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RESEARCH PAPER

COMPARATIVE STUDY OF AGE VARIATIONS ANDHUMAN SERUM CREATININE, UREA AND URIC ACID LEVELS IN PREGNANT WOMEN AT DIFFERENT TRIMESTERS OF PREGNANCY

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ABSTRACT

This study is designed to evaluate human serum levels of creatinine, urea and uric acid in the different trimesters of pregnancy. A total number of 120 subjects were recruited from primary health care centres in Ekpoma [30 pregnant women for each of the trimesters (3x30=90) and 30 non-pregnant women serving as the control]. Venous blood samples were taken from all the subjects to determine the mean serum creatinine, urea and uric acid. The method used in the measurement of creatinine was the modified alkaline picrate method while the Urease-Berthelot's method and the enzymatic colorimetric method (uricase) were used for the measurement of urea and uric acid respectively. The results showed that there was significant decrease ($p<0.05$) in the serum creatinine, urea and uric acid levels between the different trimesters and as compared to control values. It was also observed that the levels of creatinine and uric acid under the age range of 26-35 years were significantly lower ($p<0.05$) than 18-25years and 36-45 years, while the levels of urea across the various age groups were not significantly different ($p>0.05$). Conclusively, human serum creatinine, urea and uric acid levels decrease in pregnancy but progressively increase towards term.

Key Words: Pregnancy, Creatinine, Urea, Uric acid

INTRODUCTION

Pregnancy is a normal physiological condition which shows many changes in the maternal environment (Waltzer, 1981; Clark*et al.*, 2104). Adaptation to pregnancy in humans involves anatomic, physiologic and metabolic changes in the mother, to support and provide her with nutritional and metabolic needs and those of growing conceptus (Kalhan, 2000). Almost all maternal physiological system undergoes adjustments because of pregnancy, but perhaps, the greatest upheaval is caused to the renal system (Hytten, 1976; Clark *et al.*, 2104). Many changes in renal function occur in normal pregnancy, and without a proper understanding of these changes, routine clinical investigations may be easily misinterpreted (Brown and Whitworth, 1992). Such clinical investigations include estimation of serum uric acid, urea and creatinine.

Renal function is affected by the changes in other systems particularly those that occur in hemodynamic control (Blood flow control) (Milne *et al*., 2002). The systemic hemodynamic profile of pregnancy is characterized by an increase in intravascular volume, cardiac output and heart rate with marked fall in vascular resistance and tendency toward a decrease in a mean blood pressure in association with an increase in renal plasma flow (RPF) and glomerular filtration rate (GFR) (Waltzer, 1981; Mabie*et al*., 1994; Chapman *et al.,* 1998; Clark *et al.*, 2104).

Although pregnancy involves a continuous process, it is divided into three trimesters (of three months each) (Abman, 2011). The first trimester is from 0 to 13 weeks and begins the first day of the last menses. The second trimester is from 13 to 26 weeks where rapid foetal growth occurs and by the end of the second trimester, the foetus would have been weighing approximately 0.7g and 0.3m long (Abman, 2011). The third trimester is from 26 to 40 weeksand this is the period when foetal organs complete their prenatal maturation (Abman, 2011). Between the interval of 37 to 42 weeks, normal labour, rhythmic uterine contractions and birth occur and this is called Term (Wylie, 2005; Abman, 2011).

Many changes in renal function are associated with pregnancy and without a proper understanding of these changes; routine clinical investigations may be easily misinterpreted (Brown and Whitworth, 1992). Therefore, this study is justified as it is aimed to investigate the changes in renal function during pregnancy as alluded to by Waltzer, (1981).

MATERIALS AND METHODS

Area of Study: This study was conducted in Ekpoma -the administrativeheadquarters of Esan West Local Government area of Edo State, Nigeria, and host of the state-owned Edo University –Ambrose Alli University, Ekpoma. It has an undulating topography (World Gazetter, 2007); usually cold at night but very hot during the day;and located at latitude 6^{o} 45^{I}N and longitude 6^{o} 08^{I}E,(World Gazetter, 2007) with Irrua, Igueben, Ukhun, Opoji as neighbouring towns. It is moderately populated and most of the indigenes are farmers or traders. The main source of water in the locality is rainwater, which is usually collected in manmade surface wells.

