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(RESEARCH ARTICLE)

Evaluation of some biochemical changes and associated metabolic syndrome among pregnant women in Enugu Southeast of Nigeria

Ifeoma Chinwe Ikegwuonu [1, *], Lynda Chinyere Eze [1], Blessing Chidimma Okpagu [1], Nkiruka Peace Ojiako[1], Ifesinachi Joel Agbo [1], Maduka Luke Nweke [2] and Adanna Perpetua Ikebudu [3]

[1] Department of Medical Laboratory Sciences, Faculty of Health Sciences and Technology, College of Medicine, University of Nigeria Enugu Campus. Enugu State, Nigeria.
[2] Department of Physiology, Faculty of Basic Medical Sciences, College of Medicine, University of Nigeria Enugu Campus. Enugu State, Nigeria.
[3] Department of Pharmaceutical Chemistry and Medicinal Chemistry, Faculty of Pharmaceutical Sciences, Nnamdi Azikiwe University Awka. Anambra State, Nigeria.

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Abstract

Objective: Metabolic syndrome is a global health problem which involves a cluster of conditions that increases the risk of heart disease, stroke and diabetes. Pregnancy induces significant physiological, hormonal and metabolic changes in a woman. The complex of metabolic and hormonal disorders is a risk factor for clinical manifestations of cardiovascular diseases, nephropathy and retinopathy. This study assessed some biochemical changes and associated metabolic syndrome among pregnant women in Enugu, Nigeria.

Methods: A total of one hundred and thirty apparently healthy women consisting of seventy pregnant women as test group and sixty non-pregnant women as control group were recruited for this cross sectional study. Anthropometric parameters waist circumference (WC), height, weight, systolic blood pressure (SBP), diastolic blood pressure (DBP) were measured and body mass index (BMI) calculated. Five milliliters of fasting blood samples were collected and used for the determination of fasting plasma glucose (FPG) and lipid profile (TC, TG, HDL-C, LDL-C, VLDL-C) using enzymatic colorimetric methods. Metabolic Syndrome (MetS) prevalence was estimated using the National Cholesterol Education Program-Adult Treatment Panel III (NCEP-ATP III) and International Diabetes Federation (IDF) criteria. Data was analysed using the Statistical Package for the Social Sciences (SPSS) version 26.

Results: The results showed a significant (P< 0.05) increase in BMI, WC, SBP, DBP, TG, VLDL-C and a decrease in HDL-C of pregnant women compared to non-pregnant women. Using the NCEP-ATP III criteria, it was found that about twenty-eight (40%) pregnant women had metabolic syndrome and only two (3.33%) non-pregnant woman had metabolic syndrome while the IDF criteria, presented about thirty (42.9%) pregnant women and ten (16.7%) non-pregnant women with metabolic syndrome.

Conclusion: This study concludes that pregnancy predisposes women to higher risk of developing metabolic syndrome.

Keywords: Pregnancy; Metabolic syndrome; NCEP-ATP III; IDF criteria; Enugu

1. Introduction

Metabolic syndrome is one of the most prevalent heath challenges affecting humans in recent times. It is defined by the accumulation of interrelated physiological, biochemical, clinical, metabolic factors that directly increase the risk of cardiovascular disease, type 2 diabetes mellitus and dyslipidemia which all-cause mortality [1]. It is the co-occurrence

* Corresponding author: Ifeoma Chinwe Ikegwuonu

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of obesity, insulin resistance, atherogenic dyslipidemia and hypertension [2]. Definitions for Metabolic syndrome have been opined by several health institutes, of particular interest are those opined by WHO, whose definition was the first to tie together the key components of insulin resistance, obesity, dyslipidemia and hypertension, with insulin resistance a requirement of the definition; in the absence of it, an individual would not be considered to have metabolic syndrome, even if all other requirements were satisfied [3]. In 2001, the National Cholesterol Education Program – Adult Treatment panel (NCEP-ATP III) defined the metabolic syndrome as having at least three of the following abnormalities:

- Waist circumference >102cm in men and >88cm in women.
- Serum triglyceride ≥150mg/dl.
- High density lipoprotein <40mg/dl in men and <50mg/dl in women.
- Blood pressure ≥130/85mmHg.
- Serum glucose ≥110mg/dl. [4].

