f. Mother's Age expressed in years complete at birth is calculated up to the last birthday.
 Objective criteria: < 20 years at risk, $> 20 - 35$ years not at risk
- g. Parity of mothers, the number of times the mother giving birth
 Objective criteria: < 3 times normal, > 3 times the risk of
- h. Birth weight, measured in units of grams with a baby scales
 Objective criteria: ≤ 2500 grams SGA/Small for gestation, > 2500 grams of Normal

4 CONCLUSION

From the results of research using Chi Square test showed an increase of sympathetic hyperactivity between systolic and diastolic significantly. Furthermore, to assess the differences between hype reactor at PIH and normotensive groups have differences in the second trimester. While in normotensive there are significant differences in the third trimester. Results ET-1 each trimester in people who PIH and normotensive found in the third trimester is the most significant (0.000). From the results of the Chi Square test in people who PIH risk is relatively high in the second trimester ie RR = 1.375 (CI 0.14 to 13.176), in the normotensive group was found in the second trimester ie RR = 2.063 (CI 0.585 to 9.267). Overall the influence of sympathetic Hyperactivity endothelial dysfunction-1, to incidence of PIH and normotensive showed an improvement and significant difference. The influence of the increase in the value of ET-1 and CPT will affect the incidence

of small for gestational age (SGA). It is recommended that all pregnant women affordable to get antenatal service regularly, if perceived signs of persistent headache, dizzy view it can result in hypertension in pregnancy. If untreated appropriately it will become Preeclampsia and eclampsia. In connection with these problems would be able to understand the importance of the information obtained through research such as Cold Pressure Test sets include examination and blood tests to see an increase in ET-1 that can predict the occurrence of gestational hypertension. It is recommended that all pregnant women antenatal services affordable can be checked on a regular basis, if it is felt the presence of signs of head pains, settle, a dizzy view can lead to the onset of hypertension in pregnancy.

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