International Journal of Medical and Health Research
www.medicalsciencejournal.com
ISSN: 2454-9142
Received: 20-08-2021, Accepted: 03-09-2021, Published: 20-09-2021
Volume 7, Issue 9, 2021, Page No. 33-37

Serum blood urea nitrogen level of pregnant women based on their socio-demographic characteristics in Abia state Nigeria

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Abstract
This study evaluated first trimester blood urea nitrogen and risk of gestational diabetes mellitus in pregnant women in Abia State. Three (3) objectives and research questions guided the study which was a descriptive cross-sectional survey. The study population included all first trimester pregnant women accessing antenatal care in three selected Hospital at the time of conducting this study which totalled 224.The entire 224 first trimester pregnant women were selected to participate in the study using the total sampling method. The instruments for data collection consisted of a structured questionnaire and blood samples of the pregnant women. The structured questionnaire elicited information on socio-demographic characteristics of the study participants while the blood samples provided data on blood urea nitrogen levels of the pregnant women. The questionnaires were administered on the study participants by direct delivery and retrieval approach. Blood samples were collected on antenatal clinic visits after due ethical approval was granted. Data analysis was done using descriptive statistics of frequencies, percentages and mean at 0.05 level of significance. Results revealed that higher blood urea nitrogen levels were recorded in women who were older, had higher proportion of parity and gravidity; there is no significant association between marital status and serum blood urea nitrogen levels (P>.05); high levels of blood urea nitrogen were significantly associated with elevated risk of gestational diabetes irrespective of maternal age, gravidity and parity; there are significant associations between high blood urea nitrogen and gestational diabetes mellitus; Statistical tests for interactions between blood urea nitrogen and these interesting factors on outcome were not significant (P>.05). The study concluded that higher concentrations of blood urea nitrogen during the first trimester of pregnancy were positively and independently associated with increased risk of gestational diabetes. Based on the study findings routine monitoring of renal functioning of women as well as their overall endocrine and metabolic changes during pregnancy were recommended. It was also recommended that pregnant women be encouraged to attend antenatal care clinics regularly.

Keywords: blood urea nitrogen, gestational diabetes mellitus, chronic kidney disease, insulin resistance

Introduction

Almost all maternal physiological system undergoes adjustments because of pregnancy, but perhaps, the greatest upheaval is caused to the renal system (Farlex, 2020) [10]. Renal system changes during pregnancy have been associated with blood urea nitrogen levels in recent times (Allison, 2016) [1]. Blood urea nitrogen (BUN) is the main end product of protein metabolism (Feng *et al*, 2020) [11]. The deamination of amino acids produces NH_3 and CO_2, which are synthesized into urea in the liver and then filter out of the glomeruli and excrete in the urine eventually. Uric acid, blood urea nitrogen (BUN), and serum creatinine levels are crude indices of renal function. In pregnancy, plasma uric acid usually decreases by 25% beginning in the first trimester and increases during the third trimester. Upper normal limits of plasma uric acid levels are 5 to 5.5 mg/dL in pregnancy. Levels are influenced by race, multiple gestation, and time of day sampled, with higher levels in the morning. An indicator of renal filtration, the BUN normally decreases from non-pregnant levels of 12 mg/dL (4.3 mmol/L) to 9 mg/dL (3.2 mmol/L), and plasma creatinine levels decline from a non-pregnant mean value of 0.7 mg/dL (62 mmol/L) to 0.5 mg/dL (44 mmol/L) (Feng *et al*, 2020) [11]. If the plasma creatinine level exceeds 0.80 mg/dL (80 mmol/L) or the BUN is greater than 14 mg/dL at any stage in pregnancy, renal dysfunction should be suspected, and more detailed investigation should be performed.

The kidney and liver affect serum urea levels. The liver synthesizes urea, which is influenced by protein intake, metabolism, and hepatic function. Urea reabsorption is by the kidneys and varies with hydration. Therefore, it is possible for renal function to be normal in the presence of an abnormal BUN or abnormal in the presence of a normal BUN. In addition, renal function must decline by at least 50% before either the BUN or the creatinine level becomes abnormal, where clinical signs of renal insufficiency become apparent. However, blood urea nitrogen is used as a parameter to evaluate renal function since it will increase when renal efficiency is decompensated. Elevated blood urea nitrogen level had been reported to be associated with cardiovascular events and mortality in various pathophysiological conditions. Prior experimental studies suggested that increased levels of urea might induce insulin resistance and suppress insulin secretion both *in vitro* and *in vivo* (Bellamy, 2019) [5]. Recently, epidemiological evidence from the US Department of Veterans Affairs databases provided the evidence that higher levels of BUN were associated with increased risk of incident diabetes mellitus among people without diabetes and increased risk of insulin use in patients with diabetes (Dehmer, 2018) [6]. Gestational diabetes may predispose women to early-stage kidney damage, a precursor to chronic kidney disease (Farrar,

