

Original Article

Assessment of the Risk of Future Metabolic Syndrome among Non-Hypertensive and Non-Diabetic Nigerian Pregnant Women Presenting with either Glycosuria or Proteinuria at Different Trimesters

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Abstract

Background

In pregnancy, women experience physiological changes which could increase the risk of insulin resistance, and metabolic syndrome later in life. This study assessed the risk of future metabolic syndrome among pregnant women with either glycosuria or proteinuria at different gestational ages.

Methods

Eight-Six participants were recruited from health facilities in South-west, Nigeria and they were in three categories: those with glycosuria (n = 32), proteinuria (n = 27), and control (n = 27), based on urinalysis result. Data were analyzed using IBM SPSS Statistics for Windows version 25.0 (IBM Corp, Armonk, NY, USA). Groups were compared using one way ANOVA. Association between the variables was determined using Pearson correlation. Linear regression analysis was performed to predict the risk of future metabolic syndrome.

Results

Participants with glycosuria, proteinuria and control were 29.19 (SD 6.04), 27.15 (SD 4.37) and 25.74 (SD 4.67) years respectively. Glycosuria group had higher (P = 0.01) triglycerides, HOMA-IR, and a-positive association (P = 0.001) between, FBG and HBA1C. Linear regression analysis predicted future risk of metabolic syndrome (P< 0.05) for those with glycosuria and proteinuria respectively with their plasma insulin values.

Conclusion

Healthy volunteers with glycosuria and proteinuria are at greater risk of developing metabolic syndrome.

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Keywords: Glycosuria, Metabolic Syndrome, Gestational Diabetes Mellitus, Cardiovascular, Insulin Resistance, Triglycerides, Hyperinsulinemia, Hypertension and Obesity

Introduction

A waning physiologic response of the target tissues to either endogenous or exogenous insulin is referred to as insulin resistance. [1] In a typical pregnancy, maternal tissues lose sensitivity to insulin.[2] Reduction in insulin sensitivity has been observed in some pregnant individuals with increasing gestation despite having normal glucose tolerance; and, similar observation has been recorded in those with gestational diabetes.[1] In addition, during pregnancy, endogenous insulin secretion in women with diabetes is insufficient.[3]

It has been observed that insulin resistance is associated with diabetes mellitus, cardiovascular disease, dyslipidaemia, hypertension, obesity, and other abnormalities,[4,5] which are components of metabolic syndrome. Thus, insulin resistance in pregnancy has been adjudged to be the basis for many metabolic complications[6] and it is a known fact that maternal resistance to insulin during pregnancy increases as the gestational age increases.[7] This becomes necessary to improve the foetus glucose requirement during pregnancy.[8,9] Insulin resistance is a foremost cause of hyperglycemia in pregnancy which may result in gestational diabetes mellitus that is seen in about 14.0% of all pregnancies worldwide and 14.2% in Africa.[10] Unfortunately, the majority of these cases are found in developing countries.[10] It appears that the metabolic syndrome is primarily mediated by insulin resistance.[11]

Excretion of simple sugar (glucose) in the urine of humans has been termed glycosuria and this could be caused by many factors.[12] When this occurs in pregnancy, it may hint at likely impending harmful consequences in both the pregnancy and the life course. [13] Conversely, proteinuria is characterized by elevated protein in the urine. While it is generally known that proteinuria may be a sign of kidney damage and kidney disease progression,[14] the amount of proteinuria in pregnancy tends to increase; and recent

studies suggest that the severity may not impact negatively on prospective mother and baby.[14,15,16] The reoccurrence of any of these two or both (glycosuria and proteinuria) in pregnancy may be a future risk factor for the pathogenesis of metabolic syndrome among the affected pregnant women in Nigeria. Therefore, in this study, we assessed the possibility of future pathogenesis of metabolic syndrome in pregnant women with glycosuria and proteinuria at different trimesters.

