Original Article

Profile of Insulin Resistance of Pregnant Women at Late Third Trimester in Nigeria: A Descriptive Cross-Sectional Report

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Abstract

Background: Exaggerated level of insulin resistance (IR) is associated with poor pregnancy outcomes. Identifying affected women may forestall these outcomes. There are few reports on IR and its predictors among pregnant women in Nigeria. **Aim:** To determine the profile of IR, using the homeostatic model assessment of insulin resistance (HOMA-IR), and its predictors among parturient Nigerian women in third trimester. **Patients and Methods:** A cross-sectional baseline data of healthy pregnant women in third trimester, consecutively recruited into a cohort study that evaluated IR and neonatal outcomes at a tertiary maternity. Sociodemographic and clinical data were obtained. Fasting venous blood was analyzed for glucose and insulin and HOMA-IR was calculated. **Results:** We consecutively recruited 401 healthy pregnant women between 28 and 41 weeks [means ± SD = 37.4 ± 0.8 weeks]; mean age 31.52 ± 4.3 years (range: 20-41 years). Median (IQR) HOMA-IR was 1.15 (0.63, 1.96; range: 0.02–11.73). Binary multivariable logistic regression showed overweight- [aOR (95% CI) = 3.29 (1.18, 9.13)], hyperglycemia- [aOR (95% CI) = 2.98 (1.19, 6.90)], and hypertension as independent predictors of IR [aOR (95% CI) = 2.85 (1.18, 6.90)]. **Conclusion:** Among nondiabetic Nigerian pregnant women in late third trimester, IR was independently associated with overweight, hypertension, and hyperglycemia. Control of adiposity is a potential target for control of IR and consequently its outcomes.

Keywords: *Gestational diabetes, HOMA-IR, maternal hyperinsulinemia, Nigerian*

Introduction

Insulin regulates the homeostasis of blood glucose in the body. Insulin resistance (IR) has been defined as the decrease in the biological action of insulin that mainly presents as high blood levels of glucose.[1-5] Pregnancy is associated with decrease sensitivity to insulin as it advances due to the antagonistic effects of pregnancy hormones, among other factors which increase as pregnancy progresses.[3-5] This pregnancy-associated IR is associated with higher risk of caesarean section, gestational hypertension, and preterm births.[6,7] Moreover, the offspring of mothers with IR are far more likely to develop metabolic syndrome, obesity or type II diabetes.[8-12] Thus, early detection of IR in pregnant women followed by appropriate interventions may limit these adverse effects.

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Homeostatic model assessment of insulin resistance (HOMA-IR) is a simple, cheap, and indirect means of estimating IR.[13] It has the advantage of a single sampling compared with oral glucose tolerance test which requires multiple sampling. Previous researchers have documented conflicting reports on changes in IR (measured with HOMA-IR) in pregnancy; while some authors observed increasing IR as pregnancy advanced others did not.[14,15] Identification of factors

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associated with IR among pregnant women may serve as potential targets for preventive interventions such as dietary and lifestyle modification to forestall negative maternal–neonatal outcomes. In Nigeria, there are few studies on IR among pregnant women. Imoh *et al*.[16] and Imoh & Ocheke[17], respectively identified overweight and family history of DM as predictors of IR in early third-trimester pregnant women in North-Central Nigeria. However, their findings may not extrapolate to other parts of the country because of variations in factors such as dietary practices, activity level, and prevalence of obesity. This study was thus aimed at determining the profile of IR and its predictors in parturient Nigerian women in the third trimester in Lagos, Nigeria.

Methodology

Study design and location

The current report is the cross-sectional descriptive baseline data of pregnant women recruited at third-trimester into a prospective cohort study aimed at determining the association between maternal IR and neonatal outcomes. The study was carried out in the clinics and lying-in wards of a tertiary centre in South-west Nigeria.

Study population and sampling technique

We consecutively recruited pregnant women with singleton pregnancies from the ante-natal clinics. We excluded those with established or suspected pre-pregnancy or chronic diabetes, chronic hypertensive disorders, chronic medical illnesses, congenitally abnormal pregnancy and any acute illness or those on hypoglycemic medications. However, we did not exclude those found to have elevated blood pressure at recruitment.