2016) [9]. A series of animal and epidemiological research indicated that elevated BUN levels was a risk factor for insulin sensitivity reduction and increased the risk of diabetes and gestational diabetes mellitus (Levey, 211). Pregnancy does not measurably alter the time course of diabetic renal disease, nor does it increase the likelihood of progression to end-stage renal disease. Regardless of pregnancy, the progression to renal disease in diabetic patients appears to be related to duration of diabetes and degree of glycaemic control (Odutayo & Hladunewich, 2012; Park *et al*, 2018) [14].

Gestational diabetes mellitus (GDM) is defined as glucose intolerance with onset or first recognition during pregnancy (Alsahli *et al*., 2014) [2]. Gestational diabetes mellitus (GDM) is defined as any degree of glucose intolerance with an onset during pregnancy (WHO, 2015). According to the World Health Organization, the global prevalence of GDM was between 5% and 13% from 2005 to 2015. A recent meta-analysis including 79,064 pregnant women from the general population revealed that the prevalence of GDM in mainland China was 14.8% (Gao *et al*, 2019). An elevated blood glucose level during pregnancy is associated with adverse short- and long-term outcomes both for the mothers and their offspring (Arnan, *et al*, 2015). Thus, identification of the associated risk factors is urgently required to prevent gestational diabetes (Nakagawa *et al*, 2015). Women with gestational diabetes mellitus not only have increased incidence of pre‐eclampsia, macrosomia and caesarean section, but also experience higher risk of developing type 2 diabetes mellitus after pregnancy (Hua *et al*, 2020). According to Nagalakshmi *et al* (2012), women with gestational diabetes had at least a sevenfold increased risk of developing type 2 diabetes mellitus after delivery compared with those who have had a normoglycaemic pregnancy. Additionally, children with maternal diabetes exposure are more likely to develop diabetes in youth (Koppe, *et al*, 2016) [15]. Accurate identification and management of risk factors of gestational diabetes mellitus are highly desirable for optimize care and interventions (WHO, 2014).

Urea nitrogen which is generally recognized to be a biomarker of kidney function, has recently received attention because of its association with insulin resistance and diabetes. Previous experimental studies, both *in vitro* and *in vivo*, have demonstrated that elevated urea levels can promote reactive oxygen species generation, induce low-grade inflammation, and thus elicit insulin resistance and inhibit insulin secretion. A prospective cohort study of United States Veterans provided evidence to support the hypothesis that higher urea nitrogen levels are associated with an increased risk of developing diabetes mellitus (DM) and an increased likelihood of insulin use in patients who already have diabetes (Xie *et al*, 2018) [17]. Meanwhile, patients with primary aldosteronism were reported to be more likely to have DM due to increased urea nitrogen levels resulting from impaired renal function, relative to the general population.

Statement of the Problem

During the process of pregnancy, the renal workload increases due to rise in maternal and foetus metabolites. These physiological changes may lead to renal pathological damage and renal insufficiency, and the symptoms are relatively insidious (Webster *et al*, 2017). A series of studies suggested that significant impairment of kidney function was independently associated with poor obstetric outcomes particularly preterm birth and growth restriction (Park *et al*, 2018). It has been recently reported that pregnant women in the early stage of chronic kidney disease or with a mild decrease in glomerular filtration rate were at an increased risk of elevated blood urea nitrogen level and adverse maternal and fetal events (Odutayo & Hladunewich, 2012) [14]. Some studies have associated increased blood urea nitrogen concentration with gestational diabetes mellitus while others have been unable to unravel any significant association between urea nitrogen with insulin resistance and consequent gestational diabetes (Obodo *et al*, 2016; Koppe *et al*, 2018 [16]; Park *et al*, 2018; Feng *et al*., 2020 [11]; Li et, al., 2020).

Thus, there is the need to unravel this controversy especially in Nigeria where there is a reportedly high levels of hyperuricaemia, uraemia, gestational diabetes mellitus and hypertension. The association between the different health problems of pregnant women seem poorly explained and most time downplayed. According to Deng *et al* (2021) [7], women who have a pregnancy complicated by gestational diabetes have up to a 50% chance of developing type 2 diabetes in their lifetime (Deng *et al*, 2021) [7]. It would be interesting to know whether these were the women with elevated urea nitrogen in the first trimester. This possibility is supported by a study by Feng *et al* (2020) [11] in which serum uric acid was measured at a median of 16 months postpartum in women who had pregnancies complicated by gestational diabetes.

