Original Research Article

MICROALBUMINURIA IN WOMEN WITH RISK FACTORS FOR GESTATIONAL DIABETES MELLITUS IN SOME SELECTED HOSPITALS IN SOKOTO, NIGERIA

ABSTRACT

Gestational diabetes mellitus (GDM) is a common metabolic abnormality which affects approximately 2-5% of pregnancies. Risk factors such as previous infants with macrosomia, strong family history of type 2 diabetes or GDM, poor glycaemic control and high pre-pregnancy body mass index (BMI) have been implicated in the development of GDM. This study was conducted to determine the prevalence of Microalbumnuria in women with risk factors for GDM and to estimate the levels of Urinary Microalbumin in these women. Fifty (50) pregnant women with risk factors for GDM and 50 controls (pregnant women without risk factors for GDM) were evaluated for Microalbuminuria. Microalbuminuria was estimated using Turbidimetric method, Random Plasma Glucose was estimated using Glucose oxidase method, serum Urea, Creatinine and Albumin were estimated using Diacetyl Monoxime method, Jaffe Slot method and Bromo Cresol Green method respectively. The prevalence of Microalbuminuria in women with risk factors for GDM was 22%. Urinary microalbumin was significantly higher in the study subjects (56.36 ± 8.44mg/L) than in the control (17.32 ± 4.5) mg/L. The mean ± standard error of mean of random plasma glucose in the study subjects was (5.84 ± 0.16) mmol/L and that of the control was (4.33 ± 0.14) mmol/L. The mean ± standard error of mean Serum Urea, Creatinine and Albumin were (4.1 ± 0.15)mmol/L, (0.70 ± 0.03)mg/dL, and (3.06 ± 0.05)g/dL respectively while that of the control were (3.47 ± 0.13)mmol/L, (0.63 ± 0.01)mg/dL and (2.78 ± 0.09)g/dL respectively. Obesity was strongly correlated to microalbuminuria.

Key words: gestational diabetes mellitus, pregnant women, microalbuminuria, Urea, Creatinine

INTRODUCTION

Gestational diabetes mellitus (GDM), by definition is any degree of glucose intolerance with the onset or first recognition during pregnancy [1]. This definition applies regardless of whether the treatment involves insulin or diet modification alone; it may also apply to conditions that persist after pregnancy. Women with GDM have a 40-60% chance of developing diabetes mellitus over the period of 5-10 years after the pregnancy [2].

Approximately 4% of pregnant women in the United States have diabetes. Eighty-eight percent (88%) of these women have gestational diabetes mellitus (GDM; 450,000 women per year), and the remaining 12% have either type 1 (12,000) or type 2 diabetes (50,000). Normalizing blood glucose concentrations before and early in pregnancy can reduce these risks to levels of the general population [3]. All GDM severity levels will result in adverse neonatal outcome [4]. Global fetal and infant loss, perinatal mortality, neonatal mortality, and malformations rates are significantly greater if the mother is affected by diabetes than in the non diabetic population [5]. The incidence of GDM is 0.15–15%, and it corresponds to the prevalence of type 2 diabetes and Impaired Glucose Tolerance (IGT) within a given population. The predominant pathogenic factor in GDM could be inadequate insulin secretion. It has been convincingly demonstrated that GDM occurs as a result of a combination of insulin resistance and decreased insulin secretion. The cumulative incidence of Type 2 diabetes is 50% at 5 years. GDM is also a predictor, or even an early manifestation, of the metabolic (insulin resistance) syndrome. GDM is a cardiovascular risk factor and affected patients should be screened to prevent late [6].

Studies in Nigeria have shown high and low values respectively. In Ibadan, South West Nigeria the prevalence of GDM is 4.9% [7]. Consequently, in Sokoto, North-western Nigeria the prevalence of Gestational diabetes mellitus was found to be 7.7% [8].

Risks factors for gestational diabetes mellitus includes Macrosomia (≥ 4.5 kg), Family history of type 2 diabetes mellitus, Body Mass Index (BMI) ≥ 30.0, Pre diabetes, High blood pressure, Previous history of unexplained stillbirth and miscarriage and Hormonal disorders such as Polycystic Ovary Syndrome among others [9].