Then in 2005 the International Diabetes Federation (IDF) modified the WHO and ATP III definitions, stressing on visceral obesity as the core feature of the syndrome. IDF defined visceral obesity for different ethnic populations based on the waist circumference measurements obtained from epidemiologic data of various ethnic populations [5]. However, in 2009, a harmonized definition for metabolic syndrome was adopted in an effort to reconcile the disparities in definitions of metabolic syndrome. The "harmonized metabolic syndrome" proposal had the five main components [6]. It was decided that three aberrant findings out of the five components would qualify a person for the metabolic syndrome, and none will be considered obligatory.

Pregnancy is the process and series of changes that take place in a woman's organs and tissues as a result of a developing fetus. The entire process from fertilization to birth takes an average of 266–270 days, or about nine months. This condition can be indicated by positive results on an over-the-counter urine test, and confirmed through a blood test, ultrasound, detection of fetal heartbeat, or an X-ray [7]. Physiological pregnancy is a stress for β-cells of the pancreas and is characterized by oxidative stress which is one of the central mechanisms of adaptation to new conditions of vital activity of the body [8]. In the chain of metabolic and functional-morphological disorders in metabolic syndrome, the first link is hyperglycemia which has a direct glucose-toxic effect on tissues and organs also induces autoimmune reactions, the subsequent reduction in the utilization of glucose causes deficiency of energy substrates in cells. The complex of metabolic and hormonal disorders is a risk factor for clinical manifestations of pathology of internal organs, including cardiovascular diseases as well as nephropathy, retinopathy etc [9].

Diabetes is the most common metabolic disorder to affect pregnancy and is associated with increased maternal and neonatal morbidity [8]. Three types of diabetes affect pregnancy: gestational diabetes mellitus (GDM), type 2 diabetes mellitus (T2DM), and type 1 diabetes mellitus (T1DM). Type 1 and type 2 are referred to as pre-gestational diabetes because the onset predates the current pregnancy [10]. Depending on the timing of onset, inappropriate glucose homeostasis has been associated with congenital malformations, miscarriage, perinatal mortality, preeclampsia, preterm birth, increased birthweight, neonatal hypoglycemia, and respiratory distress [10]. In addition, increased insulin resistance has been associated with recurrent miscarriage even in women with no known history of diabetes. Fetal exposure to maternal hyperglycemia can lead to hyperinsulinemia, resulting in short- and long-term complications, including childhood obesity and insulin resistance [11].

In pregnant women, metabolic syndrome is a multifactorial condition and one of the major causes of maternal and neonatal morbidity and mortality worldwide. The condition is pro-inflammatory and can be a causative factor for vascular damage [12].

Obesity increases the risk for developing gestational diabetes mellitus and preeclampsia, which both associate with increased risk for type 2 diabetes mellitus and cardiovascular disease [13].

Pregnant women with metabolic syndrome have higher risk for preterm birth. Among the components of metabolic syndrome, the most significant risk factor is hypertension. An elevation of 10mmHg in diastolic blood pressure increases the relative risk of preterm by 29% [14]. The pathophysiology of metabolic syndrome is largely traceable to insulin resistance with uncontrolled flux of fatty acids implicated. Pro-inflammatory states also contribute to the syndrome. The increased risk for type 2 diabetes and cardiovascular diseases demands therapeutic attention for those at high risk [15]. Maternal dyslipidemia is linked to adverse perinatal outcomes. Hypercholesterolemia and elevated triglycerides in early pregnancy have been associated with an increased risk for spontaneous preterm delivery [16]. Variations in maternal lipid metabolism have an impact on fetal growth and a study by Schaefer-Graf et al [16] have corroborated this evidence that elevated levels of maternal TG predict macrosomia independently of other maternal factors, such as BMI and glucose levels. A study suggested that high levels of maternal HDL-C are significantly associated with a

decreased risk for macrosomia, perhaps indicating that HDL might have protective qualities for more than just maternal benefits [17]. In the context of this investigation, we assessed MetS based on the definition proposed by NCEP ATP 111[4] and IDF [5].