Study Design and Population

A case-control cross-sectional research consisting of 86 consenting pregnant women aged 18-49 attending clinic at Primary Health Centers and a Tertiary Hospital in Sagamu, Ogun state, Nigeria was undertaken. The study was conducted between July to November 2021. The participants were split into three groups: group 1 consisted of 32 pregnant women who had glycosuria in the second and third trimesters; group 2 consisted of 27 pregnant women who had proteinuria in the same trimesters; and group 3, which served as the control group, consisted of 27 pregnant women who did not have either proteinuria or glycosuria in the same trimesters. The sample size was determined based on the published prevalence of 5.8% of glycosuria and proteinuria among Nigerian pregnant women.[17]

Inclusion criteria

Volunteers included in this study were apparently healthy non-hypertensive and non-diabetic pregnant women between 18years and 49years with either glycosuria, or proteinuria and pregnant women with neither glycosuria nor proteinuria (control).

Exclusion criteria

Participants excluded from this study were pregnant women aged 18-49 with medical history of diabetes, hypertension, liver disease, kidney disease, dyslipidemia, cardiovascular disease, and haematological disorder such as sickle cell anaemia.

Sample Collection, Preservation, and analysis

About 20ml of urine was aseptically collected from the participants into labeled sterile screw-top universal bottles for urinalysis while 10ml of venous blood samples were obtained using vacutainer needles into plain tube, lithium heparin EDTA tube and fluoride oxalate tube respectively. The samples were processed and stored under appropriate temperature for further analysis. The urine glucose and urine protein were tested with dipstick urinalysis Dus combi 3 strips. Basic anthropometric measurements of height, weight, waist circumference were measured, and BMI determined. The blood pressure of each consenting volunteer was also measured.

Laboratory estimations of fasting blood glucose (FBG), glycated haemoglobin (HbA1c), fasting total cholesterol (T.Chol), Triglycerides (TG), Serum Creatinine, Urea and Insulin concentration were carried out. A mathematical model was employed to assess a possible risk of insulin resistance. [18]

Statistical Evaluation

Data generated from this study were subjected to analysis using IBM SPSS Statistics for Windows version 25.0 (IBM Corp, Armonk, NY, USA). Variables that were normally distributed were expressed as mean \pm standard deviation (M \pm SD). Analysis of variance (ANOVA) was employed to compare the mean differences between the groups studied. Post-hoc analysis was conducted to ascertain the exact point of significant difference observed in the ANOVA. Pearson correlation study was employed to determine the extent of relationships between all the parameters in each group. The future risk of metabolic syndrome was accessed using linear regression analysis. The P value less than 0.05 was set as the level of significant.

Ethical Consideration

Approval for this study was sought and obtained from the research and ethics committee of Olabisi Onabanjo University Teaching Hospital (OOUTH/HREC/428/2021AP) Sagamu Ogun State. Prior to the commencement of this study, informed consent was obtained from each participant who volunteered to be enrolled.

Results

Anthropometric Data and blood pressure values:

Eighty-six (86) participants comprising of 59 pregnant women with either glycosuria or proteinuria and 27 pregnant women with neither glycosuria nor proteinuria (control) participants were involved. Among the 59 tested pregnant women, 32 had glycosuria (urinalysis glucose positive) while 27 had proteinuria (urinalysis protein positive). Table 1 shows the anthropometric data of the volunteers. The mean age of the participants with glycosuria, proteinuria, and control participants were 29.19 (SD 6.04), 27.15 (SD 4.37), and 25.74 (SD 4.67) years respectively. The systolic and diastolic blood pressure, weight, height, and waist circumference between the participants with glycosuria, participants with proteinuria, and control group were not significantly different ($P > 0.05$).

Table 1. Anthropometric Data and blood pressure values

Variable	Glycosuria	Proteinuria	Control	F value	p-value
	Mean (SD)	Mean (SD)	Mean (SD)		
Age (years)	29.19 (6.04)	27.15 (4.37)	25.74 (4.67)	3.363	0.039
Systolic BP (mmHg)	103.59 (10.02)	101.56 (12.92)	98.70 (9.57)	1.481	0.233
Diastolic BP (mmHg)	71.25 (6.09)	68.52 (11.99)	67.78 (8.47)	1.233	0.297
Weight (kg)	63.59 (12.53)	69.89 (13.1)	63.41 (14.71)	2.093	0.130
Height (m)	1.57 (0.07)	1.58 (0.06)	1.56 (0.06)	0.505	0.605
BMI (Kg/m ²)	25.90 (4.92)	28.09 (5.23)	26.17 (6.57)	1.290	0.281
Waist circumference (in)	35.70 (5.61)	36.07 (4.22)	35.00 (4.39)	0.345	0.709

Evaluation of biochemical variables in Pregnant Women with Glycosuria and those with proteinuria

The fasting blood glucose, HBA1c, and total cholesterol in pregnant women with glycosuria and control participants were similar (P > 0.05). However, TG was significantly higher (Table 2) in glycosuria participants compared with control participants (P = 0.01).