Study Population: The subjects used forthis study were pregnant women recruitedfrom Primary Health Centers(PHC) in Ekpoma. A total of one hundred and twenty (120) pregnant women were recruited for this study; comprising 90 pregnant women -30 for each trimester respectively, and 30 non-pregnant women that served as controls. Subject data like name, age, and duration of pregnancy were obtained. The ages of the subjects rangedfrom of 18-45 years.

Sample Collection: Blood samples were collected by venipuncture into an accurately labelled plain container fromthe test and control subjects. During the collection of blood samples, it was ensured that the arm was tied with the tourniquet as recommended. The blood samples were centrifuged with a laboratory centrifuge at 1000rpm for 10minutes andat room temperature within two hours of collection and the serum separated into appropriately labeled clean plain containers.Analyses were thencarried out for creatinine, urea and uric acid.

Analytical Method: Serum creatinine was determined based on modified alkaline picrate methoddescribed by Fabiny and Ertingshausen, (1971). Urease- Berthelot method was employed for Urea, while
TheEnzymaticcolorimeric method (Uricase) was employed for uric acid.

Statistical Analysis: ANOVA were used to compare theresults in both pregnant women and control usingtheSPSScomputer program (version 17.0). The results were reported as mean ± standard deviationwith $P \leq 0.05$ considered statistically significant.

RESULTS

The tables below present the levels of human serum creatinine, urea and uric acid (Mean and standard deviation) of the test and control subjects. There was a significant decrease ($p<0.05$) in the serum levels of creatinine, urea and uric acid in first, second and third trimesters when compared with the control (Table 1).

The mean and standard deviation of human serum creatinine, urea and uric acid in according to age were compared. There was a significant decrease in the levels of creatinine under the age range of 26-35 years, the level of urea decreased but it is not significant. Also, there was a significant decrease in the levels of uric acid under the age range of 26-35 years (Table 2).

TABLE 1: HUMAN SERUM CREATININE, UREA AND URIC ACID LEVELS IN CONTROL AND DIFFERENT TRIMESTERS IN PREGNANCY USING ANOVA

Parameters (mg/dl)	Control Subjects (n=30)	1st Trimester (n=30)	2nd Trimester (n=30)	3rd Trimester (n=30)	F value	P value
Creatinine	1.03± 0.14[a]	0.63± 0.34[b]	0.68± 0.17[b]	0.83±0.26[b]	17.30	p<0.05
Urea	9.23± 6.25[a]	7.73 ±3.44[b]	8.27±3.93[b]	10.27 ± 3.66[b]	43.12	p<0.05
Uric Acid	4.65± 0.55[a]	2.44±1.38[b]	3.87 ± 0.75[b]	3.93 ± 0.69[b]	31.41	p<0.05

Values in a row with a different superscript are significantly different at P<0.05

TABLE 2: HUMAN SERUM CREATININE, UREA AND URIC ACID LEVELS OF PREGNANT WOMEN ACCORDING TO AGE

Parameters (mg/dl)	18-25 years (n=46)	26-35years (n=30)	36-45years (n=14)	F value	P value
Creatinine	0.80 ±0.28[a]	0.61 ± 0.26[b]	0.64 ± 2.0[a]	5.01	p<0.05
Urea	8.28 ± 4.06[a]	8.70 ± 3.60[a]	10.43 ±3.03[a]	1.74	p>0.05
Uric Acid	3.66 ± 1.14[a]	2.65 ± 1.22[b]	3.89 ± 0.74[a]	10.84	p<0.05

Values in a row with a different superscript are significantly different at P<0.05

DISCUSSION

The present results showed that the serum creatinine, urea and uric acid, in the 1st, 2nd and 3rd trimester of pregnancy were significantly lower in pregnant group than control group. From the results obtained in this study, it appears that the results of serum creatinine, urea and uric acid during the 3rd trimester are found to be significantly lower when compared with the control group. The results agreed with Macdonald and Good, (1971); Dunlop and Davison, (1977); Korda and Horvath, (1979); Sirajwala*et al*., (2013).

This could be explained based on the fact that Plasma volume increase during the course of pregnancy coupled with a similar increase in Glomerular filtration rate in early pregnancy (Davison, 1994; Moran, 2003). These changes in plasma volume and Glomerular filtration rate may give a possible explanation for initial increase in the clearance of serum creatinine, urea and uric acid (Dunlop and Davison, 1977; King, 2000). Based on this, all the three parameters are therefore significantly decreased in the serum of pregnant women.

