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MEASUREMENT OF PLASMA ANTITHROMBIN III IN WOMEN AND IT IS RELATION WITH PREECLAMPSIA

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ABSTRACT

This study was aimed to measure anti-thrombin III level among pregnant women with preeclampsia and compare it to normal pregnant women and correlated with pation age and gestation. Blood samples were collected from 40 pregnant women with preeclampsia beside 40 normal pregnant women who served as control group. anti-thrombin III was measured using automated chemical analyzer (Biosystem A15), data were analyzed using (SPSS). the result showed that there was statistical significant difference in anti-thrombin III between case and control P.V (0.00) also significant deference in blood pressure PV (0.00) and there was no statistical significant difference between case and control in gestation and age PV(0.61) (0.08).This study obtained significant difference according to finding. I conclude that Sudanese females with preeclampsia have low ATIII.

KEYWORDS: *Preeclampsia, Antithrombin III, blood pressure, gestation.*

INTRODUCTION

systematic review by the World Health Organization indicates that hypertensive disorders account for 16% of all maternal deaths in developed countries, 9% of maternal deaths in Africa and Asia, and as many as 26% of maternal deaths in Latin America and the Caribbean (Khan, 2006). Where maternal mortality is high, most of the deathsare attributable to eclampsia rather than preeclampsia. (Duley, 2009). Based on data from the United States National Hospital Discharge Survey, the prevalence of preeclampsia during admission for labor and delivery increased by 25% from 1987 to 2004; during the same period, the rate of eclampsia decreased by 22%, butth is was not statistically significant (Wallis, 1987) Severe morbidity associated with preeclampsia and eclampsia includes renal failure, stroke, cardiac dysfunction or arrest, respiratory compromise, coagulopathy, and liver failure (Duley, 2009).

In a study of hospitals managed by Health Care America Corporation, preeclampsia was these con leading cause of pregnancy-related intensive care unit admissions, after obstetric hemorrhage (Porreco 2010).

Preeclampsia is a pregnancy-specific disorder that affects 2–8% of all pregnancies and remains a leading cause of maternal and prenatal morbidity and mortality worldwide. Diagnosis is based on new onset of hypertension and protein urea. Multiple organ systems can be affected, with severe disease resulting. The wide range of risk factors reflects the heterogeneity of preeclampsia. Obesity, which is increasing at an alarming rate, is also a risk factor for preeclampsia as well as for later-life cardiovascular disease. Exploring common features may provide insight into the path physiologic mechanisms underlying preeclampsia among obese and overweight women.

Preeclampsia

Preeclampsia is a pregnancy-specific syndrome that affects many organ systems and is recognized by new onset of hypertension and proteinuria after 20 weeks of gestation. It is estimated to complicate 2–8% of all pregnancies. (Duley 2009**)** though the precise cause is unknown, the pathophysiologic processes underlying this disorder are described as occurring in two stages. (Roberts 1999**)** The first stage is characterized by reduced placental perfusion, possibly related to abnormal placenta ion, with impaired trophoblast invasion and inadequate remodeling of the uterine spiral arteries. The second stage refers to the maternal systemic manifestations characterized by inflammatory, metabolic, and thrombotic responses that converge to alter vascular function, which can result in multiorgan damage. (Roberts, 2005; Steegers, et al 2010) Precise classification of the various hypertensive disorders of

pregnancy has remained challenging due to changing nomenclature as well as to the geographic variation in accepted diagnostic criteria. For example, terms such as "toxemia" and "pregnancy-induced hypertension" are now considered outdated. Furthermore, varying diagnostic criteria are used in different regions of the world, with disagreement about the degree of hypertension, the presence/absence of proteinuria, and the categorization of disease severity (Steegers, et al 2010). These inconsistencies have led t-o -challenges in comparing and generalizing epidemiologic and other research findings. The most commonly used classification system in the United States is based on the Working Group Report on High Blood Pressure in Pregnancy, in which four major categories are defined: gestational hypertension, preeclampsia-eclampsia, chronic hypertension, and preeclampsiasuperimposedon chronic hypertension (Working Amjobsted 2000) Preeclampsia is defined as the new onset of sustained elevated blood pressure (≥140mmHg systolic or ≥90mmHg diastolic on at least two occasions 6h apart) and proteinuria (at least 1+ on dipstick or ≥300mg in a 24-h urine collection), first occurring after 20 weeks of gestation.