Fasting blood glucose, HBA1c, and total cholesterol in pregnant women with proteinuria and control participants were similar (P > 0.05). However, TG was higher in participants with proteinuria (Tables 2, and 3) when compared with pregnant volunteers with neither glycosuria nor proteinuria participants (P < 0.05)

Table 2. Comparative evaluation of biochemical variables in Pregnant Women with Glycosuria and those with proteinuria

Variable	Glycosuria Mean (SD)	Proteinuria Mean (SD)	Control Mean (SD)	F-value	P-value
Fasting blood glucose (mmol/L)	5.63 (1.82)	5.45 (0.64)	5.23 (0.49)	0.783	0.460
Insulin Conc. (µiU/mL)	8.26 (5.46)	6.46 (3.36)	6.30 (2.97)	2.060	0.134
HOMA-IR	2.09 (1.41)	1.59 (0.84)	1.48 (0.7)	2.841	0.064
Total. Cholesterol (mg/dl)	189.44 (35.63)	200.11 (34.3)	188.59 (42.54)	0.808	0.449
Triglyceride (mg/dl)	107.44 (45.15)	120.59 (65.51)	78.22 (40.85)	4.857	0.01
Urea (mg/dl)	21.72 (6.5)	20.33 (6.26)	18.70 (3.27)	2.120	0.127
Creatinine (mg/dl)	0.83 (0.2)	0.96 (0.65)	0.77 (0.15)	1.519	0.225
Glycated Haemoglobin (%)	5.29 (1.35)	5.08 (0.37)	4.92 (0.31)	1.321	0.272

Table 3. Tukey Post Hoc analysis for the significant ANOVA test for Triglyceride

Variable		Mean difference	P-value
Glycosuria	Proteinuria	-13.16	0.590
	Control	29.22	0.080
Proteinuria	Glycosuria	13.16	0.590
	Control	42.37	0.009
Control	Glycosuria	-29.22	0.080
	Proteinuria	-42.37	0.009

Table 4. Linear regression to predict future metabolic syndrome among the participants with glycosuria and proteinuria respectively

Independent variables	R ²	Constant	Beta	P-value	95% CI
Participants with Glycosuria					
Fasting blood glucose (mmol/L)	0.149	0.411	0.298	0.029	0.032-0.564
Fasting Insulin (mIU/mL)	0.862	0.112	0.239	<0.001	0.203-0.275
Total Cholesterol (mg/dL)	0.006	2.646	-0.003	0.685	-0.018-0.01
Triglycerides (mg/dL)	0.318	0.201	0.018	0.001	0.008-0.027
Glycated Haemoglobin (%)	0.269	-0.773	0.541	0.002	0.209-0.873
Participants with Proteinuria					
Fasting blood glucose (mmol/L)	0.000	1.529	0.012	0.965	-0.533-0.557
Fasting Insulin (mIU/mL)	0.908	0.049	0.239	<0.001	0.208-0.270
Total Cholesterol (mg/dL)	0.041	2.591	-0.005	0.309	-0.015-0.005
Triglycerides (mg/dL)	0.015	1.782	-0.002	0.546	-0.007-0.004
Glycated Haemoglobin (%)	0.001	1.290	0.060	0.897	-0.879-0.998

Dependent variable: HOMA-IR.

Among participants with glycosuria linear regression analysis, predicted the risk of future metabolic syndrome with fasting blood glucose, insulin, glycated haemoglobin and

TG values, whereas, among pregnant women with proteinuria fasting insulin value predicted the risk of future metabolic syndrome.

Pearson correlation between the variables measured in participants with glycosuria and those with proteinuria.

