

Research Article

Metabolic syndrome and serum ferritin level in postmenopausal women in urban cities in Enugu State, Nigeria

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ABSTRACT

Background: Physiological and biochemical changes that alter the general health of women are seen in menopause which include increase in adiposity and elevated serum ferritin. There is a dearth of information on the prevalence and common risk factors of MS and their association with iron stores of the body among postmenopausal women (POMW) in Enugu. Hence, this study was carried out to determine the prevalence of metabolic syndrome, the most prevalent components of metabolic syndrome and its relationship with serum ferritin level in postmenopausal women in Enugu, Nigeria.

Methods: The study was a cross sectional study, carried out from February to August 2013 among two hundred and twenty four (224) apparently healthy postmenopausal women aged 40 to 83 years. Metabolic syndrome was defined using National Cholesterol Education Programme, Adult Treatment Panel III criteria.

Results: The most frequent components of metabolic syndrome (MS) seen among the subjects were high waist circumference (WC) (70.1%), high blood pressure (66.5%) and low high density lipoprotein cholesterol (25.4%). The prevalence of metabolic syndrome among the women was 29.0% while the mean level of serum ferritin of subjects with metabolic syndrome showed no significant ($p > 0.05$) difference when compared to subjects without MS.

Conclusions: The most frequent cluster of the risk factor of MS in the population studied was high WC, high blood pressure and low high density lipoprotein cholesterol (HDL). Although serum ferritin is slightly associated with FPG and WHR, it may not be used as diagnostic tool for MS in the group studied.

Keywords: Metabolic Syndrome, Ferritin, Postmenopausal women

INTRODUCTION

The health of girls and women is affected by developmental, psychological and physiological age. Women's lives are marked by a continuous transition from intrauterine life, infancy, adolescence, menarche, reproductive life, menopausal transition, postmenopausal to the frail elderly life. Across the life span of a woman, menopause probably has the greatest impact on the health

of women.¹ Menopause is the phase of aging during which women passes from reproductive to non-reproductive stage.² Oestrogen deficiency is a major occurrence in postmenopausal women and is associated with symptoms and diseases that are of increasing importance to women's health. Physiological and biochemical changes that alter the general health of women are seen in menopause which includes an increase in adiposity, which is a risk factor for developing insulin

resistance, dyslipidaemia, breast cancer, hypertension and cardiovascular diseases.³⁻⁵ Also, due to cessation of menstruation, the iron store of the body increases, resulting in elevated serum ferritin which is the major iron storage compound in the body.⁶ Elevated serum ferritin has been associated with hypertension, hyperinsulinaemia, hyperglycaemia and central adiposity which are components of metabolic syndrome (MS).⁷⁻¹⁰ Metabolic syndrome can be defined as a cluster of metabolic abnormalities that occur together in an individual more often than is expected by chance and directly increase the risk of cardiovascular diseases, type 2 diabetes and other causes of morbidity and mortality. The abnormalities include: insulin resistance, obesity, hypertension, dyslipidaemia, glucose intolerance, prothrombotic and proinflammatory state.¹¹ Metabolic syndrome is a cardiovascular risk factor of public health significance but there is a dearth of information on the most frequent of these risk factors of MS and their relationship with body iron stores measured as serum ferritin among the postmenopausal women in urban areas of Enugu state, Nigeria. Therefore, with the increase in the rate of morbidity and mortality among postmenopausal women in this locality, it is imperative to study the relationship between serum ferritin and metabolic syndrome in this group.

METHODS

Study population

The study was a cross sectional study, conducted in two urban centres (Enugu and Nsukka) in Enugu State, South East, Nigeria, from February to August, 2013. Two hundred and twenty-four (224) apparently healthy postmenopausal women aged 40 to 83 years who gave written informed consent, were recruited for the study. Awareness was created through different women groups and institutions while the research was carried out in Chemical Pathology Department College of Medicine University of Nigeria, Enugu Campus.