Sample size

The minimum sample size was determined using the standard formula for proportions: $n = z^2/p\,q/d^2$, where n = desired sample size; z = the fraction of the area under the normal distribution curve covered by two standard deviations on either side of normal distribution which is equal to 1.96 in a two-tailed test; P = estimated or known prevalence of the condition—a value of 50% (0.5) was used as the prevalence of IR measured by HOMA-IR, $q = 1 - p$; d = tolerable margin of error (80%). The calculated sample size was 384.16 which was rounded up to 400.

Ethical considerations

Ethical approval (LREC/06/10/1323) was sought and obtained before commencement. Written informed consent was also obtained from the pregnant women prior to enrolment.

Data collection

Trained research assistants used a structured data collection form to obtain the following data from eligible women and their medical records: maternal and paternal sociodemographic characteristics (age, sex, occupation, education), anthropometric (weight, height), and clinical data (family history of diabetes). Maternal body mass index (BMI) was computed as weight (kg)/Height (m^2).

Specimen collection and preparation

Participants were bled in the morning following an 8 to 10 hours overnight fast. With the participant sitting in a comfortable position, antiseptic preparation of the antecubital region was done using methylated spirit swabs and a tourniquet applied proximal to the antecubital vein. With gloved hands, about 5 mm of venous blood was collected into vacutainer tubes using a multiple sampling needle. Three mm of venous blood was collected into plain vacutainer tubes, while 2 mm of venous blood was collected into fluoride oxalate vacutainer tubes. The samples in the plain tubes were allowed to stand for 30 min and subsequently centrifuged at 3,000 rpm for 5 min and the supernatant (serum) separated and stored at –80°C till the time of analysis; similarly, the blood samples in fluoride oxalate bottles were centrifuged at 3,000 rpm for 5 min and the supernatant (plasma) separated and stored at –80°C pending analysis. The multiple sampling needles were discarded into sharps boxes and the infranatant from the separated blood specimen were disposed through the Hospital Environmental Safety Department. Hemolyzed, icteric, and lipemic samples were excluded and repeated thawing and freezing was avoided. Analysis of specimen was carried out in the Chemical Pathology Laboratory, Department of Pathology, Lagos State University College of Medicine, Ikeja Lagos Nigeria. Laboratory analysis was done in batches and within, between and day to day precision was determined using quality control sera.

Serum insulin was analyzed using enzyme-linked immunosorbent assay (ELISA) kit for quantitative determination of insulin levels in Human serum. The principle of the assay is based on antigen antibody reaction. The results were read using a microplate reader.

Serum glucose

Glucose is oxidized by glucose oxidase to gluconic acid and hydrogen peroxide which in conjunction with peroxidase reacts with chloro-4-phenol and 4-amino-antipyrine to form a red quinonimine. The absorbance of the colored complex proportional to the concentration of glucose in the sample was measured at 500 nm.

Insulin resistance estimation

HOMA-IR was calculated as fasting insulin (μU/mL) × fasting plasma glucose (mmol/L)/22.5.

Operational definitions

We defined hyperglycemia in pregnancy as fasting serum glucose >91.0 mg/dL[18]; hyperinsulinemia as fasting serum insulin (FSI) more than 20.0 μU/Ml[19] and IR as HOMA-IR values more than the 75th percentile of the HOMA-IR values of our sample population (HOMA-IR >1.96).[20,21] In the absence of data on the women's pre-pregnancy weight or BMI (to determine true pre-pregnancy adiposity), we used the absolute weight and BMI at recruitment as surrogates; according to Imoh & Ocheke,[17] a third-trimester weight of ≥95 kg is associated with higher IR in Nigerian pregnant women in third trimester. We thus categorized weight into *overweight* (≥95.0 kg) and *normal-weight* (<95.0 kg). This value corresponded to 94th percentile of the weight distribution of our sample. The corresponding 94th percentile BMI was 36.4; hence we defined higher adiposity as ≥36.5 and lower adiposity as <36.5.

