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Research Article

Microalbuminuria and Glycosuria as Biomarkers for Renal and Cardiovascular Disorders in Pregnancy

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Abstract

Background: Microalbuminuria and glycosuria are useful biochemical parameters for the assessment of renal and cardiovascular dysfunction during pregnancy. They have high predictive value for conditions such as preeclampsia and gestational diabetes in early pregnancy. Our study sought to determine the concentrations of urinary microalbumin and glucose among pregnant women attending the Plateau State Specialist Hospital, in Jos, Plateau State as a means of possible disease prevention.

Methods: A total of 160 women who consented to the study were enrolled, 140 were pregnant women while 20 were apparently non- pregnant women. Routine spot urine samples were collected from the women and concentrations of urinary albumin and creatinine were determined using the turbidimetric and Jaffe reaction methods respectively. Microalbuminuria was then determined by calculating the urinary albumin: creatinine ratio (UACR ratio). The glucose oxidase method was used to determine the concentration of glucose in the urine using point of care glucose test strips.

Results: The Mean ± Standard deviation urinary albumin and creatinine concentrations were 2.14 ± 2.25 mg/dl and 0.08 ± 0.06g/dl respectively for the pregnant women while the non-pregnant participants had 1.92 ± 1.54mg/dl and 0.17 ± 0.09g/dl respectively. The Mean ± Standard deviation microalbuminuria concentration for the pregnant women was 47.58 ± 84.28 mg/g while the non-pregnant participants was 16.21 ± 27.02 mg/g ($p > 0.05$). The mean ± standard deviation glycosuria concentration for the pregnant women was 0.76 ± 1.07 mmol/l while that of the non- pregnant control was 0.49 ± 0.22mmol/l ($p > 0.05$). The mean ± standard deviation microalbuminuria concentrations in the first, second and third trimesters of pregnancy were (86.05 ± 189.21 mg/g), (83.46 ± 146.11) and (37.42 ± 56.47) respectively. Microalbuminuria levels were significantly elevated in the first and third trimesters respectively, with $P < 0.05$. The mean glycosuria concentrations in the first, second and third trimesters were (0.75 ± 0.80 mg/dl), (2.18 ± 4.16 mg/dl) and (1.22 ± 1.36 mg/dl) respectively, with $P > 0.05$.

Conclusion: Microalbuminuria and glycosuria may be useful biochemical markers for predicting the occurrence of renal and cardiovascular disorders in pregnancy.

Keywords: Microalbuminuria; Glycosuria; Pregnancy

Introduction

Pregnancy, also known as gestation is the period when one or more offspring grows in a woman's womb and this period requires careful monitoring by qualified healthcare providers. Special coaching classes are usually organized for pregnant women by such healthcare providers (Antenatal classes) with the aim of educating and monitoring various physiological functions of the body. Some of the biggest challenges in most antenatal clinics in Jos mostly include the non-availability of standardized biochemical screening tests for the detection of possible abnormal parameters such as microalbuminuria and glycosuria, leading to complications arising from abnormal microalbuminuria and glycosuria concentrations. This is probably because microalbuminuria screening is often not conducted on pregnant women around this environment except when renal and cardiovascular disorders are suspected or whenever the urine dipstick suggests presence of proteinuria. Microalbuminuria dipsticks are also mostly unavailable in Jos due to their high cost.

The detection of microalbuminuria and glycosuria during pregnancy is of great significance because it serves as a prognostic and preventive measure in the control of renal and cardiovascular disorders as well as in the management of the health of both the mother and child during the course of pregnancy [6]. Despite the fact that microalbuminuria and glycosuria have been established to have high predictive value for renal and cardiovascular disorders such as pre-eclampsia and gestational diabetes in early pregnancy [12], not much importance has been placed on the early detection of microalbuminuria and glycosuria among pregnant women in developing countries like Nigeria and more specifically, Jos, Plateau state. In addition, not much has been done to show any relationship between pregnancy itself, microalbuminuria and glycosuria [14].