Gestational diabetes occurs only in pregnancy and results when the level of blood sugar is too high. The condition resulting from elevated urea nitrogen level increases the risk for preterm birth and caesarean delivery, among other complications. According to Asamiya *et al* (2019) [4], there is \a significant negative relationship between blood urea nitrogen level, birth weight and gestational age. A birth weight equal to or greater than 1500 g or a gestational age equal to or exceeding 32 weeks corresponded to BUN levels of 48–49 mg/dl or less (Asamiya *et al* 2019) [4]. However, kidney disease in pregnancy is often under-recognized and under-appreciated owing to the lack of symptoms and routine kidney function testing in pregnancy (Rawal *et al*. 2018). Deng *et al* (2021) [7] noted with so much concern that there are limited data in the literature on the association between adverse pregnancy outcomes and maternal blood urea nitrogen levels. Very limited research works have paid attention to the influence of blood urea nitrogen on gestational diabetes. In fact, there from literature searches, there are no such studies in Abia State of Nigeria.

Aim and Objectives of the Study

The aim of this study is to evaluate by sensitivity analysis, first trimester blood urea nitrogen and risk of gestational diabetes mellitus in pregnant women in three health facilities in three geopolitical zones of Abia State which include Abia Central, Abia South and Abia North. Specifically, this study aims to:

1. Determine the serum blood urea nitrogen level of pregnant women based on their socio-demographic characteristics.
2. Ascertain the association between first trimester blood urea nitrogen and gestational diabetes mellitus in terms of sensitivity analysis.

Research Questions

The following research questions will be answered in this study:

1. What is the serum blood urea nitrogen level of pregnant women based on their socio-demographic characteristics?
2. What is the association between first trimester blood urea nitrogen and gestational diabetes mellitus in terms of sensitivity analysis?

Significance of the Study

Results from the study will be beneficial to clinicians, the public, government and related agencies as well as other researchers who may want to conduct a similar study. The study findings will provide clinicians with information on the prevalent blood urea nitrogen status of the pregnant population in first trimester which would motivate proactive preventive and control measures directed at ensuring that women maintain optimal homeostasis during pregnancy and beyond.

The study would by the findings and recommendations of the study by guided to make crucial health seeking, utilization and related behaviours in pregnancy as a way of ensuring overall positive outcomes. Government and related public as well as private agencies will be provided with data that would guide sensitization and related awareness creation programmes on the need for routine health check during pregnancy which may enhance health related behaviours of women and ultimately reduce morbidity and mortality associated with childbirth. Results from the study when published will be useful to other researchers who may want to conduct a similar study as it would add to already existing literatures on the association between blood urea nitrogen and gestational diabetes mellitus.

Scope of the Study

This study is delimited to all first trimester pregnant women accessing antenatal care in the three geopolitical zones of the state which include Abia Central, Abia North and Abia South at the time of conducting the research. The content scope of the study include the serum blood urea nitrogen level of pregnant women based on their socio-demographic characteristics, the association between first trimester blood urea nitrogen and gestational diabetes mellitus in terms of sensitivity analysis and the association between first trimester blood urea nitrogen and gestational diabetes mellitus in terms of sub-groups analysis.

Materials and Methods

Research Design

This study is an analytical experimental study of first trimester blood urea nitrogen and risk of gestational diabetes mellitus in pregnant women. The research design was adopted because the researcher did not intend to manipulate any of the study variables. Hopkins (2010) explained that study design aims at collecting data, describing it in systematic manner, the characteristic features of facts about a given population.

Sample and Sampling Technique

The entire 224 first trimester pregnant women were selected to participate in the study. Thus, total sampling method was adopted. Convenient sampling was used to select the sample size of 224.

Method of Data Collection

The questionnaires were administered on the study participants by direct delivery and retrieval approach. Blood samples were collected on antenatal clinic visits after due ethical approval was granted. The women were encouraged to participate in the study by educating them on the consequences of elevated blood urea nitrogen level and gestational diabetes on pregnancy outcomes. They were also informed that the results of the laboratory investigations would help recommend interventions crucial to enhancing overall positive pregnancy outcomes.

Results

The study result is based on the aims and objectives of the study.