Data management and analysis

We extracted data from data collection forms into Microsoft Excel Worksheet 2010 for data cleaning, then imported into R for analysis (using JASP version 0.16, a free open-source graphical user interphase; University of Amsterdam, Netherlands; https://jasp-stats.org/download/). After checking for outliers, implausible values, and distribution (Shapiro–Wilk test), we summarized categorical variables with frequencies and percentages and continuous variables with means ± standard deviation (SD) or medians [interquartile range (IQR)] and percentiles. Outliers were assessed for possible errors while significantly skewed variables were log-transformed and then back-transformed. Mann–Whitney *U* test was used to compare continuous variables (HOMA-IR) between two groups. Two-by-two contingency tables with Fisher's exact test was used to compare IR and categorical variables. Spearman's correlation coefficient rho (ρ) was used to determine linear association between HOMA-IR and continuous variables and scatter-plots with the line of *locally estimated scatterplot smoothing* (LOESS) to visually assess these relationships. Potential predictors with significant bi-variable association with HOMA-IR or IR were entered into multivariable linear or binary logistic regression models, respectively, to determine the independent predictors of IR. Probability (*P*) value of <0.05 was taken as statistically significant and effect sizes estimated with unadjusted and adjusted odds ratios (OR) at 95% confidence intervals (CI).

Results

Overall, we recruited 401 pregnant women between 28 and 41 weeks gestational age [mean ± SD = 37.4 ± 0.8 weeks]. However, only two women were less than 37 weeks.

Socio-demographic, anthropometric and clinical characteristics

The means ± SD (95% CI) age and gestational age (GA) were, respectively, 31.5 ± 4.3 years (95% CI: 31.1, 31.9; range: 20.0–41.0) and 37.40.8 weeks (95% CI: 37.3, 37.4; Range: 28.0–41.0). More than four-fifths (83.8%) of the women had at least tertiary education and about two-thirds of them (63.5%) were of Yoruba ethnicity [Table 1]. Almost half of them were primiparous. The mean weight and BMI were 74.13 ± 12.91 kg and 28.69 ± 4.72 kg/m^2, respectively, suggesting that they were on average a "normal-weight," "low-BMI" population. Family history of DM was present in 10.6% (42/396) and 5.8% (23/396) had elevated blood pressure at recruitment.

Biochemical characteristics: Serum glucose, insulin and HOMA-IR of study participants

The proportion of women with hyperglycemia (fasting serum glucose ≥92 mg/dL), hyperinsulinemia (fasting serum insulin >20.0 μU/Ml) and IR [HOMA-IR value greater than the 75th centile (>1.96)] were 5.29% (95% CI: 3.49, 7.95; *N* = 21/376), 6.06% (95% CI: 3.90, 8.90; *N* = 24/372), and 25.25% (95% CI: 21.23, 29.76; *N* = 100/396;), respectively. Table 2 shows the serum glucose, insulin, and HOMA-IR values

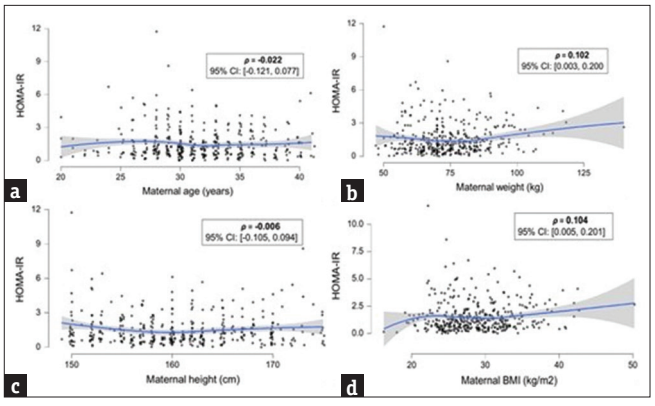

Figure 1: Scatterplots showing linear correlation between HOMA-IR and anthropometric variables. The blue curves show the line of *locally estimated scatterplot smoothing* (LOESS) showing the trend in HOMA-IR with increasing values of the independent variables (age, weight, height and BMI); the grey shaded areas show the confidence bands while the dots are data-points. Whereas HOMA-IR tended to be mostly flat for age and height, it showed a slight increase with weight from about 80 kg and BMI from about 34 kg/m^2 Abbreviations: ρ, Spearman's coefficient rho; CI, confidence interval; HOMA-IR, homeostatic model assessment of insulin resistance (a) HOMA-IR versus age, (b) HOMA-IR versus weight, (c)HOMA-IR versus height, (d) HOMA-IR versus BMI