Albumin is the most commonly excreted form of protein in urine, and the normal urinary albumin excretion rate which is usually referred to as albuminuria is less than 20mg/24hours urine collection. According to Airoldi and Weinstein, microalbuminuria is a condition characterized by abnormal increase in the level of albumin excreted in urine in the range of 30 -299 mg/24hours urine collection [1]. It may also be expressed in terms of urinary albumin: creatinine ratio as (30 - 300 mg albumin/g of creatinine) when a spot urine sample is collected. When urinary albumin levels are measured in excess of 300 mg/24hours or urine albumin: creatinine ratio measured in excess of 300mg albumin/g of creatinine, this is known as frank proteinuria. It is important to note however, that the presence of persistent microalbuminuria in pregnancy is not a disease condition in itself but persistent microalbuminuria in early pregnancy may serve as a marker for renal and cardiovascular disorders [15].

Glycosuria on the other hand, is defined as the presence of detectable concentrations of glucose in the urine [5]. Glucose is a high threshold substance and hence its detection in urine at increased concentrations indicates an abnormality especially during pregnancy. Pregnancy induced hyperglycemia may result in the detection of the excess glucose in urine, which if not properly managed may lead to gestational diabetes. Glycosuria therefore, indicates a risk of having gestational diabetes and an overly large baby such that a caesarian section becomes inevitable [6]. Our work therefore sought to compare micoalbuminuria and glycosuria concentrations of pregnant and non-pregnant women attending the Plateau State Specialist Hospital, Jos, as a means of possible disease prevention.

Materials and Methods

Study area

Our study was carried out at the Plateau State Specialist Hospital (PSSH), Jos. The Hospital is located at the city center of the Jos metropolis in Jos-North Local Government Area. It is a secondary hospital that caters for various categories of patients ranging from adults to children and also pregnant women. The sample analysis was carried out at the Chemical Pathology Laboratory of the Department of Medical Laboratory Science, University of Jos.

Study population

The study population consisted of pregnant women of various ages and trimesters attending the antenatal clinic in the hospital while the control population were non-pregnant women.

Ethical consideration

Ethical clearance was sought and obtained from ethical committee of the PSSH before commencement of the study. The inclusion criteria included Pregnant women attending the Plateau Specialist hospital, Jos, who gave their consent while those that did not consent were excluded from the study. A structured questionnaire was used to obtain information from the patients such as demographic characteristics, history of any disease and status of pregnancy.

Sample size determination

The sample size was calculated using the Thrushfield formula

$$n = \frac{Z^2 . P (1 - P)}{d^2}$$

where n = Minimum sample size

Z = Constant value at 95% confidence level (1.96)

P= Prevalence rate

d = Desired absolute precision (5%)

In this case, a 10% prevalence rate was used, with P = 0. 10 [6]. The minimum sample size obtained based on the formula was 138. A total of 160 participants were studied, 140 participants who were pregnant served as the test group while another 20 participants who were non-pregnant women served as controls. The use of very few control samples was largely due to the unavailability of participants at the time this study was carried out.

Sample collection

Participants were well guided on sample collection and 5mls of early morning spot urine was collected using chemically clean universal containers. Samples were transported to the laboratory for analysis within 30mins following standard Operating procedures without the use of preservatives.

Determination of microalbuminuria

Microalbuminuria was determined by estimation of the albumin: creatinine ratio of the spot urine samples collected. This involved the measurement of albumin concentration in mg/dl and creatinine concentration in g/dl. The albumin: creatinine ratio in mg/g obtained was equal to the total microalbumin excretion in mg/24 hours. Albumin estimation was based on the precipitation of protein, particularly albumin, in urine by 3% trichloroacetic acid. The turbidity produced from the sample was then measured against an albumin standard using a spectrophotometer at wavelength of 450nm.