Indeed, despite the existence of quite a substantial volume of information on MetS prevalence globally, there is still a paucity of data on its association with pregnant women particularly in Enugu, Nigeria. Therefore this study aimed at filling these knowledge gaps.

2. Materials and methods

2.1. Study Design/Selection

This cross sectional study involved a total number of one hundred and thirty (130) apparently healthy women aged (18-45 years) from Enugu metropolis. The test group comprised of seventy (70) pregnant women while the control group is made up of sixty (60) non-pregnant women, who freely wanted to participate in the study. The subjects that met the inclusion criteria were selected by simple random sampling. Informed consent was obtained from each participant. Questionnaires were distributed and duly filled by the participants before commencement of the study.

2.2. Inclusion and Exclusion Criteria

2.2.1. Inclusion criteria for test group

Apparently healthy pregnant women (ages 18-45 years).

2.2.2. Inclusion criteria for control group

Apparently healthy non-pregnant women (ages 18-45 years)

2.2.3. Exclusion Criteria for both test and control groups

Subjects on drugs/medications, smokers, alcoholics and HIV positive subjects.

2.3. Ethical Considerations and Informed Consents

Ethical approval was duly obtained from the ethical committee of the University Of Nigeria Teaching Hospital, Ituku-Ozalla, Enugu, with the Ref no: UNTH/HREC/2022/06/452. Written consent of willingness to participate in the study as a subject was obtained from all participants included in the study with absolute confidentiality maintained.

2.4. Anthropometric Measurements

2.4.1. Measurements of Body Mass Index (BMI)

The weight, height and BMI of the respondents were recorded. A digital weighing scale ((Beurer GmbH soflinger Straβe 218 89077 Ulm, Germany)) was used to measure the body weight (kg). A stadiometer was used to measure height (m); and the BMI was calculated by dividing the weight (kg) by the square of height (m^2). The waist circumference was measured in cm using a measuring tape.

2.4.2. Measurements of Blood Pressure (BP)

A standardized automatic BP monitor OMRON M2(HEM-7143-E-01-10/2020 5674679-4A , Brazil) was used to take the blood pressure measurements in two readings after the participants have been sat undisturbed for a minimum of five minutes and the average record was used.

2.5. Blood Collection/Handling

A qualified phlebotomist performed the collection of blood samples from the participants, using a sterile needle with a capacity of 5mls and a disposable syringe. 5mls of fasting venous blood was drawn, and 3mls was promptly transferred to a clean, appropriately labelled plain tube. Subsequently, the blood was allowed to clot and retract before undergoing centrifugation at a speed of 5000 rpm for duration of 5 minutes. The resulting serum was carefully separated into another properly labelled plain tube for analysis of lipid profile. The remaining 2 ml of fasting blood was collected in fluoride oxalate bottle for fasting plasma glucose analysis It was gently inverted several times to ensure proper mixing of the sample with the anticoagulant present in the tube. The blood collected into Potassium oxalate/Sodium fluoride

tubes was centrifuged at 1500rpm for 10 minutes to obtain plasma which was transferred into an aliquot vial for fasting plasma glucose estimation.

2.6. Laboratory Analyses

The lipid profile was analyzed using the Enzymatic Colorimetric Method: TG [18], TC [19], HDL-C [20], and LDL-C [21]. VLDL-C was estimated using friedewald formula [22]. Fasting plasma glucose estimation was done using Glucose Oxidase method [23].

2.7. Assessment of Metabolic syndrome (MetS)

National Cholesterol Education Program-Adult Treatment Panel 111 (NCEP-ATP 111) criterion [4] and International Diabetes Federation criterion (IDF) [5] were used to assess the MetS. NCEP-ATP criterion states that the presence of three or more of the following components WC ≥ 88cm, SBP ≥ 130mmHg, DBP ≥ 85mmHg, FPG ≥ 110mg/dl (6.1 mmol/l), fasting TG ≥ 1.7mmol/l, and HDL-C < 1.29 mmol/l in a woman diagnosis MetS. IDF states that MetS is diagnosed with the presence of central obesity (defined as waist circumference with ethnicity specific values WC ≥ 80cm) plus two or more of the following factors: Raised triglycerides ≥ 150mg/dl (1.7mmol/L), Reduced HDL cholesterol < 50mg/dl (1.29mmol/L), Raised blood pressure ≥ 130/85mmHg and FPG ≥ 100mg/dl (5.6mmol/L) in a woman.

