COMPARISON OF SERUM ENDOTHELIN-1 AND SERUM LEPTIN LEVELS IN PRE-ECLAMPTIC AND CONTROL SUBJECTS IN THIRD TRIMESTER OF PREGNANCY

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ABSTRACT

Background: Pre-eclampsia is one of the leading causes of maternal and foetal morbidity and mortality. The pathophysiology of pre-eclampsia is not fully understood , however, Endothelin-1 (ET-1) and leptin are assumed to play important role in the severity of pre-eclampsia.

Objectives: To determine the levels of ET-1 and leptin in pre-eclamptic patients and compare them with normotensive subjects.

Materials and Methods: This study was conducted in Gyneacology Ward of Hayatabad Medical complex (HMC) under the supervision of Khyber Medical University (KMU), Peshawar, Pakistan, in the time period of January-September 2014. The study involved 40 pre-eclamptic and 40 normotensive women in their third trimester of pregnancy. Serum samples were obtained from all the individuals for determination of ET-1 and leptin concentration.

Results: Mean serum ET-1 and mean serum leptin levels in pre-eclamptic and control groups were 213±76.0mg/mL vs 97.5±0.1mg/mL, P<0.001 and 288.5±153ng/mL vs 158±55.9ng/mL, P<0.05 respectively. The mean systolic blood pressure (SBP) and mean diastolic blood pressure (DBP) in pre-eclamtic and control groups were 175.4±16.9mmHg vs 112.6±11.3mmHg, P<0.001, and 118.0±9.8mmHg vs 73.1±6.9mmHg, P<0.001 respectively. The urinary albumin excretion was greater in pre-eclamptic women of age group of 34-41years.

Conclusion: As a conclusion, significant high levels of serum ET-1 and leptin in pre-eclamptic women indicates possible role of ET-1 and leptin in the pathogenesis of pre-eclampsia. Also the elevated level of ET-1 and leptin may help in the prediction of the disease and may serve as a marker of severity of pre-eclampsia.

Keywords: Endothelin-1, Urinary albumin, Leptin, Pre-eclampsia,

INTRODUCTION

Pre-eclampsia is a syndrome defined as the onset of hypertension and proteinurea after 20 weeks of gestation in previously normotensive and non proteinuric women.[1] Pre-eclampsia involves abnormality of multiple body systems. The abnormalities in pre-eclamptic patients are high blood pressure, gestational hypertension, high frequency of urine having protein as well as disturbed liver and renal functions. In pre-eclamptic patients the platelet count remains considerably very low so disturbed coagulation may be present in pregnant women.[2] Pre-eclampsia occurs mostly in second or third trimester of pregnancy in normotensive women when there are symptoms of protenuria and high blood pressure. Therefore pre-eclampsia is considered to be the most severe and life threating complication worldwide.[3] The ratio is about two to ten percent in worldwide population. In Pakistan as well as around the globe pre-eclampsia is considered as a major cause of maternal morbidity and mortality, complicating 7–10% of pregnancies.[4]

The pathophysiology of pre-eclampsia is not fully understood but some contributing factors are family history, age, parity, immunity, abdominal pregnancies, multiple pregnancies, microvascular disease, and abnormalities in trophoblastic implantation, placental perfusion and large placenta. Endothelial cell injury in pre-eclampsia causes endothelial dysfunction leading to vasopasm, low plasma volume and oxidative stress.[5]

Some hormones like endothelin -1 (ET-1) and leptin are assumed to play important role in the severity of pre-eclampsia. ET-1 is a powerful and potent vasoconstrictor hormone which is derived from endothelium of smooth muscles of blood vessels. ET-1 is made up of 20 aminoacids which is then proteolytically cleaved to form active ET-1 of 21 amino acids. A lot cardiovascular diseases like congestive cardiac failure, chronic kidney failure and high blood pressure are due to high

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level of ET-1.[6] Leptin is recently identified polypeptide hormone of 167 amino acids, derived from obese gene (Ob gene). Leptin act as anti-obesity hormone which elevate energy consumption of the body, decrease body weight/adiposity, increase sensitivity of insulin, activation of sympathetic nervous system and reduces eating habits. Previous studies have reported that increased level of serum leptin in early pregnancy may leads to high risk for developing pre-eclampsia in women in their third trimester of pregnancy.[7] However, some studies have suggested no effect to the level of ET-1 and leptin in pregnancy induced hypertension.[8] Therefore, in the connection of all the controversial studies in literature we based our study to compare the level of ET-1 and leptin in pre-eclamptic and healthy pregnant women in their third trimester of pregnancy.