Exclusion criteria

Subjects on lipid lowering drugs, iron replacement therapy and those who received or donated blood within the past four months prior to the study were excluded.

Inclusion criteria

Apparently healthy Postmenopausal women, who reported absence of menstruation for one year or more, living in Enugu urban who gave written informed consent were included in the study.

Ethical consideration

Ethical approval was sought and obtained from the Ethics Committee of Enugu State Ministry of Health. Written informed consent was obtained from the respondents who

met the inclusion criteria prior to the study. The right and welfare of the participant were observed as stated in the Helsinki declaration.¹²

Demographic data collection

Questionnaire and oral interview were used to interview the women in order to elicit information on age, ethnicity, educational background, and menopausal status, history of blood donation or reception and medications.

Anthropometric measurements

The body weight, height, waist and hip circumferences were measured to the nearest 1 kg, 0.1 m, 0.1 cm, 0.1 cm respectively using standard protocols. The BMI was calculated as the ratio of body weight in kg to height in meter squared (kg/m^2). The blood pressure was measured and the reading taken in nearest one millimetre of mercury (1 mmHg) using sphygmomanometer.

Blood sample collection and analysis

Five millilitres of venous blood sample was collected from each subject after an overnight fast of 8-12 hours using a standard method. Two millilitres of the sample were placed in a fluoride oxalate bottle for the estimation of fasting plasma glucose while 8 ml was placed in a clean dry plain tube, and the serum separated after clotting. The serum was used to assay the levels of ferritin, triacylglycerol and high density lipoprotein cholesterol. Fasting plasma glucose concentration was determined using the glucose oxidase method.¹³ Serum triacylglycerol (TG) concentration was measured by enzymatic method while the concentration of high density lipoprotein cholesterol (HDLCC) was measured using phosphotungstic acid precipitation and cholesterol oxidase method.^{14,15} Serum ferritin concentration was measured using solid phase enzyme linked immunosorbent assay (ELISA) based on sandwich principle.¹⁶ Commercially prepared kits by Teco USA were used to assay for glucose, triacylglycerol and high density lipoprotein cholesterol while ferritin was assayed using a commercially prepared kit by DRG, Germany.

Diagnosis of metabolic syndrome

An individual was identified as having metabolic syndrome if she presented with any three or more of these risk factors blood pressure (BP) $\geq 130/85$ mmHg, waist circumference (WC) >88 cm, high density lipoprotein cholesterol (HDLCC) <1.3 mmol/l, triacylglycerol (TG) ≥ 1.7 mmol/l and fasting plasma glucose (FPG) ≥ 5.6 mmol/l. This is the revised National cholesterol education programme adult treatment panel III criteria¹¹.

Statistical analysis

Statistical package for social sciences (SPSS) version 16 and graph pad prism software were used to analyze the

data obtained. The results were presented as mean±standard deviation for continuous variables while absolute numbers and percentages were used to present the categorical variables. Student’s t-test, Spearman correlation and ANOVA were used to compare the data and inferences made at 95% confidence limit (p <0.05).

RESULTS

Out of 224 subjects, 65 of them had three or more of the risk factors of MS giving a prevalence of 29%. According to the result in Table 1, the most frequent risk factor was central obesity measured as high WC (70.1%). It was followed by HBP and low HDLC while the least were high TAG and high FPG. The same pattern of cluster of the risk factors were seen when the subjects were grouped into the postmenopausal women with metabolic syndrome (POMW+MS) and those without (POMW-MS). Other measures of obesity, WHR and BMI recorded a lower frequency than WC, but were relatively high among subjects with MS. Therefore, the most predominant cluster of the risk factors of MS in the population studied was high WC, HBP and low HDLC.

Table 1: Frequency of the risk factors of metabolic syndrome in the groups studied.