2.8. Data Analysis

The data was analyzed using IBM Inc.'s Statistical Package for Social Science (SPSS) version 26. Pearson's correlation was used to determine the relationship between the parameters. To determine the differences between the means of the two groups, the Student's T-test was utilized. All tests were conducted with a two-tailed approach, and a p-value of less than 0.05 was deemed statistically significant.

3. Results

Table 1: **S**hows the Anthropometric parameters of pregnant and non-pregnant women. The result shows a significant increase ($P < 0.05$) in the mean ± standard deviation of systolic blood pressure (109.90 ± 9.99, 103.63 ± 10.72), diastolic blood pressure (92.29 ± 10.83, 70.40 ± 9.37), body mass index (26.51 ± 3.93, 23.08 ± 3.91), waist circumference (88.27 ± 9.21, 75.93 ± 8.65) of pregnant and non-pregnant women respectively.

Table 1 Anthropometric parameters of pregnant and non-pregnant women

Groups	Body mass index (kg/m^2)	Waist circumference (cm)	Systolic blood pressure (mmHg)	Diastolic blood pressure (mmHg)
Pregnant women N=70	26.51 ± 3.93	88.27 ± 9.21	109.90 ± 9.99	92.29 ± 10.83
Non-pregnant women N=60	23.08 ± 3.91	75.93 ± 8.65	103.63 ± 10.72	70.40 ± 9.37
t-statistics	3.441	6.114	2.461	4.207
p-values	0.002*	0.000*	0.020*	0.0001*

Values are given as mean ± SD * = Significant value (P<0.05)

Table 2: shows the levels of biochemical parameters of pregnant and non-pregnant women. This table shows a significant (P<0.05) increase in the mean ±SD of TG (1.62 ± 1.51, 0.76 ± 0.31) and VLDL (0.71 ± 0.29, 0.41 ± 0.15) and a decrease of HDL (1.35 ± 0.35, 1.56 ± 0.28) while a non- significant deference (P>0.05) exist in FPG (101.90 ± 13.41, 101.03 ± 9.81), TC (4.88 ± 0.63,4.67 ± 0.79) and LDL (2.82 ± 0.68, 2.69 ± 0.72) of the pregnant and non-pregnant women respectively.

Table 2 Biochemical parameters of pregnant and non-pregnant women

Groups	Fasting Plasma Glucose (mmol/L)	Total cholesterol TC (mmol/L)	Triglycerides TG (mmol/L)	High density lipoprotein HDL (mmol/L)	Very low density lipoprotein VLDL (mmol/L)	Low density lipoprotein LDL (mmol/L)
Pregnant women N=70	5.66 ± 13.41	4.88 ± 0.63	1.62 ±1.51	1.35 ± 0.35	0.71± 0.29	2.82± 0.68
Non-pregnant women N=60	5.61 ± 9.81	4.67± 0.79	0.76 ± 0.31	1.56 ± 0.28	0.41± 0.15	2.69 ± 0.72
t-statistics	0.283	1.123	3.035	-2.700	4.606	0.652
p-values	0.779	0.271	0.005*	0.011*	0.000*	0.520

Values are given as mean ± SD * = Significant value (P<0.05)

Table 3: shows classification of metabolic syndrome in pregnant women according to NCEP-ATP 111 criterion [4], The result shows that 24 women had FPG ≥ 6.1mmol/l, 26 had TG ≥ 1.7mmol/l, 0 had SBP ≥ 130mmHg, 14 had DBP ≥ 85 mmHg; while 40 women had WC ≥ 88cm, 34 had HDL-C < 1.29mmol/l. Out of the 70 pregnant women, 28 (40%) had presence of three or more components therefore were defined as having metabolic syndrome (MetS).

