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Comparative study of serum creatinine levels amongst pregnant women attending antenatal clinic in a tertiary heath centre in Sokoto

Jelani I[1*], Tsado P A[1], Mahmud R I[3], Abacha FZ[4], Bello S S[2]
[1] Department of Chemical Pathology, School of Medical Laboratory Sciences, College of Health Sciences, Usmanu Danfodiyo University, Sokoto, Nigeria
[2] Department of Anatomy, Faculty Basic Medical Sciences, College of Health Sciences, Usmanu Danfodiyo University, Sokoto, Nigeria
[3] Department of Medical Laboratory Science, School of Basic Medical Science, Skyline University Nigeria, Kano, Nigeria
[4] Department of Medical Laboratory Science, Faculty of Allied Health Sciences, College of Medical Sciences, University of Maiduguri, Maiduguri, Nigeria

Abstract
Pregnancy is characterized by so many anatomical and physiological adaptations, of which the kidney is implicated. However, no much attention has been given to this aspect, especially in Northern Nigeria. The study compared the serum creatinine levels of pregnant women across the trimester and its correlation with glomerular filtration rate. This study is a comparative cross-sectional study. Sixty-one (61) pregnant women were enrolled. The comparisons of serum creatinine among trimester groups were performed. Serum creatinine was measured by Jaffe's end-point and Jaffe's Kinetic method respectively. A significant negative correlation was recorded between Glomerular filtration rate and serum creatinine. A significant decrease was noticed in creatinine levels using the Jaffe's Kinetic when compared with Jaffe's endpoint method. This study finds that the decrease in serum creatinine levels in pregnant women is normal physiological changes. However, an abnormal increase is a pointer to pregnancy related acute kidney Injury.

Keywords: Glomerular filtration rate, serum creatinine, pregnancy

Introduction

Pregnancy is a condition in which one or more offspring develops in the womb of a woman [1]. Pregnancy may be confirmed with ultrasound or a pregnancy test by detecting a hormone in a woman's blood or urine Human Chorionic Gonadotropin (HCG), as it is an ideal marker for pregnancy since it rises rapidly and consistently in early pregnancy [2]. Pregnancy is divided into three trimesters, each lasting for approximately 3 months characterized by specific events and developmental markers [1].

During pregnancy, the pregnant mother undergoes significant anatomical and physiological changes in order to nurture and accommodate the developing foetus. The pregnancy plasma volume increases progressively throughout normal pregnancy [3]. Consequently, renal vasodilatations, renal plasma flow and glomerular filtration rate (GFR) will increase, compared to non-pregnant levels, by 40-65 and 50-85%, respectively [4]. In addition, the increase in plasma volume causes decreased oncotic pressure in the glomeruli, with a subsequent rise in GFR [4].

Glomerular filtration rate (GFR) represents the flow of plasma from the glomerulus into bowman's space over a specified period and is the chief measure of kidney function [5]. The kidneys receive 20% to 25% of the cardiac output (about 1.0 to 1.1 litres per minute) with the blood entering individual glomerular tufts via the afferent arteriole and exiting through the efferent arteriole [6]. The useful measure for approximating the GFR is creatinine clearance rate which is the volume of blood plasma that is cleared of creatinine per unit time [7]. The physiological increase in GFR during pregnancy normally results in a decrease in concentration of serum creatinine which falls by an average of 0.4 mg/dl to a pregnancy range of 0.4 to 0.8 mg/dl [8].

Beforehand creatinine has been a useful metabolic marker to ascertain the functionality of the renal system. However, during pregnancy various physiological and anatomical changes occur to the kidney, which may alter serum creatinine estimations leaving an impact on the serum creatinine concentrations of pregnant women, and may not actually portray the functioning of the kidney. As such, making it difficult to either include or exclude abnormal kidney function in pregnancy. Moreso, due to the changes expected during pregnancy estimating GFRs will inconsistently underestimate renal function and should not be used as a focal determinant for renal function. Therefore, serum creatinine concentration remains the only standard, single point assessment for kidney function in pregnancy, hence the need to estimate serum creatinine rather than solely depending on GFR estimation. The aim of this study was to compare serum creatinine along trimesters in pregnant women.