Antithrombin III (ATIII)

Antithrombin III (ATIII) is an important endogenous anticoagulant protein which functions at the level of serine protease inhibition. ATIII inactivates thrombin, factor Xa and other enzymes in the intrinsic coagulation pathway, thereby decreasing fibrin formation. Inhibition occurs when stable, stoichiometric ATllI-enzyme complexes form as a result of interactions between the reactive site of ATIII and the active site of the protease target. (Rsenberg, 1973). The rate of complex formation increases substantially in the presence of heparin sulfate proteoglycans on the surface of the vascular endothelium in vivo, (Marcum, and Rosenberg 1987) or after addition of heparin in vitro or pharmaceutically. (Marcum and, Rosenberg 1973).

ATIII is synthesized in the liver and has a half life of almost three days in the circulation's The plasma concentration of ATIII is approximately 125ug/m19 and does not vary widely among normal people. There is an increased risk of thrombosis when ATIII levels are subnormal (Thaler, and Lechner 1981).

ATIII works as an anticoagulant by forming stable complexes with thrombin, factor Xa and other serine proteases of the intrinsic pathway. Complex formation involves interactions between the reactive site of antithrombin III and the active sites of its target proteases. The anticoagulant activity of antithrombin III is substantially increased by exposure to heparin sulfate proteoglycans on the vascular endothelium (Marcum, and Rosenberg 1987) and by pharmaceutical application of heparin in clinical settings. Binding of these anionic polysaccharide cofactors to ATIII induces a conformational change in the inhibitor, which is then able to form complexes with target proteases at rates as much as 1000-fold faster than the "progressive" rate. (Rsenberg, 1973). Complexes composed of antithrombin III and inactive target enzyme are finally cleared from the circulation by hepatic receptors that recognize neoepitope present in the complex.

Blood pressure

Blood pressure should be measured on at least two occasions four hours apart using an appropriately sized cuff and validated device for use in women with preeclampsia (Duley 2009; Conrad et al, 1998). For women at high risk, guidelines recommend monitoring blood pressure at increased frequency in antenatal clinics, however no exact frequency is recommended. Recent studies have addressed the potential for women to self-monitor their blood pressure at home to improve the detection of hypertension in pregnancy, particularly in women with elevated risk. It appears that self-monitoring is feasible (Founds et al 2008) acceptable to pregnant women (Stewart Fm), may reduce clinic visits (Founds et al 2008**)**, and be efective for detecting hypertension in pregnancy and distinguishing white coat hypertension (Wallstrom et al 2001). A current RCT (BUMP) hopes to provide a larger evidence base to determine the impact of self-monitoring on maternal and neonatal outcomes and advise how self-monitoring can be implemented into clinical practice.

MATERIAL AND METHOD

Study Population

This study was carried out on Sudanese females, 40 from preeclampsia (study group), and 40 from normal pregnant woman's(control group).

Inclusion criteria

In Sudanese female with preeclampsia adult (20-45) years old.

Exclusions criteria

On pregnant women, non-Sudanese or pregnant suffering from any other diseases.

Sample Size and Sampling

5ml of venous blood was collected from pregnant women with preeclampsia by clean phleptomy into avacotainer containing 3.2% sodium citrate. The volume of blood drawn into the syringe should be exactly 9 times the volume of the sodium citrate solution. Mix the blood sample immediately after collection avoiding formation of foam. Transfer to a centrifuge tube and centrifuge for 10 minutes at approx...2000g. Centrifugation should be performed within 2 hours of blood collection. Transfer the supernatant in plaincontainer.

Methods

Quantitative determination of antithrombin III in human plasma was measured by turbidimetric immunoassay measurement of antigen antibody reaction by the end method using biosystem A15 analyzer.

Principle of ATIII

ATIII is an inhibitor of thrombin, factor xa and factor vIIa. There is more ATIII in blood than prothrombin, blood is able to clot only because the reaction of the inhibitor with thrombin is much slower than the action of thrombin on fibrinogen. The reactivity of ATIII is regulated by combination with its activator heparin

Procedure of ATIII

Pipette 5ml of sample, control or calibrator into test cuvette. add reagent 1=250ml mix, incubate for 2minutes, read absorbance. then add reagent2. mix incubate and read absorbance after 5 minutes. Wave length 340nm.