Table 3 NCEP-ATP III classification of metabolic syndrome in pregnant women

Components	Criteria	Number of women affected	Number of women not affected	Women with MetS	Women without MetS
FPG (mmol/l)	≥ 6.1	24	46	28 (40%)	42 (60%)
Fasting TG (mmol/l)	≥ 1.7	26	44		
SBP (mmHg)	≥ 130	0	70		
DBP (mmHg)	≥ 85	14	56		
WC (cm)	≥ 88	40	30		
HDL-C (mmol/l)	<1.29	34	36		

Table 4: shows classification of metabolic syndrome in non-pregnant women according to NCEP-ATP 111 criterion [4]. The result shows that 14 had FPG ≥ 6.1mmol/l, 0 had TG ≥ 1.7mmol/l, 0 had SBP ≥ 130mmHg, 8 had DBP ≥ 85 mmHg; 6 had WC ≥ 88cm, and 10 had HDL-C < 1.29mmol/l . Out of these 60 women only 2 (3.3%) had the presence of three or more components therefore were labeled as women with metabolic syndrome.

Table 4 NCEP-ATP III classification of metabolic syndrome in non-pregnant women

Components	Criteria	Number of women affected	Number of women not affected	Women with MetS	Women without MetS
FPG (mmol/l)	≥ 6.1	14	46	2 (3.3%)	58 (96.7%)
Fasting TG (mmol/l)	≥ 1.7	0	60		
SBP (mmHg)	≥ 130	0	60		
DBP (mmHg)	≥ 85	8	52		
WC (cm)	≥ 88	6	54		
HDL-C (mmol/l)	<1.29	10	50		

Table 5 IDF classification of metabolic syndrome in pregnant women

From the result gotten, according to the IDF criteria [5] for classification of metabolic syndrome, thirty (42.9%) out of the seventy pregnant women have metabolic syndrome while the remaining forty (57.1%) do not have metabolic syndrome.

Table 5 IDF (2005) classification of metabolic syndrome in pregnant women

Components	Criteria	Number of women affected	Number of women not affected	Women with MetS	Women without -MetS
WC (cm)	≥ 80	62	8	30 (42.9%)	40 (57.1%)
Fasting TG (mmol/L)	≥ 1.7	26	44		
SBP (mmHg)	≥ 130	0	70		
DBP (mmHg)	≥ 85	14	56		
FPG (mmol/L	≥ 5.6	34	36		
HDL-C (mmol/L)	< 1.29	34	36		

Table 6 IDF classification of metabolic syndrome in non-pregnant women

From the result obtained from the analysis, according to the IDF criteria [5]. It was found out that ten (16.7%) women out of the sixty non-pregnant women have metabolic syndrome while the remaining fifty (83.3%) do not have metabolic syndrome.

Table 6 IDF (2005) classification of metabolic syndrome in non-pregnant women

Components	Criteria	Number of women affected	Number of women not affected	Women with MetS	Women without MetS
WC (cm)	≥ 80	24	36	10 (16.7%)	50 (83.3%)
Fasting TG (mmol/L)	≥ 1.7	0	60		
SBP (mmHg)	≥ 130	0	60		
DBP (mmHg)	≥ 85	8	52		
FPG (mmol/L)	≥ 5.6	36	24		
HDL-C (mmol/L)	< 1.29	10	50		

4. Discussion

Metabolic syndrome (MetS), a series of symptoms, including abdominal obesity, impaired glucose tolerance and insulin metabolism, hypertension and dyslipidemia, is considered as the risk of developing cardiovascular diseases and diabetes that can predispose pregnant women to serious health problem [24]. This study assessed the biochemical changes and associated metabolic syndrome in pregnant and non-pregnant women using the NCEP-ATP III and the IDF criteria.