MATERIALS AND METHODS

A total of 80 women in their third trimester of pregnancy were recruited in which 40 women were taken as Pre-eclamptic group (PE group) and 40 women were taken as control group (normotensive). Women with already hypertension, diabetic and renal failure were excluded from the study. The pre-eclamptic patients were diagnosed through pregnancy induced hypertension and proteinuria. The patients were selected from Hayatabad Medical complex (HMC), Khyber Teaching Hospital (KTH), and Lady Reading Hospital (LRH) which are the three main Tertiary Hospital in Peshawar, Pakistan. The data and samples collection was started after taking written consent from the third trimester pregnant women on printed consent form already designed. History, clinical examination and laboratory investigations were taken according to the well designed questionnaires. This study was conducted in Khyber Medical University (KMU) in the time duration of January 2014- September 2014.

Blood samples were taken in disposable plastic syringes both from the PE and control groups. The blood samples were collected by adopting the aseptic procedure from the antecubital vein and then centrifuged (AJ-IE08 China). The samples were centrifuged at 3,000 rpm for ten minutes. The clear serum extracted was then shifted to new eppendorf tubes and labeled. The labeled serum samples were then stored at -20 to -80^{0}C till analysis. Human ET-1 and huma leptin serum ELISA kits were purchased from Hangzhou East Bio Pharm Company Limited China. The kit utilized a doubly-antibody sandwich enzyme-linked immunosorbent assay (ELISA) to analyze the levels of serum ET-1 and leptin in the samples.[9] The data was analyzed by SPSS version 17.

RESULTS

This study included a total of 80 samples. Forty normotensive women were compared with forty pre-eclamptic women in third trimester of pregnancy. Table-1 shows demographic data of pre-eclamptic and control group. Except the mean maternal age, all the demographic variables like duration of marriage, gestational age, number of deliveries, height and weight were nonsignificant among the two groups. The mean maternal age of pre-eclamptic women was 28.85±0.90 as compared to control subjects, 26.10±0.51, P<0.05.

Table-2 shows that mean SBP, and mean DBP of pre-eclamptic women was significantly higher at P<0.001. Mean SBP and mean DBP of PE group was 175.4±16.9mm Hg, 118.0±9.8 mm Hg as compared to control group, 112.6±11.3 mm Hg, 73.1±6.9 mm Hg respectively. The mean ET-1 level in pre-eclamptic women was 213±76.0mg/mL as compared to 97.5±0.1mg/mL in control subjects, P<0.001. The mean serum leptin level in pre-eclamptic women was 288.5±153ng/mL which was significantly higher at P<0.05 as compared to normal pregnant women in which the serum leptin level was 158.0±55.9ng/mL.

Figure-1 shows that the number of pre-eclamptic women in age group of 34-41years was greater as compared to control subjects. Figure -2 shows that only 5%

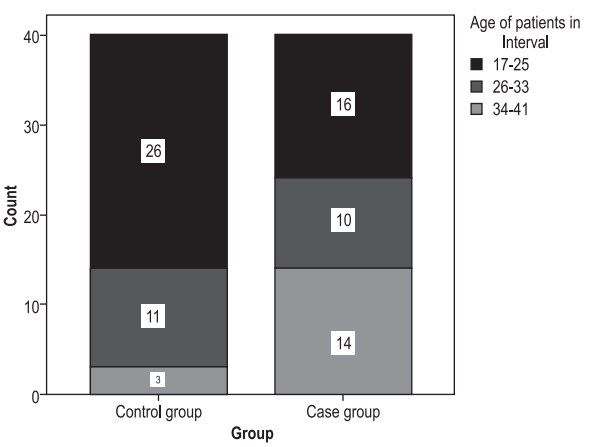

Figure-1: Distribution of Pre-eclamptic and Control Subjects in Different Age Groups

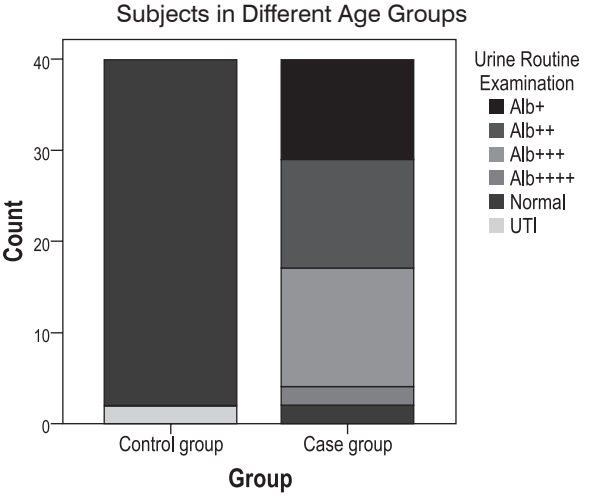

Figure-2: Urine Routine Examination of Pre-eclamptic and Control Subjects

Table-1: Demographic Data of Pre eclamptic and Control (Normal Pregnant Women) Groups