Data Collection and analysis

Data will be collected by questionnaire and analyzed using statistical package for social science (SPSS)

Ethical Consideration

Ethical approval was taken from Alneelain University institution Review board and consents were obtained from the study participants and they were informed about the research objective and results.

RESULT AND DISCUSSION

Table (4.1): Significant between antithrombin III as control and tests cases in experiments samples. use independent –T-test.

Parameters	N	Mean	Std. dev	T- value	P-value	The Inference
Control	40	28.487	4.77	8.219	0.000	There is significant difference
Test	40	20.470	3.91			

Table (4.2): Comparison Between Antithrombin III and Gestation at Different Period. Use Anova –One-Way Analysis.

Gestation period (months)	6		7		8		9	
Antithrombin (III)	control	test	control	test	control	test	control	test
	26.52±2.95	21.65±2.75	26.99±4.38[a]	21.33±1.51[b]	27.81±4.38[a]	20.59±3.66[b]	29.71±4.64[a]	19.74±4.96[b]

Data are presented as means ±Std. deviation

[a, and b,] value with different superscripts in the same row and column are significantly different at ($P \leq 0.05$).

this table showed that there was significant deference between control and tested samples at gestation period (7, 8, and 9 months) and antithrombin. But there is no significant between then at six months.

Table (4:3): Pearson Correlation to Determine the Relationship between antithrombin III and age, Pressure and on Gestation (n=40).

Compatibility Variables	The correlation coefficient with antithrombin III levels	Probability value	Conclusion
Age	0.009	0.727	There is a negative correlation between the two variables
Pressure	0.656	0.000	There is a positive correlation between the two variables
Gestation	0.174	0.0282	There is a negative correlation between the two variables

Correlation is significant at the 0.01 level

DISCUSSION

In this study, the ATIII in women with preeclampsia is significantly lower from that in women with normal pregnancy. The present study confirm the strong correlation between antithrombin and preeclampsia because the coagulation system is impaired in pregnant women with preeclampsia. The increase of blood pressure reflected the severity of disease. The different grades of micro thrombi formation and fibrin deposition affect multiple maternal organs, including the uteroplacental vesels. this findings of study agree were agree with the finding of study done by (Sakar et al, 2013). Also agree by (Heilman et al 2007).

We found that, overall, AT levels were lower than baseline during pregnancy. Additionally from the analysis we learned that there was significant deference between control and tested samples at gestation period (7, 8, and 9 months) and antithrombin. But there is no significant between then at six months. there was difference between levels obtained at the end of the second trimester and levels obtained in the third trimester, but there was a remarkable difference between AT levels obtained during pregnancy and AT levels obtained before pregnancy. From the we found that from mid trimester to term (25 to 40 weeks gestation), AT levels were negatively correlated with gestational age with a drop during this period of time. Previous investigators have found decreased AT levels in the third trimester of pregnancy or immediately postpartum and others have found no change (Cerneca *et al* 1997; Wickstrom *et al* 2004). This variation in results is likely because the decreases in AT levels are not large until the immediate postpartum period and then the dramatic

decreases are fleeting. The more changes observed in the immediate postpartum periodmay be easier to explain than the smaller changes observed during pregnancy.

It is possible that the changes observed during pregnancy can be explained by hemodilution, altered synthesis, increased clearance or even a consumptive process. These were normal subjects who did not have renal disease or preeclampsia and would not have been expected to have lost antithrombin through urinary excretion.

In conclusion, found that AT levels are below base line during pregnancy. It appears that this decrease is present by the end of the last trimester. There is a further decline of approximately after midtrimester. Then, it appears that antithrombin is consumed at the time of pregnant consistent with temporary thrombus formation These findings may have implications for the management of AT replacement in patients with either AT deficiency or an AT-deficient disease state such as severe preeclampsia and may have implications for anticoagulation for all patients at risk for pregnancy-related thrombosis.