A positive association existed between HOMA-IR and TG as presented in Figure 1 ($r = 0.564, P = 0.001$), and Figure 2 showed a strong positive relationship between fasting blood glucose and glycated haemoglobin ($r = 0.830, P < 0.001$) in pregnant women with glycosuria.

A similar relationship (Figure 3) was seen between FBG and HBA1c ($r=0.854, p<0.001$) in pregnant women with proteinuria. However, contrary to what was observed in pregnant women with glycosuria, there was no association between HOMA-IR and Triglyceride in pregnant women with proteinuria (Figure 4).

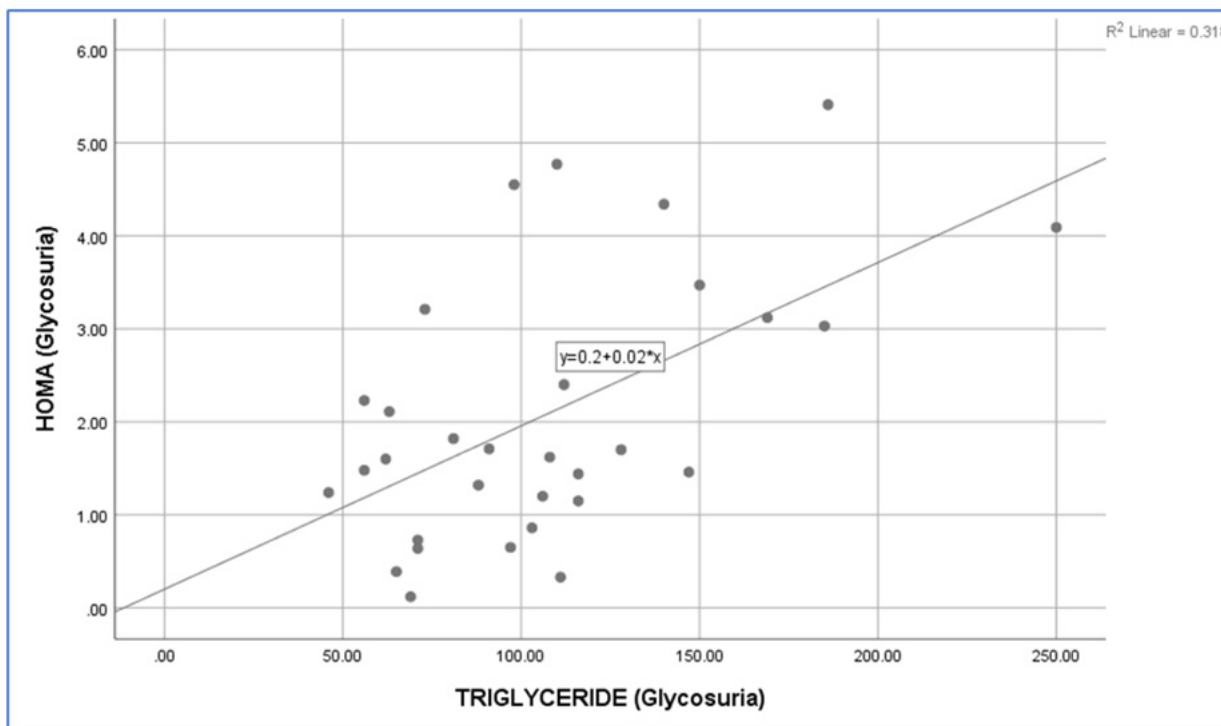


Figure 1. Pearson Correlation between HOMA-IR and Triglycerides in Pregnant Women with Glycosuria

