Comparison of testosterone hormone in the sera of patients with preeclampsia and healthy pregnants women

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Abstract:

Objective: to determine the level of serum testosterone in preeclamptic(PET) groups and normotensive pregnants women in second and third trimister.

Methods: Fifty five pregnant women with preeclampsia (PET) (twenty five of them in the second trimester of pregnancy while the rest of them were in the third trimester of pregnancy and the same number for healthy pregnant women.

Results: serum testosterone was significantly higher in preeclamptic groups compared with normal pregnants women groups($p<0.001$).Also serum testosterone was significantly higher in the third trimester compared with second trimester for preeclamptic groups ($p<0.001$), and also shows nonsignificant decrease in third trimester compared with second trimester for healthy pregnant women($p=0.36$).

الخلاصة:

لتقدير مستوى هرمون الذكورة في النساء الحوامل المصابات بمرض قبل الشنج ومجموعة السيطرة في الفصلين الثاني والثالث من الحمل . وقد انتقينا ٥٥ امراة مر يضة حامل ،خمسة وعشرون منهن في الفصل الثاني من الحمل بينما الباقي منهن كانوا في الفصل الثالث من الحمل و اخذ نفس العدد للنساء السليمات الحوامل .

وقد اظهرت النتائج زيادة معنوية في هرمون الذكورة في النساء المصابات بمرض قبل الشنج بالمقارنة مع الحوامل ذوات الضغط الطبيعي ($p<0.001$) وكذلك هناك زيادة معنوية في مستوى هرمون الذكورة في الفصل الثالث مقارنة مع الفصل الثاني للنساء الحوامل المصابات بمرض قبل الشنج ($p<0.001$) وايضا وجد هناك نقصان غير معنوي في الفصل الثالث مقارنة مع الفصل الثاني للنساء السليمات الحوامل ($p=0.36$).

Introduction :

Hypertension in pregnancy is a significant problem , if it is associated with proteinuria (which indicates multisystemic disease, known as preeclampsia , it will be associated with increased morbidity and mortality for both mother and baby (Sheinam ,2007). Hypertension in 20 weeks of gestation(Sheinam,2007). Major preexisting risk factors for PET include primigravida state , history of PET in previous pregnancy , large body size, a family history of PET, multiple pregnancy , preexisting maternal hypertension, pregestational diabetes , antiphospholipid antibody syndrome , vascular or connective tissue disease and advanced maternal age (> 35 to 40 years)(Chan, etal ,2006) .

The aetiology of this disease is still in debate and many theories were introduced in this field by many investigators in different countries. One of these theory which relates the disease to uteroplacental ischemia, suggests the following :-

1- Preeclampsia begins with uteroplacental ischemia , which is an increase intramural resistance in the myometerial vessels, leads to hightened myometerial tension produced by large fetus in a primipara, twins or hydramnios(Ficioglu, etal 2003) .

2- The uteroplacental ischemia leads to the production of vasoconstrictor substance , which enters the circulation and produces renal vasoconstriction leading to increased production of renin - angiotensin and aldosterone(Ficioglu, etal 2003) .
3-The renin-angiotensin system produces a generalized vasoconstriction and aggravates further the uteroplacental ischemia (Takeuchi, etal ,2004) . It is followed

by systemic of cytotoxic products that damage maternal vascular endothelium (Buhimschi,etal,2006) .
4- Aldosterone leads to water and electrolyte retention and generalized edema(John,2008) .

Androgen are responsible for the manifestation of primary and secondary sex characteristics and preservation of libido , sense of well being(Gronowki, etal,1999), lean mass and bone density (Nini,etal,2000). Androgens are involved in a negative biofeed back mechanism on the hypothalamic pituitary axis to inhibit gonadotropin secretion(Bagatell,,etal,1994) . They are group of C_{19} steroid, androgen precursor by the adrenal cortex is dehydroepiandrosterone (DHEA) (Chape-DC, Harvey-RA and Ferries-DR) . Adrenal androgen themselves are weak , they are converted in peripheral tissue to testosterone (as strong androgen) and to estradiol (Chape, etal,2003).

Testosterone is the major male hormone secreted from the leydig cells (interstitial cells) , under the influence of luteinizing hormone (LH) (Ivanova, etal ,1994). In female , the follicular theca cells produce C_{19} androgens . These are converted to C_{18} estrogens by granulosa cells (Vasudevan and Sreekuman-S.). In human male the peripheral aromatization of testosterone to estradiol (E2) account for 80% of the production of the latter(Murray, etal ,2011). In female , adrenal androgens are important substrates , since as much as 50% of the estradiol E2 produced during pregnancy comes from the aromatization of androgens(Murray, etal , 2003). Aromatase activity is present in adipose cells and also in liver, skin and other tissues(Ojeda, etal ,2007) . Increased activity of this enzyme may contribute to the estrogenization that characterizes such disease as cirrhosis of the liver , hyperthyroidism and obesity(Ojeda, etal, 2007) .