Materials and methods

Study Area

This study was carried out in Sokoto, North-Western Nigeria. Sokoto state is located in the extreme northwest of Nigeria, near to the confluence of the Sokoto River and the Rima River. The state is bounded in the North by Niger Republic, Kebbi state to the south west and to East by Zamfara [9]. The state covers a total land area of about 25,973 square kilometers and a population of 5.4 million based on 2017 estimation [10]. Sokoto state has semi-arid climate and vegetation is largely Sudan Savannah with an annual rainfall between 500 – 1300 mm and temperature ranges between 15^{o}C and over 40^{o}C during warm days [9].

Study Population
Sixty-one (61) apparently healthy pregnant women were recruited for the study, of which thirty-one (31) were in their third trimester, eighteen (18) were in their second trimester and twelve (12) in their first trimester.

Inclusion Criteria
Apparently healthy pregnant women without any form of kidney impairment, diabetes mellitus and pre-eclampsia were recruited for the study following informed consent.

Exclusion Criteria
Unhealthy non pregnant and pregnant women with kidney disease, pre-eclampsia, eclampsia and diabetes mellitus were excluded from the study.

Informed Consent
Informed consents were sought from each participant with proper explanation given as regards the aim and objectives of the study.

Ethical Consideration
Ethical approval was obtained from the Research and Ethical committee of the Specialist Hospital Sokoto, Sokoto State (SHS/SUB/133/Vol.1).

Sample Size
The resource equation described by Charan and Biswas [11] was used to calculate minimum sample size as 45.

Study Design
The research design was a comparative cross-sectional study.

Sampling techniques
Subject Selection
The study involved pregnant women attending antenatal clinic in Specialist Hospital Sokoto with the use of a structured interviewer administered questionnaire to elicit data on subject's socioeconomic characteristics following informed consent.

Blood sample collection and processing
Two (2) mL of venous blood sample was collected into a plain container using a disposable plastic syringe from antecubital vein after which the blood was centrifuged at 4000 rpm for 5 minutes. The serum was harvested into a cryovial and analyzed.

Analytical methods
Determination of Serum Creatinine
The determination of serum creatinine was performed using the conventional Jaffe's Endpoint and Kinetics Method described by Jaffe [12] and Lipitskaia *et al* [13]. respectively. Creatinine reacts with picric acid in alkaline medium to give yellow to red colored complex which absorbed light at 520 nm. The intensity of the colour is proportional to the concentration of creatinine.

Data analysis
Statistical Product for Service Solution (SPSS) version 26.0 was used for the statistical analysis. Kruskal Walis tool was used for multiple comparisons across trimesters. Correlation analysis was done with the Pearson's correlation tool.

Results

Serum Creatinine levels and GFRs of study participants
The values of subjects' serum creatinine concentration across trimesters were significantly decreased ($p<0.007$) for kinetic methods as depicted in Table 1. However, creatinine concentrations by Jaffe's method and GFRs of test participants increased but not statistically significant as observed amongst the trimesters ($p>0.05$) as indicated in Table 1 and 2 respectively. Table 3 shows an extremely negative statistically significant correlation between Creatinine Jaffe's method and GFRs.

Table 1: Mean Comparison of creatinine concentrations of pregnant women

	Mean of Ranks by trimesters				
Parameter/methods	First	Second	Third	KWS	p-value
Cr Kinetic (mg/dL)	44.96[a]	36.08 [ab]	26.21[b]	9.962	0.007
Cr Jaffe (mg/dL)	34.71	35.44	26.98	3.600	0.165

Values are presented as Sum of Ranks, KWS=Kruskal Wallis Statistics, Cr=Creatinine, GFR=Glomerular filtration rate, Values with different superscript per row are statistically significant.