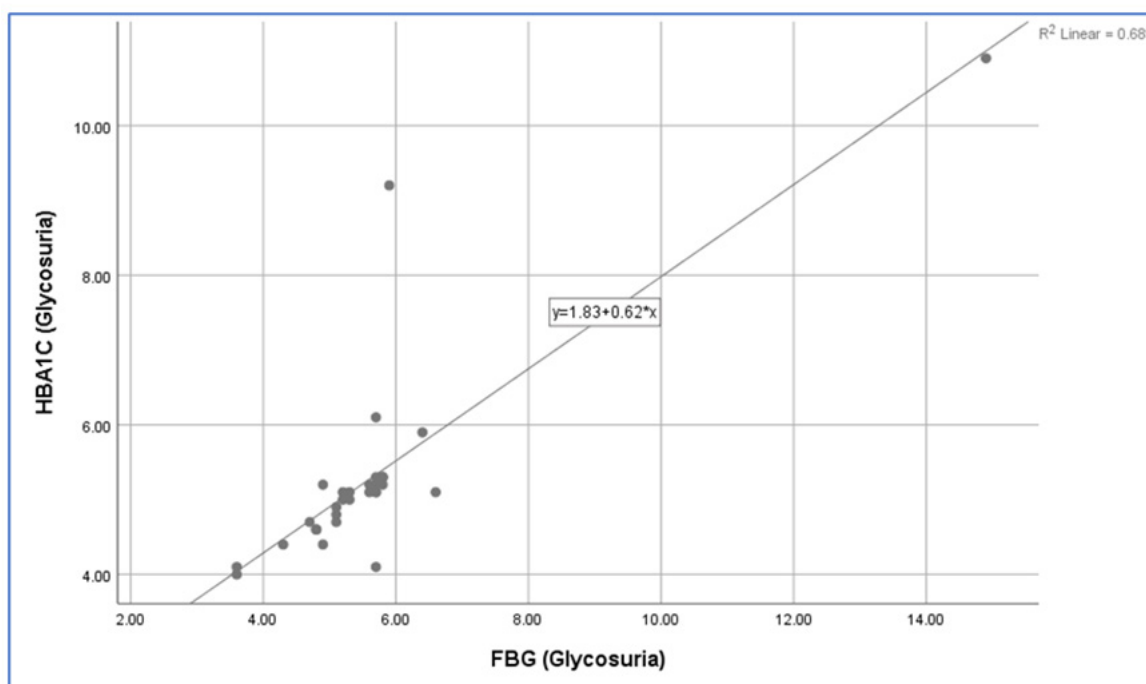


Figure 2. Pearson Correlation between FBG and HBA1C in Pregnant Women with Glycosuria