Microalbuminuria is an increased excretion of albumin above the reference range for healthy non diabetic subjects, but undetectable by the Albustix dipstick test, or as modified by expert group, as a urinary albumin excretion rate between 20 - 200μg/min (3-30 mg/mmol ACR) in an overnight or 24 hours sample on at least 2 of three occasions within a period 6 months [10]. Microalbuminuria is also defined as the urinary excretion of 30-300 mg of albumin per day [11][12]. The patients with longer duration of diabetes mellitus, hypertension, older age, higher body mass index (BMI) and adverse lipid profile are more prone to develop microalbuminuria [13]. Screening tests for microalbuminuria are recommended annually for patients with type 1 diabetes of greater than 5 years duration and for all patients with type 2 diabetes from the time of diagnosis.

Normal human urine contains only very small quantities of albumin, less than 30mg of albumin being excreted by healthy adults in 24 hours. The appearance of large amounts of albumin in the urine is a cardinal sign of renal damage, especially glomerular diseases, and is not detectable by screening techniques using urinary dipsticks. Early detection of microalbuminuria allows early intervention with a goal of delaying the onset of overt diabetic nephropathy [14].

This study was therefore designed to investigate microalbuminuria in pregnant women with the risk factors for the development of gestational diabetes.

MATERIALS AND METHODS

Study Area

The study was carried out in the Department of Chemical Pathology, Usmanu Danfodiyo University Teaching Hospital (UDUTH) Sokoto, Nigeria. Usmanu Danfodiyo University Teaching Hospital is a Tertiary Health Facility located in Sokoto, the Sokoto State Capital, Nigeria. It serves as a referral centre for more than 10 million people of the Nigerian States of Sokoto, Zamfara and Kebbi, and neighboring Niger and Benin Republic in the West African sub region.

Sokoto state is located at the extreme part of the North-Western Nigeria, (longitude 11^{o}-30 to 13^{o}-50 east and latitude 4-6^{o} north). Sokoto state shares a border with Niger republic to the North, Kebbi state to the West, and South and Zamfara state to the south and east. Sokoto state occupies an area of short-grass savannah vegetation in the South and thorn shrub in the North generally of Arid zone. The State covers a total land area of about 32,000 square kilometers and a population of 4,953,078 million based on 2013 projection [15].

Study Subjects

Pregnant women were recruited from population of patients attending the antenatal clinic (ANC) in Specialist Hospital and Maryam Abacha Women and Children Hospital, Sokoto. A structured questionnaire was administered to each patient and relevant bio data and clinical information were obtained. Informed consent for inclusion into the study was obtained from each subject using the standard protocol. Subjects were selected by simple random sampling method.

Ethical Approval

Ethical approval was obtained from the Ethical Committee of Specialist Hospital, Sokoto and Maryam Abacha Women and Children Hospital, Sokoto before the commencement of the study.

Study Design

It is a case control study. The subjects were grouped into 2:

Group 1: fifty (50) pregnant women without risk factor for Gestational Diabetes Mellitus (control)

Group2: fifty (50) pregnant women with risk factors for Gestational Diabetes Mellitus

Sample Collection and Processing

A total number of one hundred blood samples and urine samples were collected. Fifty numbers of blood and urine samples were collected from women with risk factors for Gestational Diabetes Mellitus, 50 numbers of blood and urine samples were collected from pregnant women without gestational diabetes (controls). Spot urine sample (2 mL) was collected into a universal container for the estimation of microalbuminuria while 3ml of blood sample was collected into fluoride oxalate container for the estimation of glucose and 3mL of blood into a plain container for the estimation of urea, creatinine and albumin respectively. The blood in the plain container was allowed to clot after which it was centrifuged, separated and the serum was stored in a freezer at -20^0C till analysis. The urine sample was analyzed immediately for Microalbuminuria, glucose was also estimated immediately after separation of plasma from the whole blood.

Biochemical Analysis

Urinary microalbumin was estimated using Turbidimetric method [16]. Blood glucose was estimated by glucose oxidase method [17]. Serum Urea was estimated by Diacetyl Monoxine Method**,** serum albumin was estimated using Bromocresol green Method [18]. Serum Creatinine was estimated using Jaffe's Method [19].