Methods :

This study was conducted in Babylon Maternity and Pediatrics Teaching Hospital . Fifty five pregnant women with preeclampsia (twenty five of them in the second trimester of pregnancy(G1) while the rest of them were in the third trimester of pregnancy(G2)) and the same number for healthy pregnant women (twenty five of them in the second trimester of pregnancy(G3) and thirty of them were in the third trimester of pregnancy(G4) .

All the patients were nonsmokers, have no other diseases (ie, cardiac, hepatic, renal, endocrine and other disease)which may have effect on the measured parameters were excluded from the study. Pregnancy is divided into 1st trimester (1-12 week), 2nd trimester (13-28 week) and 3rd trimester more than 28 weeks. Depending on the gestational age.

Blood samples (5ml) were collected by venipuncture , and sera were separated by centrifugation at l500 xg for 2 minutes. And sera were transferred into eppendrof tube and was used for measurement of testosterone by enzyme Linked immunosorbant assay (ELISA) . The statistical analysis is based on ANOVA test to determine the differences between groups and within groups. Normal value for tesoterone level in female is (0.2 -0.8 ng/ml).

Result :

Serum testosterone was significantly higher($p<0.001$) in preeclamptic groups(G1&G2) compared with normal pregnant women groups (G3&G4) ($p=0.36$) .Also serum testosterone was significantly higher in G2 compared with G1,and also shows nonsignificant decrease in G4 compared with G3 ,[Fig(1),Table(1), Table (2)]

Table (1): Serum data of testosterone in preeclamptic and normal pregnant women (2nd and 3rd trimester)

Measured parameter	G1	G٢	G3	G4
(Testosterone(ng/ml) *± SD)	1.46±0.199	2.41±0.54	0.82±0.198	0.74±0.24

(mean ± SD)*

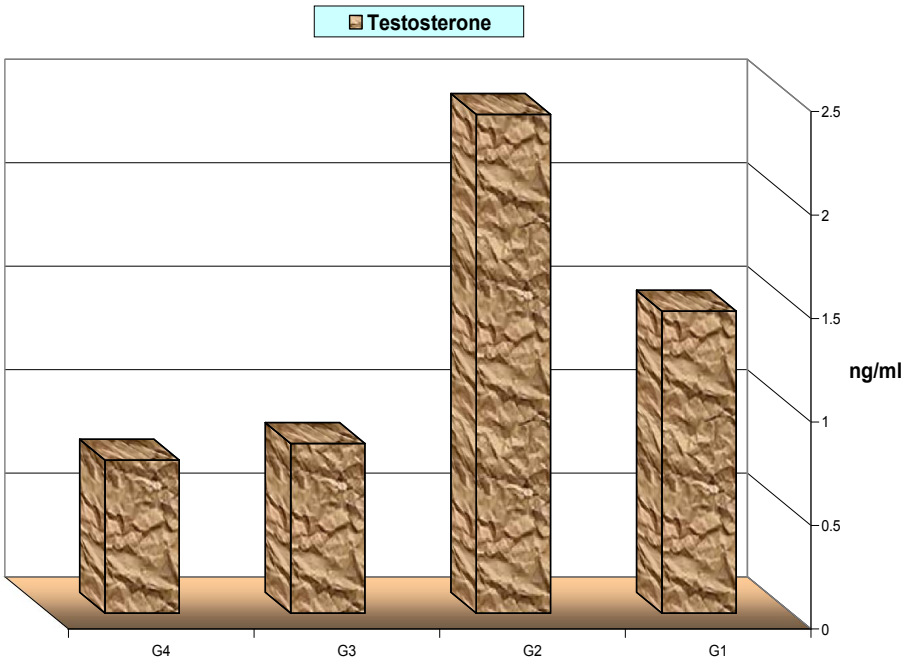

Figure (1): Serum data of testosterone in preeclamptic and normal pregnants women (2nd and 3rd trimester)

Table (2): Significance value for testosterone in different groups

Groups	P value
G1 vs G2	<0.001
G1 vs G3	<0.01
G1 vs G4	<0.001
G2 vs G3	<0.01
G2 vs G4	<0.01
G3 vs G4	=0.36

Discussion :

Many previous studies reported the changes in estrogen levels during normal and complicated pregnancy .Besides , there are numerous studies concerning the role of metabolic syndrome in the aetiology of preeclampsia (Iou, etal, 2005), (Reyes, etal, 2006),(Rebecca, etal ,2003). In our study , levels of serum testosterone were found to be significantly higher in women with preeclampsia than in normotensive women with similar gestational age . Such increase in hormone level in both 2nd and 3rd trimester can be attributed to :

1- Low expression of the aromatase gene due to small or impaired for the conversion of testosterone to estrogen . The decrease of enzyme activity lead to a subsequent increase in testosterone level(Rebecca, etal ,2003) .
2- In the late pregnancy , when the fetal adrenal gland become mature it will result in further increment in the level of testosterone by conversion of DHEA to testosterone(Rebecca, etal ,2003) .
3- Human chorionic gonadotropin increase in PET and this will stimulates the ovarian thecal cell to synthesis androstenedione and testosterone(Steier, etal ,2007).
4- The decrease in testosterone clearance in normal pregnancy is intensified in PET patients . This will lead to increase in serum testosterone levels(Bammann, etal ,1980) .
5- Insulin stimulate the production of testosterone by ovarian tissue which suggests that hyperinsulinemia could be primary change that triggered the increased release of testosterone (Ahmed-I, etal, 2009). However , hyperinsulinemia should also stimulate the production of adrenal androgen (Lemieux,etal, 2012) .