Variables	Groups		P-value
	PE (n=40) Mean±SD	Control (n=40) Mean ±SD	
Age(Years)	28.85±0.90	26.10±0.51	<0.05
Duration of Marriage (Years)	6.9±4.72	6.5±5.28	NS
Gestational Age (Weeks)	34.7±2.24	34.90±2.96	NS
Number of Delivery	0.79±0.82	0.84±0.78	NS
Height (m)	1.57±0.74	1.56±1.12	NS
Weight (Kg)	68.26±0.99	65.98±1.78	NS

NS: Not significant. All of the values are indicated as median± SD.

Table-1: Demographic Data of Pre eclamptic and Control (Normal Pregnant Women) Groups

Variables	Groups		P-value
	PE (n=40) Mean±SD	Control (n=40) Mean ±SD	
Systolic Blood Pressure (mmHg)	175.4±16.9	112.6±11.3	<0.001
Diastolic Blood Pressure (mmHg)	118.0±9.8	73.1±6.9	<0.001
Serum Leptin (ng/mL)	288.5±153	158±55.9	<0.05
Serum Endothelin-1 (mg/mL)	213.1±76.0	97.5±0.1	<0.001

NS: Not significant. All of the values are indicated as median± SD.

of the healthy pregnant women (control) were having Urinary Tract Infection (UTI) while 95% were having normal urine routine examination. In case group (PE group) majority of individuals were having abnormal urine routine examination, that is, different concentration of albumin in urine was reported as compared to control group.

DISCUSSION

Globally, pre-eclampsia is the most important cause of maternal morbidity and mortality. It is a pregnancy syndrome having hypertension and protenuria. The cause of hypertensive disease is not yet clear; it includes immunological, genetic, environmental and placental abnormalities. The current study was conducted to report the level of serum ET-1 and serum leptin in pre-eclamptic women in their third trimester of pregnancy and to compare the results with control group. In our study both serum ET-1 and serum leptin levels were significantly higher in PE group as compared to control group. These results suggests that ET-1 has potent role in the pathophysiology of pre-eclampsia, which is in agreement with the previous studies done on the level of ET-1 in other ethenic population. According to George and Granger in pre-eclampsia the placental tissues secrete some soluble secretions to the maternal blood. These secretions are the important pathological factors which causes high blood pressure by secretion of ET-1, a strong vasoconstrictor in blood.[10]

The results of our study also suggest that serum leptin level increases with increase in blood pressure both systolic and diastolic. Similar findings were seen in a study done by Anim-Nyame et al, however Martinez- Abundis et al contradicts our study and according to them serum leptin levels were similar in the patients with different grades of pre-eclampsia and normotensive pregnant women.[11,12] High leptin level may be increased in women with increased gestational age because not only adipose tissue is a source of leptin, but also in pregnancy foetus, placenta, amniotic fluid, increase in plasma volume and extra vascular fluid accumulation leads to increase in maternal weight and also the body mass index (BMI) is responsible for increase in serum leptin level.[13,14] Our study suggested that BMI value has no significant impact on serum leptin levels, while increase maternal age may be one of the low risk factor for pre-eclampsia. Maternal urinary albumin excretion was greater in pre-eclamptic women with increase maternal age.[15] Impaired renal function is a pathophysiological component of pre-eclampsia and the measured increase in plasma leptin concentration may reflect reduced renal clearance.[16] Also high leptin levels may be due to the possible haemoconcentration in pre-eclampsia caused by association of preeclampsia with reduced plasma volume.[17]

CONCLUSION

It has been concluded that in third trimester of pregnancy, the levels of ET-1 and leptin increases significantly in pre-eclamptic women due to increase in both systolic and diastolic blood pressure. No significant correlation was made between gestational age,

BMI and number of deliveries while increase maternal age may be considered as one of the low risk factor in the severity of pre-eclampsia. Unstable ET-1 and leptin levels in normal pregnancy and in gestational trophoblastic diseases indicate that these hormones can play an important role in human pregnancy. Further studies are required to understand the significance of these hormones and its correlation with other parameters of biochemistry in preeclampsia.

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