Table 1: Baseline socio-demographic and clinical characteristics of pregnant Nigerian women at late third trimester

	n (%)	Mean±SD	95% CI of Mean (Upper, Lower)	Range
Anthropometric				
Weight, kg	396	74.13±12.91	72.86, 75.41	47.00, 140.00
Height, cm	395	160.69±6.58	160.04, 161.33	149.00, 175.00
BMI, kg/m^2	395	28.69±4.72	28.23, 29.16	16.20, 50.20
Educational level				
Primary	1 (0.3)			
Secondary	63 (15.9)			
Tertiary	314 (79.3)			
Postgrad	18 (4.5)			
Ethnic Group				
Yoruba	250 (63.5)			
Igbo	125 (31.7)			
Others	19 (4.8)			
Parity				
1	182 (46.3)			
2	124 (31.6)			
3	67 (17.0)			
4	18 (4.6)			
5	2 (0.5)			
Weight category*				
Overweight	27 (6.82)			
Normal-weight	369 (93.18)			
BMI category†				
High adiposity	24 (9.09)			
Low adiposity	360 (90.91)			

n, frequency; CI, confidence interval; GA, gestational age at enrolment; BMI, body-mass index in kg/m^2. * overweight was defined as weight at recruitment ≥95.0kg and normal-weight as<95.0kg. †high adiposity was defined as BMI ≥36.5 kg/m^2 and low adiposity as BMI <36.5 kg/m^2

Table 2: Descriptive data of biochemical characteristics of all study participants (*n*=401) and subset of normoglycemic, normotensive, normal weight participants

Variable	*n*	Mean±SD	Range	Percentile values				
				5th*P*	25th*P*	50th*P*	75th*P*	95th*P*
All participants								
FSG	397	78.22±7.96	56.00, 124.00	67	73	78	83	92
FSI	396	7.88±7.01	0.100, 59.40	1.1	3.3	6.1	10	21.5
Log insulin*	396	0.743±0.40	-1.027,1.774	0.038	0.521	0.787	1.001	1.333
HOMA-IR	396	1.54±1.38	0.020, 11.73	0.19	0.63	1.15	1.962	4.103
Log HOMA-IR*	396	0.026±0.41	-1.820,1.069	-0.716	-0.201	0.0612	0.293	0.613
Normoglycemic, normotensive, normal-weight participants (*n*=320)								
FSG	320	77.00±6.42	56.0, 91.0	66.95	73	77	81	88
FSI	319	7.34±6.58	0.1, 59.4	1.09	3.1	5.6	9.1	21.5
Log insulin*	319	0.713±0.391	-1.027, 1.774	0.021	0.495	0.752	0.958	1.333
HOMA-IR	319	1.41±1.31	0.02, 11.73	0.189	0.6	1.06	1.73	4.045
Log HOMA-IR*	319	-0.009±0.400	-1.802, 1.069	-0.722	-0.22	0.026	0.239	0.607

FBG, fasting blood glucose in mg/dl; FSI, fasting serum insulin, HOMA-IR, homeostatic model assessment for insulin resistance; log, logarithm to base 10. * the geometric means and percentile values derived from back-transformation of the logarithm of insulin and HOMA-IR yielded values similar to their arithmetic means and percentiles of the untransformed values

of all study participants. The mean ± SD (95% CI) fasting blood glucose level was 78.22 ± 7.96 mg/dL (77.44, 79.01), while the median (IQR) fasting insulin was 6.10 (6.70) Miu/L (95% CI: 7.19, 8.57). The median (IQR) HOMA-IR, the mean, median, and percentile values of FSG, FSI, log FSI, HOMA-IR, and HOMA-IR remained essentially unchanged even after exclusion of women with overweight, hyperglycemia

Table 3: Comparison of HOMA-IR based on categorical factors

	n (%)	Median	IQR	W	*P*
Hyperglycemia*					
Yes	21	1.78	1.9	4929	0.052
No	375	1.12	1.26		
Weight†					
Overweight	27	2.41	1.565	6844.5	< 0.001
Normal-weight	364	1.1	1.192		
BMI‡					
High adiposity	24	1.775	1.798	5312	0.086
Low adiposity	366	1.12	1.232		
Family history of DM					
No	334	1.15	1.373	9420	0.901
Yes	57	1.16	1.01		
§Elevated BP					
No	368	1.115	1.255	3177	0.045
Yes	23	1.56	1.7		
Ethnicity					
Yoruba	247	1.22	1.44	19238.5	0.111
Others	142	1.09	1.14		
Parity					
Primiparous	181	1.19	1.43	20007	0.248
Multiparous	207	1.11	1.20		

n, frequency; IQR, interquartile range; BMI, body-mass index in kg/m^2; DM, diabetes mellitus; BP, blood pressure; W, Mann-Whitney *U* value. *hyperglycemia: FBG >91 mg/dL. †Overweight was defined as weight at recruitment ≥95.0kg and normal weight as <95.0kg. ‡High adiposity was defined as BMI ≥36.5 kg/m^2 and low adiposity as BMI <36.5 kg/m^2. §Elevated BP: systolic BP >139 mmHg or diastolic BP >89 mmHg

and hypertension [Table 2]. Also, the back-transformed values of the mean, SD and percentile values of log insulin and log HOMA-IR yielded values almost exactly as the untransformed values.