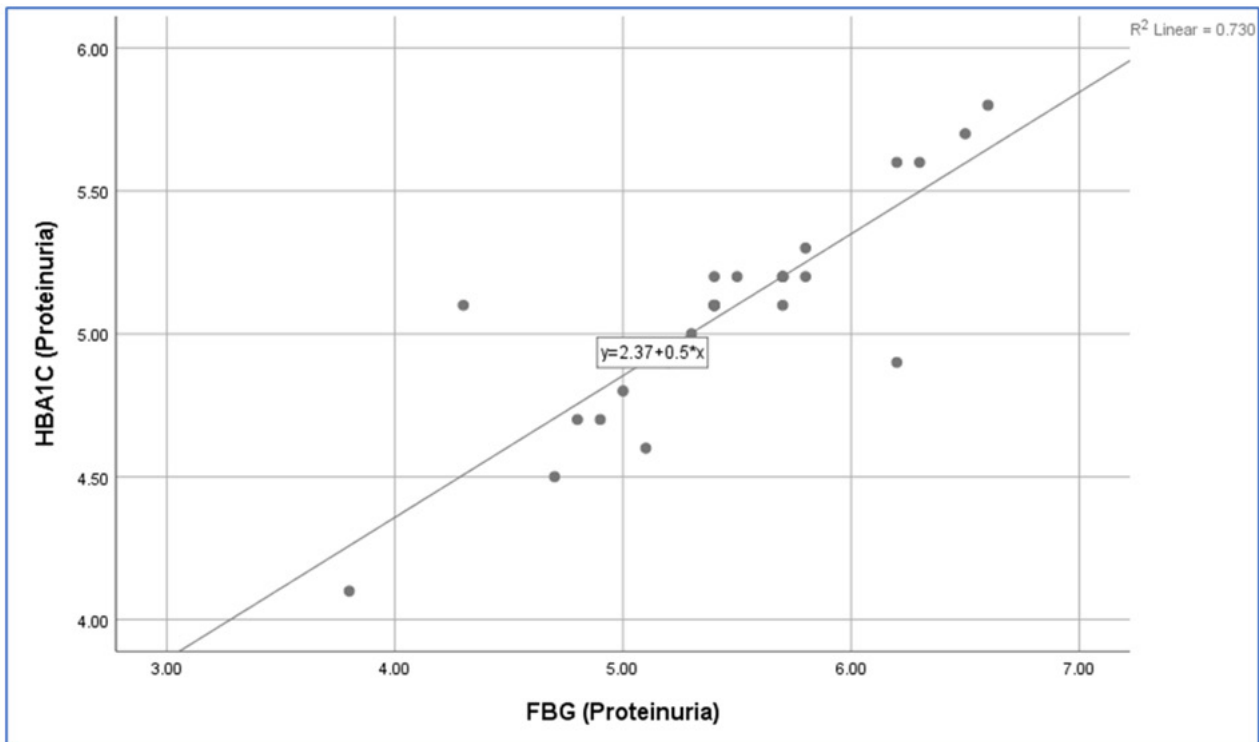


Figure 3. Pearson Correlation between FBG and HBA1C in Pregnant Women with Proteinuria

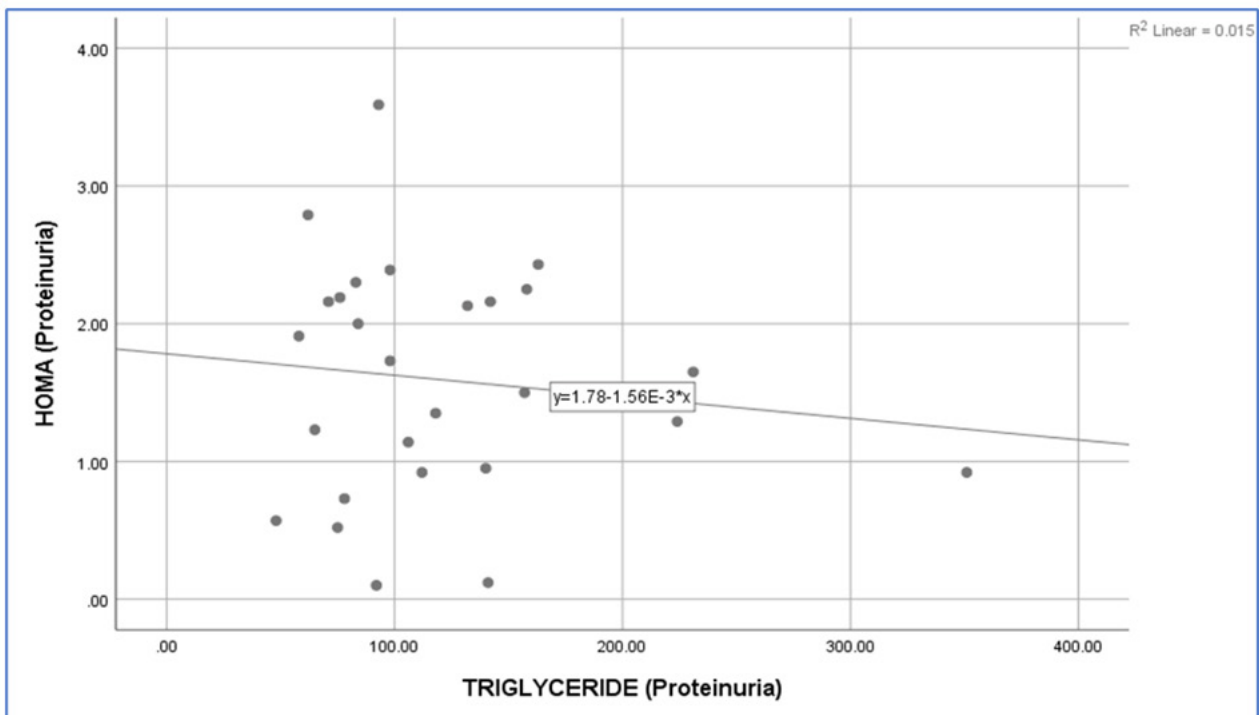


Figure 4. Pearson Correlation between HOMA-IR and Triglycerides in Pregnant Women with Proteinuria