Consequently, the increased renal plasma flow, decreased serum albumin values and raised serum progestogen levels (Paaby, 1959; Davey *et al.*, 1961; Lindheimer and Katz, 1975) produce an increase in the Glomerular filtration rate (GFR) during pregnancy (Paaby, 1959; Davey *et al.*, 1961; Lindheimer and Katz, 1975 King, 2000) which is matched by markedly increased clearances of creatinine, urea and uric acid (Paaby, 1959; Hytten and Leitch, 1971; Lindheimer and Katz, 1975; Moran, 2003).This results in decreased serum levels of these products (Sims, 1968; Lindheimer and Katz, 1975; Biswajit*et al*., 2016). Also, serum uric acid levels have been shown to be decreased in early pregnancy and to have a tendency to rise towards term (Boyle *et al*., 1966). The same tendencies were demonstrated in this study, with urea also being found to decrease to the most marked extent. This cannot be explained by the increased GFR only, but also due to the dilution effect as well as a decreased production of urea because of the positive nitrogen balance associated with pregnancy (Lindheimer and Katz, 1975; Biswajit*et al*., 2016).

The positive protein and purine balance during growth of the foetus, and the increase of GFR, result in lowered maternal plasma urea and uric acid levels (Burtis and Ashwood, 1999; Tran, 2005). In the 3rd trimester the GFR begin to decrease toward non-pregnant values (Burtis and Ashwood, 1999; Tran, 2005), so that serum urea and creatinine concentration rise slightly during the last weeks of pregnancy. During this times, tubular reabsorption of uric acid increase dramatically (Burtis and Ashwood, 1999; Tran, 2005) which increase serum uric acid concentration. Also, the decrease in plasma volume causes a decrease in renal plasma flow (RPF) to the secretary site which leads to decrease in the secretion of uric acid from proximal and more distal parts of tubule (Dunlop and Davison, 1977; Dennen*et al*., 2011; Tran, 2005). This reflects the increase of serum uric acid in late pregnancy.

Comparatively, serum creatinine and urea levels were found to be higher in the second trimester when compared with the first trimester. Also, serum uric acid levels were found to be significantly higher in the second trimester when compared with the first trimester. Also, observed in this study is a significant higher levels of serum creatinine, urea and uric acid in the third trimesters when compared with the first trimester. Similarly, comparing second and third trimesters, it was also noted that serum creatinine and urea levels were significantly higher in the third trimester while that of uric acid was also high in the third trimester but not significant. Also, serum creatinine, urea and uric acid were also compared according to age. The levels of creatinine and uric acid were significantly reduced in the age range of 26-35 years while there was no significant difference in urea levels within the age ranges.

From this study, it could be concluded that human serum creatinine, urea and uric acid levels are affected by pregnancy and these alterations tends to come to normal values as the pregnancy progresses to term. This could be explained based on the fact that Plasma volume increase during the course of pregnancy coupled with a similar increase in Glomerular filtration rate in early pregnancy. In view of the outcome of this work, more research work should be carried out on human serum creatinine, urea and uric acid levels in pregnancy as this could serve as a more specific tool in the management of renal function in pregnant women.

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REFERENCES

Abman, S.T. (2011): Fetal and Neonatal physiology (4th Edition). Philadelphia: Elsevier/ Saunders. Pp 46-47.

Biswajit, D., Manidipa, C., Asif, M., Debasish, P. and Dipak, K. (2016): A Study on Serum Urea, Creatinine and Uric Acid Levels in Normal Pregnancy (First and Third Trimester) in Rohilkhand Region, Uttar Pradesh. *Scholars Journal of Applied Medical Sciences (SJAMS).* 4(9A):3236-3241.

Boyle, J.A., Campbell, S., Duncan, A.M., Greig, W.R. and Buchanan, W.W. (1966): Serum uric acid levels in normal pregnancy with observations on the renal excretion of urate in pregnancy. *J. Clin. Pathol.,* 19: 501-503.

Brown, M.A. and Whitworth, J.A. (1992): "The Kidney in Hypertensive Pregnancies" *Am. J. Kidney*. Dis, 20(5): 427-442.

Burtis, C.A. and Ashwood, E.R. (1999): "Tietz –TextBook of Clinical Chemistry" 3rd ed., W.B. Saunders Company: 1239-1250.

Chapman, A.B., Johnson, A.M. and Gabow, P.A. (1998): Pregnancy outcome and its relationship to progression of renal failure in autosomal dominant polycystic kidney disease. *J Am SocNephrol.,* 5:1178–1185.