Our results were in agreement with the results reported by Golmahamed ,2005 and Jasim, 2008) .

The increase in serum testosterone levels in the second trimester of normal pregnancy in comparison with those values of the 3rd trimester can be attributed to the increase of aromatase activity with progressive course of pregnancy (Rebecca, etal ,2003) .

References:

Ahmed- I, Hisham-M. and Khaled A. 2009. Androgen Pattern in Patients With Type 2Diabetes-associated Erectile Dysfunction: Impact of Metabolic Control. J Urology. 74(3): 552–559.

Bagatell-C.J, Heiman-J.R and Matsumate-A.M,etal. 1994.Metabolic & Behavioral effects of high dose,exogenous testosterone in Healthy men. Am J clin chemistry.;8:212-215.

Bammann-B.L, Goulam-C.B and Jiang-N.S.1980 . Androgen production and metabolism in normal pregnancy.Am J Obestet Gynecol ;137(3):293-298.

Buhimschi-C.B, Maglorri-L and funai-E,etal. 2006. Fractional excretion ofAngiogenic factors in women with severe preeclampsia. Am College obstet & Gynecol.;107(5):1103-11130.

Chan-P.D and Hahnson-S.M. 2006. Current clinical strategies publishing. 6th ed. Laguna Hills. California.

Chape-D.C,Harvey-R.A and Ferries-D.R.2005.Lippincott's Illustratedreviews:Biochemistry.3rd ed. Awolters Kluwer.;237-238.

Ficioglu-C and Kutlu-T. 2003. The role of androgens in the aetiology and pathology of preeclampsia.J Obstet Gynecol.;23:134-137.

Golmahammad-I.S, Salari-S and Eskandari-M, etal. 2005. Evaluation 0f androgen and progesterone levels in women with preeclampsia. Iran J Med Sci.;30(4):186-189.

Gronowki-A.M and Levine-M.L. 1999. Tietz text book of clinical chemistry3rd ed.Sunders company,philadeiphia.;1601-1611.

Iou-S.G, Eskandari-M and Dabiri-A.2005. Evaluation of estrogen level ofWomen with preeclampsia in third trimester. Medical J Islamic World Academy of Sciences.;15(1):19-22.

Ivanova-E.A. 1994. Effect of testosterone on rate of total protein synthesis In the fetal rabbit reproductive tract in vitro.Bulletin of Experimental Biology & medicine.1994;98(8):233-234.

Jasim-F.G.2008. Role of sex hormones in preeclampsia. PhD thesis. College of Medicine. Al-Nahrain University.

John-P. 2008. Evalution of priteinuria in pregnant women. Am J obstet &Gynecol.;57:611.

Lemieux-M.V, DiVasta-AD. 2012. Severe Hyperandrogenemia and Resistance in a 12-Year-Old Girl. Journal of Pediatric and Adolescent Gynecology. 25(4): 99-101.

Murray-R.K, Granner-DK, Mayes-PA and Rodwell-VW. 2011. Harper's illusterated Biochemistry.28th ed. Mc Graw-Hill, New York.;440-445.

Nini-A.F,Riggs-B.L and Alkinson-E.J,etal. 2000. Relative contributions oftestosterone & estrogen in regulatating bone resorption & formation in normal elderly men. Am soci clin invest. 1553-1560.

Ojeda-N.B, Grigore-O and Yanes-L.L, etal. 2007.Testosterone contributes to marked elevations in mean arterial pressure in adlt male intrauterine grouth restricted offspring. Am J Physiol Regul Integr Comp Physiol.;292:758-763.

Rebecca-T Postischman-N, Roberts-JM and Ness-R. 2003. Maternal serum estrogen and androgen concentrations in preeclamptic and uncomplicated pregnancies. Intern J Epidem.;32: 455-460.

Reyes-M.R, Alvarez-S.A and Lazalde-B. 2006. Estrogens are potentially the only steroids with an antioxidant role in pregnancy. Acta obstet Gynecol Scand.;85(9):1090-1093.

Sheinam-A.Dewhurst's.2007. Text book of obstetrics & Gynecology for Postgraduates. 8th ed. Graphicraft,Hong Kong.;227.

Steier-J.A,Ulstein-M and Myking-O.L. 2002. Human chorionic gonadotropin and testosterone in normal and preeclamptic pregnancies in relation to fetal sex. Obstetric gynecol.; 100:552-556.

Takeuchi-K , Zhang-B and ideishi-M , etal. 2004. Influence of age &Hypertension on the association between small artery Compliance & coronary artery disease. Am J Hypertension. ;17(12);1188-1191.

Vasudevan and Sreekuman-S. 2001. Text book of biochemistry for medical Students.3rd ed.Jaypee brothers,New delhi ; 417-422,218.