Socio Demographic Data

Table 1: Socio-Demographic Characteristics of the Study Participants (n=224**)**

Variable	Category	Frequency	Percentage (%)
Age (years)	18-28	64	28.6
	29-39	124	55.4
	40-44	36	16.0
	Total	224	100
Marital status	Single	4	1.78
	Married	212	94.6
	Divorced/separated	8	3.57
	Total	224	100
Parity	None	16	7.14
	1-2	112	50.0
	3-4	136	60.7
	5 and above	8	3.57
	Total	224	100
Gravidity	1-2	139	61.6
	3-4	69	31.3
	5 and above	16	7.14
	Total	224	100

The table above shows the socio-demographic characteristics of the study participants. Out of the 224 subjects studied, 64(28.6%) were aged 18-28 years, 124(55.4%) were aged 29-39 years while 36(16.0%) were aged 40-44 years. 4(1.78%) were single, 212(94.6%) were married while 8(3.57%) were divorced/separated. 16(7.14%) had no child, 112(50.0%) had 1-2 children, 136(60.7%) had 3-4 children while 8(3.57%) had 5 children and more. 139(61.6%) had gravidity of 1-2 while 69(31.3%) had gravidity of 3-4 while 16(7.14%) had gravidity of 5 and above respectively.

What is the serum blood urea nitrogen level of pregnant women based on their socio-demographic characteristics?

Table 2: Characteristics of the Study Subjects based on Serum Blood Urea Nitrogen Quartiles (n=224)

Characteristics	*BUN (mmol/L*				
	Q1 (<2.40)	Q2 (2.40-2.91)	Q3 (2.92-3.50)	Q4 (≥3.50	P-value
No of subjects	56	60	52	56	
Age (years)	34.83 ± 3.05	34.77 ± 4.00	33.86 ± 4.17	34.80 ± 3.08	.001

Marital status					
Single	2(3.57)	-	2(3.84)	-	.222
Married	52(92.9)	58(97.0)	48(92.3)	54(96.4)	.121
Divorced/separated	-	4(6.67)	2(3.84)	2(3.57)	.202
Parity					
None	2(3.57)	4(6.67)	4(7.69)	6(10.7)	.000
1-2	2(64.3)	4(66.7)	2(57.7)	26(46.4)	.001
3-4	26(57.1)	48(80.0)	26(61.5)	24(42.9)	<.001
5 and above	-	-	4(7.69)	4(7.14)	<.001
Gravidity					
1-2	40(71.4)	28(46.7)	32(61.5)	38(67.9)	<.001
3-4	16(28.6)	20(33.3)	20(38.5)	14(25.0)	<.001
5 and above	2(3.57)	4(6.67)	6(11.5)	4(7.14)	<.001

The above table shows the characteristics of the study subjects based on serum blood urea nitrogen quartiles. 224 study participants were included in the study with mean age of 34.83±4.08 and the median serum BUN concentration was 2.95 mmol/L (IQR, 2.40-3.50 mmol/L). From table 4.2, those with higher BUN levels tended to be older, had higher proportion of parity and gravidity (≥2). However, there is no significant association between marital status and serum blood urea nitrogen levels (P>0.05).

Ethical Consideration

Ethical clearance for the study was obtained from the ethical committee of the Imo State University Owerri. Permission to conduct the study was obtained from the research ethics committee of IMSU. Informed consent was obtained from all the participants after explaining the purpose of the study. The pregnant women were requested to participate in the study voluntarily without coercion. The women were also informed that their participation will not negatively affect their care. They were assured of anonymity, privacy and confidentiality.

Conclusion

This study concluded that higher blood urea nitrogen levels were recorded in women who were older, had higher proportion of parity and gravidity. However, there is no significant association between marital status and serum blood urea nitrogen levels. High levels of blood urea nitrogen were significantly associated with elevated risk of gestational diabetes irrespective of maternal age, gravidity and parity. There are significant associations between high blood urea nitrogen and gestational diabetes mellitus. However, statistical tests for interactions between blood urea nitrogen and these interesting factors on outcome were not significant.

Recommendations

Based on the study findings, the following are hereby recommended.

1. Routine monitoring of renal functioning of women during pregnancy
2. Routine monitoring of endocrine and overall metabolic changes that takes place in women during pregnancy

Contribution to Knowledge

This study has contributed to existing knowledge on first trimester blood urea nitrogen and risk of gestational diabetes mellitus in pregnant women. It has specifically contributed to the body of knowledge on serum blood urea nitrogen level of pregnant women based on their socio-demographic characteristics, the association between first trimester blood urea nitrogen and gestational diabetes mellitus in terms of sensitivity analysis and sub-groups analysis.

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