Data obtained from this study were analyzed using statistical package for social sciences (SPSS) for Windows version 20 (SPSS Inc., Chicago, IL, USA). The data were expressed as the mean ± standard error of mean. Paired comparison was made using student T- test, and less or equal to 0.05 ($P < .05$) was regarded as statistically significant.

RESULTS

The prevalence of microalbuminuria in women with risk factors for gestational diabetes mellitus was found to be 22%.

Table 1 shows the Socio- economic and Demographic characteristics of pregnant women with and without risk factors for gestational diabetes mellitus. Majority of the study population were Hausa (80%), among which most of them (44%) had no Formal Education and 62% of them are married to peasant farmers.

Table 1

Characteristics	Pregnant Women +RFGDM (n= 50)	Pregnant Women RFGDM (n= 50)
Tribes		
Hausa	43(86%)	40(80%)
Yoruba	3(6%)	4(8%)
Igbo	2(4%)	3(6%)
Others	2(4%)	3(6%)
Educational status		
Primary	20(40%)	18(36%)
Secondary	6(12%)	8(16%)
Tertiary	4(8%)	2(4%)
Informal	20(40%)	22(44%)
Occupation of husbands		
Farmer	30(60%)	31(62%)
Trader	15(30%)	14(28%)

Civil servants	3(6%)	3(6%)
Others	2(4%)	2(4%)

Values are number of subjects with percentage in parenthesis, n= number of subjects, -RFGDM = No Risk factor for gestational diabetes mellitus, +RFGDM= with risk factors for gestational diabetes mellitus. Majority of the study population were Hausa (80%), among which most of them (44%) had no formal education. Majority of them (62%) were women married to peasant farmers.

Table 2 shows the age distribution (in years) and gestational ages (in weeks) of pregnant women with and without risk factors for gestational diabetes mellitus. Majority of the study population had pregnancies with gestational age between 24- 28 weeks. Majority of the study population (60%) were within the age group of 18-25 years.

Table 2:

Variable	**Pregnant Women +RFGDM (n= 50)**	**Pregnant Women -RFGDM(n= 50)**
Gestational age (weeks)		
16-20	10(10%)	14(28%)
20-24	14(28%)	13(26%)
24-28	26(52%)	23(46%)
Total	50(100%)	50(100%)
Age Class of Pregnant Women (years)		
18-25	18(36%)	30(60%)
26-32	25(50%)	8(16%)
33-39	5(10%)	10(20%)
40-46	2(4%)	2(4%)
Total	50(100%)	50(100%)

Values are number of subjects with percentage in parenthesis, n= number of subjects, -RFGDM = No Risk factor for gestational diabetes mellitus, +RFGDM= with risk factors for gestational diabetes mellitus. Majority of the study population (46%) had pregnancies with gestational age between 24-28 weeks. Majority of the study population (60%) were within the age of 18-25 years.

Table 3 shows the mean urinary levels of microalbumin and serum levels of random plasma glucose, albumin, urea and creatinine in pregnant women with and without risk factors for gestational diabetes mellitus.The mean ± standard error of mean urinary microalbumin level in pregnant women with risk factors for gestational diabetes mellitus was significantly higher than controls p- value < 0.05. The difference between pregnant women with and without risk factors for gestational diabetes mellitus of serum concentrations of random plasma glucose, albumin, urea and creatinine were not statistically significant ($p>0.05$)

Table 3:

Parameters	**Pregnant Women – RFGDM (n= 50)**	**Pregnant Women + RFGDM (n= 50)**
RPG (mmol/L)	4.33 ± 0.14	5.84 ± 0.16
MA(mg/L)	17.31± 0.64	56.36 ± 8.44*
Albumin(g/dL)	2.78 ± 0.09	3.06 ± 0.05
Urea (mmol/L)	3.47 ± 0.13	4.10 ± 0.15
Creatinine(mg/dL)	0.63 ± 0.01	0.70 ± 0.03

* ($P < .001$). n= number of subjects.
-RFGDM = No Risk factor for gestational diabetes mellitus, +RFGDM= with risk factors for gestational diabetes mellitus,RPG- Random plasma Glucose, MA- Microalbuminuria

Table 4 shows the mean levels of BMI, blood pressure, family history of diabetes and family history of hypertension in pregnant women with and without risk factors for gestational diabetes mellitus. The mean ± standard error of mean BMI of the study population was significantly higher in pregnant women with risk factors for gestational diabetes mellitus than in controls, p-value < 0.05. The mean ± standard error of mean systolic blood pressure and diastolic blood pressure shows no difference across the groups, p- value > 0.05.