Discussion

In this study we assessed the likelihood of developing diabetes mellitus, and by extension metabolic syndrome among non-diabetic pregnant Nigerian women with glycosuria, and those with proteinuria at second and third trimesters gestational ages. Based on anthropometric data obtained from the consented volunteers, it was observed that the mean ages of pregnant women who presented with glycosuria and those who presented with proteinuria were more advanced than those who had neither glycosuria nor proteinuria. This observation aligns with the earlier literatures where it was reported that ageing was a major factor predisposing women within the reproductive age to gestational diabetes.[19-21] Thus, older pregnant women may present with advanced risk of insulin resistance and gestational diabetes leading to glycosuria.[22]

Also, the systolic and the diastolic blood pressure measurements were similar among all the group volunteers studied. However, it has been observed that excess proteinuria in pregnancy may be a sign of preeclampsia.[23] Preeclampsia during pregnancy results in complications. Proteinuria as observed in this study may indicate isolated de-novo proteinuria.[14] Nevertheless, because the pregnant women with proteinuria had gestational age greater than 20 weeks, this suggests a subset of isolated de-novo proteinuria known as gestational proteinuria.[14,24] A possible explanation for this has been attributed to the maternal factors other than those associated with the initiation of preeclampsia.[14] It has been reported that about half of individuals with this type of proteinuria may present with preeclampsia despite the normal blood pressure measurement.[25]

Furthermore, pregnant women with proteinuria had higher levels of triglycerides (TG) compared with the other groups studied. Elevated triglyceride in pregnancy has been reported to cause complications in both the mother and fetus.[26,27]

An elevated triglycerides in pregnancy has been related to greater threat of preeclampsia to the woman and other complications to the fetus.[28] In addition, elevated triglycerides is associated with an increased risk of future type 2 diabetes mellitus.[29] In a recent study, it was concluded that elevated triglyceride in rare cases could trigger acute pancreatitis among pregnant women with a possible devastating outcome.[30]

Moreover, it was observed that pregnant women with glycosuria, presented with highly significant positive association between HOMA-IR and triglyceride. This observation is similar to the finding from a recent study where elevated level of triglyceride was positively related to hyperinsulinemia observed after meal.[31] This was not so in pregnancy with proteinuria. Although, this study found no significant link between HOMA-IR and total cholesterol in both pregnancy with glycosuria and proteinuria, however, it did observe a relationship between fasting blood glucose and HBA1c in pregnant women with glycosuria. A compelling positive connection between fasting blood glucose and HOMA-IR was also observed in pregnant women with proteinuria. This finding points to the fact that elevated blood glucose may predispose pregnancy to gestational diabetes mellitus (GDM), force the kidney to over work, thereby leading to kidney damage and may allow protein to leak into the urine. Proteinuria is a well-established biological marker for the diagnosis and monitoring of the course of kidney diseases as well as a predictive risk factor for cardiovascular disease and death.[32]

The risk of future metabolic syndrome among the pregnant women at different stages of trimester was assessed using the regression analysis model. It was noted that fasting plasma insulin concentration predicted the risk of metabolic syndrome among pregnant women with glycosuria and those with proteinuria. Among pregnant women with glycosuria, plasma insulin, fasting blood glucose,

glycated haemoglobin and plasma triglycerides all showed strong prediction of metabolic syndrome. Our findings are in consonance with a recent study.[33] Thus, the linear regression analysis results suggested that insulin, glycated haemoglobin, fasting blood glucose and triglyceride could provide firsthand information regarding the future risk of metabolic syndrome in these categories of individuals.

Conclusion

This study clearly showed that pregnant women with glycosuria and those with proteinuria in the absence of diabetes and hypertension may present with elevated HOMA-IR and triglyceride values. The outcome of this study showed that glycosuria and proteinuria in pregnancy in the absence of diabetes mellitus and high blood pressure could predispose these individuals to a greater risk of developing metabolic disorders in the nearest future. Therefore, early antenatal screening and monitoring of pregnant women from the first semester is advised.

Authors' contribution

OAE: Conceived and design the study, contributed to analysis tool, performed analysis, wrote the manuscript; final review of the draft. FKA: Conceived the study idea, collected the data, contributed to analysis tool, performed analysis, and participated in the writing of the manuscript. NOO: Collected data, contributed analysis tool, performed analysis, and participated in the writing of the manuscript. ENA: Collected data, contributed analysis tool, performed analysis, and participated in the writing of the manuscript.

Conflict of interest statement

All authors declared that they had no conflict of interest with respect to this study.

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