The result in table 1of this study, shows that pregnant women have higher blood pressure (both SBP and DBP), body mass index and waist circumference compared to non-pregnant women. These differences indicate potential health risks associated with pregnancy. The rise in systolic and diastolic blood pressure could be as a result of increase visceral fat (WC) and BMI, where fats accumulate within and around the kidney leading to the alteration of renin-angiotensin system causing increasing salt retention and elevated blood pressure. This finding agrees with previous studies by [14, 25]. The increase WC and BMI in pregnant subjects could be as a result of increase lipid accumulation within and around

the liver and the abdominal skeletal muscle which could result from ingestion of fatty and energy laden processed food as well as sedentary lifestyle. This finding is in line with previous study [26],

The result presented in our table 2 shows a significantly ($P < 0.05$) higher TG, VLDL-C and lower HDL-C values in pregnant women when compared to the non-pregnant women. Normal pregnancy is a pro-inflammatory, pro-thrombotic, highly insulin resistant [27], and hyperlipidemic state [26]. Circulating TG, fatty acids, cholesterol and phospholipids are altered during pregnancy due to metabolic alterations in the liver and adipose tissue [28]. This finding is in line with other previous studies [17, 26, 29] who reported also higher triglycerides and lower HDL-C in pregnant women.

Assessment of MetS and a broader range of pregnancy complications in women is very crucial since metabolic syndrome in pregnant women leads to pregnancy complications such as preeclampsia and gestational diabetes mellitus and later life T2DM and CVD [30].Tables 3 and 4 of this study show the prevalence of MetS in Pregnant and non-pregnant women respectively according to NCEP-ATP 111 criterion. This study reveals that the prevalence of metabolic syndrome was higher in pregnant women (40%) compared to non-pregnant women (3.3%). We observed using NCEP-ATP 111 criterion of MetS that the most prevalent trait for MetS in pregnant women was high WC followed by low HDL-C and high TG. This increase in WC could be as a result of excessive gestational weight gain while low HDL-C and high TG may result from hormonal changes, sedentary lifestyle and dyslipidemia associated with pregnancy. Elevated triglycerides contribute to hardening of the arteries or thickening of the artery walls (arteriosclerosis) which increases the risk of stroke, heart attack and heart disease. Extremely high triglycerides can also cause acute inflammation of the pancreas [31]. Remarkably, it was found that the most prevalent trait for MetS in non-pregnant women was high FPG followed by low HDL-C and high diastolic blood pressure though, these were quite insignificant.

Using the IDF criterion (table 5) for MetS classification among pregnant women, WC which is a pre-requisite risk factor was the highest trait with a prevalence of 88.6% followed by low HDL-C and high fasting plasma glucose with a prevalence of 56.7% respectively. While among the non-pregnant women (table 6), high FPG was the highest with a prevalence of 60% followed by WC and HDL-C with a prevalence of 40% and 16.7% respectively. In over all, the study observed that pregnant women had higher prevalence of MetS 42.9% compared to non-pregnant women 16.7%.

In addition, this study revealed that central obesity (WC) was the most prevalent component in both the NCEP-ATP 111 and IDF criteria for MetS among pregnant and non-pregnant women with MetS, suggesting that increase in central adiposity may predispose woman to MetS. Therefore, there is need to reduce this risk among women both pregnant and non-pregnant by upholding a healthy lifestyle and increasing physical activities.

5. Conclusion

This study observed that there was an increase in body mass index (BMI), waist circumference (WC), blood pressure (SBP and DBP), triglyceride (TG), very low density lipoprotein (VLDL-C) and lower HDL-C levels in pregnant women when compared to non-pregnant women. These biochemical changes were related to metabolic syndrome. In addition, the study demonstrated that there were variations in the metabolic syndrome between the two groups. The study concludes that the prevalence of metabolic syndrome amongst pregnant women in comparison to non-pregnant women was notably high in NCEP-ATP criterion (40%, 3.3%) and IDF criterion (42.9%, 16.7%) respectively and that surprisingly; pregnancy may be associated with an increased risk of metabolic syndrome.

Compliance with ethical standards

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Disclosure of conflict of interest

The authors declare no conflict of interest, financial or otherwise.

Statement of ethical approval

Ethical approval was duly obtained from the ethical committee of the University Of Nigeria Teaching Hospital, Ituku-Ozalla, Enugu (UNTH/HREC/2022/06/452).

Statement of informed consent

Informed consent was obtained from all participants in this study before commencement.

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