Table 2: Mean Comparison of GFRs of pregnant women

	Sum of Ranks by trimesters				
Parameter/methods	First	Second	Third	KWS	p-value
GFRs (ml/min/1.73m^2)	316.50	479.50	1095.0	3.742	0.154

Values are presented as Sum of Ranks, KWS=Kruskal Wallis Statistics, Cr=Creatinine, GFR=Glomerular filtration rate, Values with different superscript per row are statistically significant.

Table 3: Correlation analysis of GFRs and Jaffe's Creatinine Concentrations of pregnant women

	Creatinine (mg/dL) by trimesters		
GFRs (ml/min/1.73m^2)	First (n=12)	Second (n=18)	Third (n=31)
rho-value	- 0.94	- 0.93	- 0.38
p-value	0.0001	0.0001	0.02

Discussion

The results obtained show a significant decrease in serum creatinine across the trimester using Jaffe's kinetic method, on a general bases this agrees with the findings of Liki *et al* [14]. The progressive decrease in creatinine levels across the different periods of gestation which can be attributed to the increased GFR and reduced clearance seen in pregnancy [15, 16]. However, it was observed that the Jaffe method used to determine serum creatinine across the trimester showed a decrease in serum creatinine level, although not statistically significant; this may be due to the fact that various variables interfere with the test method of which timing is inclusive. This is in consonant with a study carried out by Jelani *et al* [17].

In comparing between the Jaffe's kinetic method and Jaffe's endpoint method, there was a marked level of accuracy using the Jaffe's kinetic method to estimate serum creatinine levels in pregnancy, this may be due to the fact that most interferences are overcome using this method. [18, 17]

According to Ziv *et al*. [19] findings, sCr concentrations rapidly declined in the first trimester, reached a plateau in the second, and slowly increased in the third trimester toward the pre-pregnancy concentration. This is contrary to the results obtained, as it shows a marked increase in sCr concentration in the second trimester as compared to the third trimester. The results agree with the findings of Patricia *et al*. [15] and Tran. [16] The reason why the result obtained might not agree with Ziv *et al*. [19] may be due to the fact that the study group for the third trimester might have involved women who were in their 26th -34th week of gestation. This according to Ziv et al. 19 will demonstrate a decrease in serum creatinine concentration.

It was also seen that Glomerular filtration rate increased across the trimester although this increase was not statistically significant (>0.05). The finding also agrees with the study of Cheung and Lafayette [4] however, this is contrary to a study carried out by Eiya and Obika [20] According to their findings, Glomerular filtration rate picks at the second trimester. The result obtained from this study suggests otherwise which may be due to the fact that serum creatinine-based equation was used instead of the conventional creatinine clearance measurement which would require a 24 hr-urine collection of which is not practicable.

From the results obtained it was observed that there was an extremely negative statistically significant correlation between Creatinine Jaffe's method and GFRs. This implies that there was an inverse relationship between serum creatinine and GFRs. The nexus could be explained based on the fact that plasma volume increases during the course of pregnancy coupled with a similar increase in Glomerular filtration rate in early pregnancy. [21, 22] These changes in plasma volume and Glomerular filtration rate may give a possible explanation for initial increase in the clearance of serum creatinine. [23, 24] Consequently, the increased renal plasma flow, decreased serum albumin values and raised serum progesterone levels [25] which produces an increase in the Glomerular filtration rate (GFR) during pregnancy [25, 24] which is matched by markedly increased clearances of creatinine [25, 22]. This results in decreased serum levels of serum creatinine [26, 25, 27].

Conclusion

From this study, it could be concluded that human serum creatinine is affected by pregnancy and this alteration tends to come to normal values as the pregnancy progresses to term. This could be explained based on the fact that plasma volume increases during the course of pregnancy coupled with a similar increase in glomerular filtration rate in early pregnancy. In this study, the kinetic method for estimating serum creatinine, proved to be more accurate as compared to the End-point method.

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