Correlates and predictors of HOMA-IR

Table 3 shows that women with overweight and elevated blood pressure had significantly higher HOMA-IR compared, respectively, with their normal weight and normotensive counterparts. In contrast, median HOMA-IR levels were similar between groups based on BMI, hyperglycemia and family history of DM.

As shown in Figure 1, HOMA-IR showed a significantly positive but weak linear correlation with BMI [Spearman's rho (ρ) = 0.104, N = 390, P = 0.040] and weight (ρ = 0.102, N = 391, P = 0.043) but not with age (ρ = –0.022, N = 391, P = 0.664) or GA (ρ = 0.043, N = 390, P = 0.397). However, a multivariable linear regression model showed that neither weight or BMI independently predicted HOMA-IR values [standardize beta (95% CI) = 0.017 (–0.050, 0.075, P = 0.875 and standardize beta (95% CI) = 0.042, P = 0.698, respectively)

Table 4 shows that, with variables dichotomized, each of overweight (≥95 kg), adiposity (≥36.5 kg/m^2), hypertension (SBP ≥140 and/or DBP ≥90 mmHg), and hyperglycemia (≥92 mg/dL) had significant bi-variable association with IR, whereas age, gestational age, parity, and ethnicity had no significant association. In a binary multivariable logistic regression model, overweight, hyperglycemia, and hypertension remained as independent predictors of IR.

Discussion

This report describes the cross-sectional profile of IR, measured with HOMA-IR, in pregnant women in late third trimester and the maternal factors associated with it. Their mean fasting serum glucose level and median insulin were 78.22 ± 7.96 mg/dL and 6.10 (6.70) Miu/L, respectively, while their median (5th, 75th, 95th percentiles) HOMA-IR was 1.15 (0.19, 1.96, 4.10). The prevalence of hyperglycemia (fasting serum glucose ≥91 mg/dl), and hyperinsulinemia (fasting serum insulin >20.0 μU/Ml), were 5.3%, and 6.1%, respectively. IR was independently associated with overweight, hyperglycemia, and hypertension—each associated with about 3-fold increased odds of IR; however, the triad jointly explained only 7% of the variance in the IR.

Insulin resistance in pregnancy has been linked to complications like gestational diabetes mellitus, preeclampsia, neonatal macrosomia, preterm births, and increased risk of abdominal delivery.[18,22] It has also been associated with the risk of developing type II diabetes, obesity, and metabolic and cardiovascular disease later in life.[17]

HOMA-IR ranges in pregnancy

The HOMA-IR in our sample population ranged widely from 0.02 to 11.73, with median (IQR) of 1.15 (0.63, 1.96). Imoh *et al*.[16] reported a similar mean HOMA-IR of 1.3 among mid-trimester pregnant women in Jos (north-central Nigeria), with 23% having IR. The HOMA-IR range observed in our study is also comparable with that documented by Mahjabeen *et al*.,[23] Sonogra *et al*.,[3] and Reyes-Munoz *et al*.[24] among women in their third trimester and 0.57–3.97 among Iranian pregnant women as documented by Jahromi and co-workers.[25] However, a community-based study of nonpregnant Nigerian women in Enugu (Eastern Nigeria) by Young *et al*.[15] reported a slightly higher median (IQR) HOMA of 1.45 (0.82–4.06) with about 45% of the women having IR; the higher IR prevalence may be due to the fact that the women were recruited during a free-health screening at a faith-based conference resulting in a clustering effect with higher risk women accessing such opportunity than healthier persons.