Preeclampsia women have decreased ATIII level as compared to normal pregnant women. These findings suggest that there is an excessive hyper coagulable state in preeclampsia and is involved in pathogenesis of the condition. Thus the reduction of ATIII is the main predictor to predict and monitor the severity of the condition.

This study Recommend that Anti- thrombin III should be, scheduled as protocol for pregnant women to avoid the disease. Blood pressure measurement are be routinely used to screen for thromboythis and anti-thromboythis factors levels. Estimation of Glomerular filtration rate for pregnant women. Anti hypertensive treatment for pations with mild to moderate to prevent eclampsia. Pregnant women with personal or family history of DVT, Placental abruption, Preeclampsia, Recurrent miscarriage and IUGR, should be considered for thrombophilia screening and antenatal prophylaxis. Future large prospective studies are urgently needed to validate the use of current approaches and perhaps define safer and more accurate strategies to reduce maternal thrombotic episodes during pregnancy and after delivery.

REFERENCES

1. Cerneca F, Ricci G, Simeone R, Malisano M, Alberico S, Guaschino S. Coagulation and fibrinolysis changes in normal pregnancy. Increased levels of procoagulants and reduced levels of inhibitors during pregnancy induce a hypercoagulable state, combined with a reactive fibrinolysis. Eur J Obstet Gynecol Reprod Biol., 1997; 73(1): 31–6.
2. Conrad KP, Miles TM, Benyo DF. Circulating levels of immunore active Kupferminc MJ, Peaceman AM cytokines in women with preeclampsia. Am J Reprod Immunol., 1998; 40: 102–111.
3. Duley L. The global impact of pre-eclampsia and eclampsia. Semin Perinatol., 2009; 33: 130–137.
4. Founds SA, PowersRW, Patrick TE, Acomparison of circulating TNF-alphain obese and lean women with and without preeclampsia. Hypertens Pregnancy, 2008; 27: 39–48.
5. Helimann L, Rath W, Pollow K. Hemostatic abnormalities in patients with severe preeclampsia. Clin Appl Thromb Hemost, 2007; 13(3): 285-291.
6. Khan, S. Dickerman, J. ؛ Hereditary Thrombophilia, Thrombosis journal, Licence Biomed Center Ltd., 2006; 4(15): 3.
7. Marcum JA, Rosenberg RD. Anticoagulant active heparin sulfate proteoglycan and the vascular endothelium. Seminars in Thrombosis and Haemostasis, 1987; 13: 464-474.
8. Porreco RP, Barkey R. Peripartum intensive care. J Matern Fetal Neonatal Med., 2010; 23: 1136–1138.
9. Roberts JM, Gammill HS. Preeclampsia – recent insights. Hypertension, 2005; 46: 1243–1249.
10. Roberts JM, Hubel CA. Is oxidative stress the link in the two-stage model of pre-eclampsia?[comment]. Lancet, 1999; 354: 788–789.
11. Rsenberg RD, Damus Ps. The purification and mechanism of action of antithrombin-heparin cofactor. J. Biol. Chem., 1973; 248: 6490-6505.
12. Steegers EAP, von Dadelszen P, Duvekot JJ. Pre-eclampsia. Lancet, 2010; 376: 631–644.
13. Thaler E, Lechner K. AntithrombinIII deficiency and thromboembolism. Clin. in H aematrol., 1981; 10: 369-390.
14. Wallis AB, Saftlas AF, Hsia J. (1987). Secular trends in the rates of preeclampsia, eclampsia, and gestational hypertension, United States. Am J Hypertens. 2008; 21: 521–52.
15. Wallstrom P, Wirfalt E, Lahmann PH, Serum concentrations of Chappe llLC, betacarotene and alpha-tocopherol are associated with diet, smoking, and general and central adiposity. Am J ClinNutr., 2001; 73: 777–785.
16. Wickstrom K, Edelstam G, Lowbeer CH, Hansson LO, Siegbahn A. Reference intervals for plasma levels of fibronectin, vonWillebrand factor, free protein S and antithrombin during third-trimester pregnancy. Scand J Clin Lab Invest, 2004; 64(1): 31–40.
17. Working Group on Research on Hypertension in Pregnancy. Report of the National High Blood Pressure Working Group on Research on Hypertension in Pregnancy Am J Obstet Gynecol., 2000; 183: S1–S22.