The concentration of albumin in the urine samples was calculated using the formula:

$$\text{Creatinine concentration (g/dl)} = \frac{\text{Optical density of test x Concentration of standard}}{\text{Optical density of standard}}$$

Reference Range: (0 - 2 mg/dl)

Urine creatinine was analysed using the Jaffe reaction based on the principle that creatinine reacts with picrate ion formed in alkaline medium to develop a red-orange colour. The colour produced from the reaction was then compared in a spectrophotometer at wavelength of 520nm with that produced by a known concentration of creatinine under the same condition.

The concentration of creatinine in the urine samples were calculated using the formula:

$$\text{Creatinine concentration (g/dl)} = \frac{\text{Optical density of test x Concentration of standard}}{\text{Optical density of standard}}$$

Reference Range: (0.05 - 0.14g/dl)

The albumin: creatinine ratio was calculated by dividing albumin concentration in milligrams with creatinine concentration in grams.

Determination of glycosuria

Glycosuria was determined using the glucose oxidase method via a Point of care glucose meter which detects the level of glucose in urine semi- quantitatively. The reaction is based on the principle of the glucose oxidase reaction, where glucose is oxidized to glucoronic acid by the enzyme glucose oxidase with the release of hydrogen peroxide. The hydrogen peroxide formed reacts with phenol and a chromogen (4 - aminophenazone) under the catalysis of peroxidase enzyme. The peroxidase enzyme converts the chromogen from a reduced colourless state to a pink coloured oxidized state.

$$\text{Glucose} + O_2 + H_2O \xrightarrow{\text{Glucose Oxidase}} \text{Glucoronic acid} + H_2O_2$$

$$2H_2O_2 + \text{4 - aminophenazone} + \text{phenol} \xrightarrow{\text{Peroxidase}} \text{Pink-coloured complex}$$

Reference range: (0 - 0.8mmol/l)

Statistical analysis

The data generated was analyzed using the Statistical Package for Social Sciences (SPSS) version 23.0. Mean (± SD) was used to describe continuous variables and proportions for categorical data. The one-way ANOVA analysis of variance was used to ascertain the significance between the means of the two groups. Probability values less than 0.05 ($P < 0.05$) were considered significant.

Results

Out of the 140 pregnant participants, 66(47.1%), 27 (19.3%), 43 (30.7%) and 4 (2.9%) belonged to the ≤ 25 years, 26 - 31years, 32 - 36 years and ≤ 37 years age groups respectively. 12(8.6%), 22 (15.7%) and 106(75.7%) of the pregnant participants were in their first, second and third trimesters of pregnancy respectively while 74(52.9%), 31(22.1%), 18 (12.9%) and 17(12.1%) had been pregnant for ≤ 2 times, 3 - 4 times, 5 - 6 times and ≥ 7 times respectively. 95 (67.9%) of the pregnant participants engaged in physical exercises while 45 (32.1%) did not. Also, 3(2.1%), 101(72.2%), 34(24.3%) and 2(1.4%) of the pregnant participants had body mass index values of ≤ 18.4kg/m2, 18.5 - 29.8 kg/m2, 29.9 - 41.3kg/m2 and ≥ 52.8 kg/m2respectively. This is shown in table 1.

	No. of Pregnant Participants	Percentage (%)
Age group		
≤ 25	66	47.1
26 - 31	27	19.3
32 - 36	43	30.7
≥ 37	4	2.9
Total	140	100.0
Trimesters		
First	12	8.6
Second	22	15.7
Third	106	75.7
Total	140	100.0
Parity		
≤ 2	74	52.9
3 - 4	31	22.1
5 - 6	18	12.9
≥ 7	17	12.1
Total	140	100.0
Physical exercise		
Yes	95	67.9
No	45	32.1
Total	140	100.0
Body Mass Index		
≤ 18.4	3	2.1
18.5 - 29.8	101	72.2
29.9 - 41.3	34	24.3
≥ 52.8	2	1.4
Total	140	100.0

Table 1: Demographic characteristics of the study participants.