Table 4: Categorical bivariate and multivariable determinants of HOMA-IR*

Factors	Insulin resistance		Total	*P*†	OR	Aor
	Higher HOMA-IR *n* (%)	Lower HOMA-IR *n* (%)				
Age						
<=30 years	46 (26.12)	130 (73.86)	176 (100.00)	0.725	1.11 (0.70, 1.76)	Na
>30 years	52 (24.19)	163 (75.81)	215 (100.00)			
Total	98 (25.06)	293 (74.94)	391 (100.00)			
GA						
<38 weeks	67 (24.27)	209 (75.72)	276 (100.00)	0.7	0.90 (0.55, 1.48)	Na
>=38 weeks	30 (26.32)	84 (73.68)	114 (100.00)			
Total	97 (24.87)	293 (75.13)	390 (100.00)			
Parity						
Primiparous	50 (27.62)	131 (72.38)	181 (100.00)	0.291	1.30 (0.82, 2.06)	Na
Multiparous	47 (22.70)	160 (77.29)	207 (100.00)			
Total	97 (25.00)	291 (75.00)	388 (100.00)			
Weight						
Overweight	16 (59.26)	11 (40.74)	27 (100.00)	< 0.001	5.00 (2.23, 11.20)	3.29 (1.18, 9.13)
Normal	82 (22.53)	282 (77.47)	364 (100.00)			
Total	98 (25.06)	293 (74.94)	391 (100.00)			
BMI						
High adiposity	12 (50.00)	12 (50.00)	24 (100.00)	0.006	3.31 (1.43, 7.63)	1.52 (0.51, 4.50)
Low adiposity	85 (23.22)	281 (76.78)	366 (100.00)			
Total	97 (23.87)	293 (75.23)	390 (100.00)			
BP						
High	11 (47.83)	12 (52.17)	23 (100.00)		2.96 (1.26, 6.95)	2.85 (1.18, 6.90)
Normal	87 (23.64)	281 (76.36)	368 (100.00)			
Total	98 (25.06)	293 (74.94)	391 (100.00)			
Family hx of DM						
No	86 (25.75)	248 (74.25)	334 (100.00)		1.30 (0.66, 2.57)	Na
Yes	12 (21.05)	45 (78.95)	57 (100.00)			
Total	98 (25.06)	293 (74.94)	391 (100.00)			
Ethnicity						
Yoruba	70 (28.34)	177 (71.66)	247		1.61 (0.98, 2.65)	NA
Others	28 (19.72)	114 (80.28)	142			
Total	98 (25.19)	291 (74.81)	389			
Hyperglycemia						
High	10 (47.62)	11 (52.38)	21 (100.00)	0.021	2.88 (1.18, 7.00)	2.98 (1.19, 6.90)
Normal	90 (24.00)	285 (76.00)	375 (100.00)			

OR, crude odds ratio from a 2 x 2 contingency tables; aOR, adjusted odds ratios from a binary logistic multivariable regression model conducted with HOMA-IR as dependent variables and weight, BMI, hypertension and hyperglycemia as independent variables; na, not applicable- not included in logistic regression because of bivariate non-significance. *R^2 for the multivariable logistic regression model explained 6.9 of the variance in the outcome variable; R^2 for overweight increased to 4.7 (95% CI: 2.1, 10.6) when BMI was deleted. There was no significant multi-collinearity among the variables (highest variable inflation factor was 1.5). †*P* value from Fisher's exact test

Risk factors for IR

Interestingly, the mean, median, and percentiles of fasting blood glucose (FBG), fasting serum insulin (FSI), and HOMA-IR for our cohort remained essentially same after we excluded those with hyperglycemia, elevated BP, and overweight. This was further corroborated by our observation that variables like weight and BMI had weak, largely nonlinear influence on our sample's HOMA-IR levels. Our observation of overweight as an independent risk factor for IR agrees with similar finding by Imoh *et al*.[26] in north-central Nigeria. Although overweight, hypertension and hyperglycemia were independently associated with the presence of IR in a multivariable logistic regression, their overall contribution to IR was as they jointly explained only about 7% of its variance. Thus, we hypothesize that other factors, especially the pregnancy state itself known to be a state of IR, may account for the remaining variance.