Clark, N., Tal, R., Sharma, H. and Segars, J. (2014): Microbiota and Pelvic Inflammatory Disease". *Seminars in Reproductive Medicine*. **32** (1): 43–49.

Davison, J.M. (1994): Pregnancy in renal allograft recipients: problems, prognosis, and practicalities. *ClincObstetGynaecol (Balliere),* 8:511–535.

Davey, D.A., O'Sullivan, W.J. and McClure Browne, J.E. (1961): Total exchangeable sodium in normal pregnancy and in pre-eclampsia. *Lancet,* 519-523.

Dennen, F.R., Martinez-Ocana, J., Kawa-Karasik, S., Villanueva-Egan, L., Reyes-Paredes, N. and Olivo-Diaz, A. (2011): Comparison of hemodynamic, biochemical and hematological parameters of healthy pregnant women in the third trimester of pregnancy and the active labor phase. *BioMed Central Pregnancy and Childbirth*; 11:33.

Dunlop, W. and Davison, J.M. (1977): "The Effect of Normal Pregnancy upon the Renal Handing of Uric Acid" *Br. J. Obstet. Gynecol*., 84: 13-21.

Fabiny, D.L. and Ertingshausen, G. (1971): Automation reation-rate method for determination serum creatinine with centrifichem. *Clin. Chem.,* 17: 696-700.

Hytten, F.E. and Leitch, I. (1971): The Physiology of Human Pregnancy. 2nd ed.

Hytten, F.E. (1976): "Renal Physiology in Normal Pregnancy". 1st ed., a wiley Medical Publication, USA: 23-42.

Kalhan, S.C. (2000): "Protein Metabolism in Pregnancy" *Am. J. of Clin. Nutr.*, 71(5): 1249- 1255.

King, J.C. (2000): Physiology of Pregnancy and Nutrient Metabolism. *Am. J. of Clinical Nutrition*, 71(5): 1218-1225.
Korda, A.R. and Horvath, J.S. (1979):" Renal Physiology", 2nd ed., London, Black Well Scientific Publication: 376-409.

Lindheimer, M.D. and Katz, A.I. (1975): Renal changes during pregnancy: their relevance to volume homeostasis. *ClinObseerGyneco.,* 2: 345-364.

Mabie, W.C., Disessa, T.G., Crocker, L.G., Sibai, B.M. and Arheart, K.L., (1994): "A longitudinal Study of Cardiac Output in Normal Human Pregnancy "*Am. J. Obstet. Gynecol*., 170: 849-856.

Macdonald, H.N. and Good, W. (1971): "Changes in Plasma Total Protein, Albumine, Urea and aminonitrogen Concentration in Pregnancy and the Puerperium" *.J. Obset. Gynecol. Br. Common Wealth*, 78: 912-917.

Milne, J.E.C., Lindheimer, M.D. and Davison, J.M. (2002): "Glomerular Heteroporous Membrane Modeling in Third Trimester and Post-Partum Before and During Amino Acid Infusion "*Am. J. Renal. Physiol.* 282: 170 –175.

Moran, P., Baylis, P.H., Lindheimer, M.D. and Davison, J.M. (2003): Glomerular Ultra Filtration in Normal and Preeclampsia. *J. Am. Soc Nephrology,* 14(3): 648-652.
Paaby, P. (1959): Changes in the water content of serum and plasma during pregnancy. *AcraObseeeGynecolScand,* 38: 297-314.
Sims, E. A. (1968): Renal function in normal pregnancy. *ClinObseee Gyneeol1968;* 11: 461-472.

Sims, G.K. (2006): Using the berthelot method for nitrite and nitrate analysis soil sci. soc.*Am.J.* 70(3): 1038.

Sirajwala, H. B., Dinesh, S. and Ashishkumar, M. A. (2013): A study of serum total calcium and uric acid levels in preeclampsia. *Indian Journal of Basic and Applied Medical Research.,* 1 (3):50-56.

Tran, H.A. (2005): Biochemical tests in pregnancy. Australian Prescriber, (28): 98-101.

Waltzer, W.C. (1981): "The Urinary Tract in Pregnancy" *J. Urol*., 125: 271- 76.

World Gazetteer (2007): Population of Cities, news, divisions. htt://world gazetteer.com/ng.php.
Retrieved on 23/05/2008.

Wylie, L. (2005): Essential Anatomy and physiology in maternity care. (2nd Edition). Edinburgh: Churchill Livingstone. P. 172.

AUTHOR'S CONTRIBUTIONS

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