The mean urinary concentrations of albumin, creatinine, microalbumin (UACR ratio) and glucose of pregnant and non- pregnant participants as shown in table 2, indicates that mean ± SD urinary albumin, creatinine and microalbumin concentrations were 2.14 ± 2.25 mg/dl, 0.08 ± 0.06 g/dl and 47.58 ± 84.28mg/g respectively. On the other hand, that of the non-pregnant participants were 1.92 ± 1.54mg/dl, 0.17 ± 0.09 g/dl and 16.21 ± 27.02 mg/g respectively. In addition, the Mean ± SD urinary glucose concentration for the pregnant participants was 0.76 ± 1.07 mmol/l while that of the non- pregnant control was 0.49 ± 0.22mmol/l.

Analyte	Pregnant participants	Non- pregnant participants
Albumin (mg/dl)	2.14 ± 2.25	1.92 ± 1.54
Creatinine (g/dl)	0.08 ± 0.06	0.17 ± 0.09
Microalbumin		
(UACR Ratio mg/g)	47.58 ± 84.28	16.21 ± 27.02
Glucose (mmol/l)	0.76 ± 1.07	0.49 ± 0.22

Table 2: Mean urinary concentrations of albumin, creatinine, microalbumin (UACR ratio) and glucose of pregnant and non- pregnant participants.

Table 3 represents a comparison of the mean microalbuminuria (UACR Ratio) and glycosuria concentrations of the pregnant and non-pregnant women (control). Our result showed a non-significant increase in the mean microalbuminuria concentration (47.58 ± 84.28 mg/g) and glycosuria concentration (0.76 ± 1.07mmol/l) of the pregnant participants when compared to the non-pregnant participants (16.21 ± 27.02mg/g) and (0.49 ± 0.22mmol/l) respectively with P > 0.05.

	Pregnant Participants	Non-Pregnant participants (Controls)	F - Value	P - value
Microalbumiuria (UACR Ratio mg/g)	47.58 ± 78.71	16.21 ± 27.02	164.75	0.06
Glycosuria (mmol/l)	0.76 ± 1.07	0.49 ± 0.22	1.78	0.18

Table 3: Comparison of the mean microalbuminuria (UACR Ratio) and glycosuria concentrations of pregnant and non - pregnant participants (control).

Table 4 represents a comparison of the mean microalbuminuria (UACR Ratio) values of the control group with the mean first, second and third trimester values. Our result showed a significant increase in the mean microalbuminuria concentrations in the first trimester (86.05 ± 189.21mg/g) and third trimester (37.42 ± 56.47) when compared to the non-pregnant participants (16.21 ± 27.02mg/g) with P < 0.05. The value for the second trimester was (83.46 ± 146.11) with P > 0.05.

	Control	First trimester	Second trimester	Third trimester
Microalbuminuria (mg/g)	16.21 ± 27.21	86.05 ± 189.21	83.46 ± 146.11	37.42 ± 56.0
p- value		**0.01**	**0.06**	**0.01**

Table 4: Comparison of the mean microalbuminuria (UACR Ratio) concentration of the non-pregnant control with the mean first, second and third trimeters of pregnancy.

Table 5 represents a comparison of the mean glycosuria values of the control group with the mean first, second and third trimester values. Our result showed a non-significant increase in the mean glucosuria concentrations in the first (0.75 ± 0.80 mg/dl), second (2.18 ± 4.16 mg/dl) and third trimester (1.22 ± 1.36 mg/dl) values when compared to the non-pregnant participants (0.47 ± 0.24 mg/dl) with P > 0.05.

	Control	First trimester	Second trimester	Third trimester
Glycosuria (mg/dl)	0.47 ± 0.24	0.75 ± 0.80	2.18 ± 4.16	1.22 ± 1.36
p- value		0.88	0.51	0.60

Table 5: Comparison of the mean glucosuria concentrations of the non-pregnant control with the mean first, second and third trimeters of pregnancy.