HOMA-IR and GDM

The women in our cohort who had hyperglycemia may be regarded as having GDM because they satisfied one of its diagnostic criteria-fasting serum glucose between 92 and 125 mg/dL (World Health Organisation, 2013).[16] According to Olumodeji *et al*.,[27] this single criterion is almost 100% sensitive to detect pregnant Nigerian women with GDM. Hence, we may consider that the prevalence of GDM in our cohort was 5.3%, which is similar to 7.7% reported by Olumodeji and colleagues among Nigerian pregnant women accessing ANC at 24–32 weeks in south-west Nigeria.[27] In our study, the median HOMA-IR was similar between the subsets of participants with hyperglycemia and normoglycemia, in contrast to finding by Mohammed *et al*.[28] who noted that pregnant women with GDM had significantly higher HOMA-IR than those without GDM in northern Nigeria, and Wang *et al*.[10] who reported similar observation among Chinese mothers. Our observation of nondifference between the HOMA-IR of the GDM and normoglycemic groups may be because we used only FSG to identify those with hyperglycemia, possibly missing others who could have been identified with the other criterion for the diagnosis of GDM:(World Health Organisation, 2013)[18] 2-h postprandial glucose. In contrast to the finding by Imoh *et al*.,[16] a family history of DM was not independently associated with IR in our study.

HOMA-IR and adiposity

In a strikingly similar agreement with an earlier study by Imoh and Ocheke[17] in north-central Nigeria, we found overweight, based on absolute weight of pregnant women (≥95 kg) rather than their BMI, to be associated with a three-fold increased odds of IR. Our finding also suggests that, in pregnant women, weight is a better determinant of IR than BMI. It may be interesting thus to determine if weight is a better measure of adiposity than BMI. Of the triad of factors associated with IR in our cohort, while overweight may be regarded as a predisposing or potentiating factor for IR, hypertension and hyperglycemia may be regarded as complications or outcomes of the physio-pathological processes underlying IR.[30,31] Thus, the prevention or amelioration of pre-pregnancy overweight or excessive weight gain during pregnancy is a potential target for the prevention of IR and its maternal consequences (including hyperglycemia and hypertension) and subsequent peri-neonatal complications.[31] Higher maternal physical activity, especially pre-pregnancy, is associated with lower risk of pregnancy-associated IR.[22]

HOMA-IR and gestational age

We had expected that HOMA-IR would correlate positively with GA because hyperinsulinemia and HOMA-IR generally tend to increase with increasing gestational age. However, HOMA-IR was not associated with GA in our cohort, perhaps because we studied a relatively narrow range of GA. Nonetheless, while some authors reported increasing IR with increasing GA, others did not. For example, while Sonagra *et al*.[3] reported that pregnant women at second and third trimester had serum insulin levels that were 29% and 61% higher than levels of age-matched nonpregnant counterparts, Jahromi *et al*.[25] found no association or correlation between IR and gestational age in Iranian third-trimester pregnant women, presumably due to small sample size or ethnic variations in other risk factors. Similarly, Sonagra *et al*.[3] in their study did not observe any relationship between age and incidence of IR in all the trimesters.

Limitations

Unlike previous studies on HOMA-IR in pregnancy, we did not compare the clinical and biochemical characteristics of our cohort, including their HOMA-IR, with nonpregnant healthy controls thus limiting a better evaluation of the effect of pregnancy on IR. However, we explored the possible association between HOMA-IR and GDM and hypertension, despite the small proportion of these subsets. The absence of pre-pregnancy weight limits our ability to delineate if the association between overweight and IR was as a result of excess pre-pregnancy weight or excess intra-pregnancy weight gain or both; nonetheless, we confirmed a previous observation that absolute weight, even in late trimester, is a useful alternative measure of adiposity in the absence of pre-pregnancy weight.

Suggestions for further studies

There is need for larger population studies, preferably multi-centric, comparing the clinical and biochemical characteristics and HOMA-IR in healthy pregnant and nonpregnant women, as well as prospectively investigate effect of maternal IR on perinatal, neonatal and long-term maternal outcomes.

Conclusion

In this cross-sectional report of predictors of IR among nondiabetic Nigerian pregnant women in late third trimester, IR was independently associated with overweight, elevated blood pressure, and hyperglycemia. Thus, control of adiposity may be a potential target for the control of IR and, consequently, its potential outcomes.

Authorship criteria/contribution

I hereby declare that Joy Chionuma and Ibironke Akinola play a major role in the concept and design

of the study. We were all involved in literature search and conduct of the study. Samples were analyzed by Dr Dada. Dr Chionuma and Dr Ubuane played a larger role in data analysis and interpretation. They also supervised the manuscript writing. Editing and review of manuscript was by all authors supervised by Dr. Chionuma. We all agreed on the final version of the manuscript for submission.

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Conflicts of interest

There are no conflicts of interest.

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