Table 4:

Parameter	**Pregnant Women - RFGDM (n= 50)**	**Pregnant Women + RFGDM (n= 50)**
BMI (kg/m^2)	22.98 ± 0.48	37.89 ± 0.60*
Systolic blood pressure (mm Hg)	124 ± 5.8	128.36 ± 11.3
Diastolic blood pressure (mm Hg)	79.2 ± 5.9	79.2 ± 10.1
Gravidity	P: 23(46%), M: 27(54%)	P: 29(58%), M: 21(42%))
Familyhistoryof diabetes	0	50
Familyhistoryof hypertension	3	35

* ($P < .001$)
n= number of subjects. BMI= Body Mass Index.
-RFGDM = No Risk factor for gestational diabetes mellitus, +RFGDM= with risk factors for gestational diabetes mellitus. mm Hg= millimeters of mercury. Kg= kilograms. M^2 =meters square.
P= primigravida. M= multigravida.

Table 5 shows the correlation of urinary microalbumin to serum urea, creatinine, albumin and random plasma glucose.

Table 5:

	Urea	Creatinine	Albumin	RBG
Microalbuminuria	r= 0.261	r= 0.087	r= 0.045	r= 0.126
	p= 0.09	p= 0.387	p= 0.656	p= 0.212

DISCUSSION

In this study, the prevalence of microalbuminuria in women with risk factors for gestational diabetes mellitus was found to be 22%. This is similar to the findings of 22% prevalence of microalbuminuria in diabetic patients in UDUTH, Sokoto [20]. Current study is also similar to the 20% prevalence found in a cohort of African- American women with GDM [21]. This similarity could be due to the geographical location and also the socio economic status of the population. Our finding is lower than the prevalence of 25% reported in 40 type II diabetic patients from Illorin, Nigeria, [22]. This is also in contrast to the prevalence of 38% reported in Port Harcourt[23], 37.6% in Lagos [24]. These variations in prevalence might be attributed to factors such as differences in populations, method of urine collection or differences in ethnic susceptibility [25].

In the this study, urine microalbumin levels was higher ($P<0.001$) in pregnant women with risk factors for gestational diabetes than in the control, and this is associated with increased in body mass index (BMI) of patients as compared to that of controls. Increased BMI is closely associated with microalbuminuria. Study on Type 2 diabetes mellitus patients reported a correlation between obesity and microalbuminuria[26]. The high mean urinary microalbumin level gotten from this study is similar to the findings of Shenaz [27] in type II diabetes mellitus in Karachi.

Random plasma glucose concentration for both women with risk factors for gestational diabetes mellitus and the control shows no statistically significant difference ($P<0.001$). The slightly insignificantly lower random glucose level could be attributed to stress the women undergo while trekking to the antenatal clinic, or long hours of waiting at the clinic before been consulted by a clinician or the socio economic status of the study population.

In the current study, the slightly low serum albumin levels in the study population and that of controls shows no statistically significant difference ($P<0.001$). This is similar to the report of [28] which reported low serum albumin level in pregnant women. The decrease in serum albumin of the study population could be due to alteration in protein metabolism which is associated with gestational diabetes mellitus, or the socio economic status.

In the current study, serum urea and creatinine levels of the study population and the control shows no statistically significant difference ($P<0.001$). Similar findings [29] [30] reported normal serum urea and creatinine levels in these category of patients but is lower than the one reported by [28]. This variation can be due to environmental factors and the socio economic status of the study population.

It could be concluded from the present study that the prevalence of microalbuminuria in women with risk factors for gestational diabetes mellitus in Sokoto, Nigeria was found to be 22%. The urinary microalbumin level is higher in pregnant women with risk factors for gestational diabetes mellitus than in the controls (pregnant women without risk factors for gestational diabetes mellitus).There is a significant positive correlation between microalbuminuria and obesity (BMI $\geq 30 Kg/m^2$).

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