Discussion

This study showed that the concentration of urinary albumin among the pregnant women, was slightly above the established normal range (0-2 mg/dl) while that of the control was within the reference range. This increase can be attributed to increased blood volume during normal pregnancy, which leads to an increase in the glomerular filtration rate and subsequent increase in albumin excretion [10]. Also, a greater percentage of the study population, were above the age of 25. Given that the number of functional nephrons decrease with advancing age, leading to increased glomerular filtration in the remaining nephrons, this might also result in increased albumin excretion [7]. Creatinine concentrations were however within the established normal range (0.05 - 0.14 g/dl) for both the pregnant and non-pregnant participants, although much higher values were observed in the test group.

Urinary albumin to creatinine ratio obtained, was within the reference range for microalbuminuria among the pregnant participants (UACR ratio 30 - 300 mg/g) indicating positive microalbuminuria levels during pregnancy, while the control group remained below the reference range (> 30 mg/g). Increased glomerular filtration rate may be responsible for the detection of microalbuminuria among the test subjects. Glycosuria however remained within the established normal range for both the test group and control group (0 - 0.8 mmol/l), even though the values obtained for the pregnant women were quite higher than the control. Despite the above increased concentrations among the pregnant women, there was however no significant difference in the mean concentrations of microalbuminuria and glycosuria when compared to the non-pregnant control, as indicated by the p value obtained. This is in line with the findings of similar studies carried out by Armstrong, in 2009 [2], which showed that no significant difference existed when the urine albumin: creatinine ratio of pregnant women was compared to the non- pregnant control and that of William., *et al*. (2005) [16], which showed that no significant difference existed when the urine glucose concentrations of pregnant women were compared with the non-pregnant control. Possible contributing factors to the non-existence of a significant difference could include the very few number of control samples collected compared to the test samples, and the fact that the pregnant women may have had no underlying renal or cardiovascular disorders. Furthermore, the very few numbers of pregnant women with increased glucose concentrations, and an association with the fact that the renal threshold for glucose was variable; resulting in a positive result for glycosuria despite normal blood sugar levels may also serve as contributing factors.

However, when the microalbuminuria and glycosuria concentrations of the non-pregnant participants were compared to that of the pregnant participants based on trimesters of pregnancy, a

significant increase in the concentration of microalbuminuria was observed among the pregnant women in their first and third trimesters of pregnancy. There was however no significant increase in glycosuria concentrations. These findings are in line with similar studies by Kaur., *et al*. in 2016 [11], Mishra., *et al*. in 2017 [13], and Baweja., *et al*. in 2011 [3] who stated that the detection of microalbuminuria and elevated protein creatinine ratio in first trimester could be a predictor for the development of preeclampsia. This is because persistent microalbuminuria indicates endothelial dysfunction and a high probability of damage to the glomerular filtration capacity of the kidney. In another study by Hae-Il Park., *et al*. in 2002 [8], microalbuminuria excretions increased significantly in the third trimester of pregnancy and this was also similar to findings in our study. Possible reasons for this increase could be due to the presence of an underlying disease condition such as diabetes and the presence of pre- existing microalbuminuria as stated by the findings of Biesenbach., *et al*. in 1994 [4]. The finding of a non-significant difference in the glycosuria concentrations despite elevations of the test group as compared to the control group, was in line with the studies carried out by Harold and Stanley, in 1973 [9], which stated that increased glycosuria observed during pregnancy was consistent with the alterations in the renal hemodynamics that occurred at that time, but no significant difference may exist, as a wide variance in the quantitative excretion of glucose can occur depending on individual renal thresholds.

Conclusion

Findings of no significant differences in the concentrations of microalbuminuria and glycosuria for the pregnant and non-pregnant participants, has led to the conclusion that unless there is an underlying health disorder, the concentrations of microalbuminuria and glycosuria among pregnant women would remain the same with the non-pregnant state. However, the observance of significantly increased microalbuminuria concentrations in the first and third trimesters of pregnancy, as well as elevated glycosuria values among the pregnant women may suggest the usefulness of microalbuminuria and glycosuria as markers for renal and cardiovascular disorders during pregnancy. Therefore, it is important that these parameters be introduced as routine antenatal screening tests as a means of possible disease prevention.

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