Variables n (%)	POMW (n = 224)	POMW+MS (n = 65)	POMW-MS (n= 159)
WC	157 (70.1)	64 (98.5)	93 (58.5)
WHR	139 (62.1)	53 (81.5)	86 (54.1)
BMI	76 (33.9)	40 (61.5)	36 (22.6)
HBP	149 (66.5)	59 (90.8)	90 (56.6)
TAG	21 (9.4)	15 (23.1)	6 (3.8)
HDLC	57 (25.4)	42 (64.6)	15 (9.4)
FPG	45 (20.1)	34 (52.3)	11 (6.9)

Abnormality was identified using revised NCEP ATP III criteria and frequency is expressed in absolute number and percentage. WC= waist circumference, WHR= waist to hip ratio, BMI= body mass index, HBP= high blood pressure, TAG= triacylglycerol, HDLC= high density lipoprotein cholesterol and FPG= fasting plasma glucose, POMW= postmenopausal women, POMW+MS= postmenopausal women with metabolic syndrome, POMW-MS= postmenopausal women without metabolic syndrome.

The mean values of WC, WHR, BMI, SBP, DBP, TAG and FPG were significantly (p <0.05) higher among the POMW+MS compared with the POMW-MS while that of the HDLC was significantly (p <0.05) lower among the POMW+MS.

The result in Table 3 which shows the prevalence of MS in subjects with high values of the parameters measured reveals that subjects with high fasting plasma glucose recorded the highest prevalence of metabolic syndrome (77.8%), this was followed by HDLC and TAG. Although high FPG and TAG were the least frequent abnormalities seen among the subjects, greater number of

subjects with these abnormalities had MS. However, subjects with high level of serum ferritin recorded the least prevalence for MS (34.6%).

Table 2: Comparison of the means of all the parameters studied between the POMW+MS and POMW-MS.

Variables	POMW+M S (n = 65)	POMW-MS (n = 159)	P value
Age (years)	56.11±1.10	54.94±0.63	P >0.05
WC (cm)	100.8 ± 1.12	90.18±0.90	P <0.05
WHR	0.92 ± 0.01	0.86±0.01	P <0.05
BMI (kg/m²)	31.82 ± 0.50	27.71±0.41	P <0.05
SBP (mmHg)	144.80±2.56	133.2±1.72	P <0.05
DBP (mmHg)	88.22±1.44	82.99±1.00	P <0.05
TAG (mmol/L)	1.39±0.06	1.10±0.03	P <0.05
HDLC (mmol/L)	1.23±0.03	1.55±0.03	P <0.05
FPG (mmol/L)	6.41±0.33	4.80±0.11	P <0.05
Ferritin (µg/l)	96.57±8.38	93.42±5.72	P >0.05

Variables are as mean±standard error of mean.

Table 3: Prevalence of metabolic syndrome among subjects with various risk factors of metabolic syndrome and high serum ferritin level.

Variables	Abnormality n	MS + n (%)	MS – n (%)
WC (>88cm)	157	65 (41.4)	92 (58.6)
WHR (> 0.85)	139	53 (38.1)	86 (61.9)
BMI (> 30kg/m²)	76	40 (52.6)	36 (47.4)
HBP (≥130/85mmH)	149	59 (37.1)	90(60.4)
TAG (≥1.7mmol/L)	21	15 (71.4)	6 (28.6)
HDLC (<1.3mmol/L)	57	42 (73.7)	15(26.3)
FPG (≥5.6mmol/L)	45	35 (77.8)	10 (22.2)
Ferritin (>120µg/l)	52	18 (34.6)	34(65.0)

Revised NCEP ATP III criteria was used to identify abnormal variables and the frequency was expressed in number and percentage.

Subjects were grouped according to the number of risk factors acquired, those without any risk factors (0), those

with 1 to 2 number of risk factors (1-2) and those with ≥ 3 number of risk factors (≥ 3). One way analysis of variance was used to ascertain the effect of the increase in the number of risk factors of MS on the mean level of the biochemical parameters. The result as represented in Table 4 showed that mean levels of TAG and FPG increases significantly ($p < 0.05$) and HDLC decreases significantly ($p < 0.05$) with increase in the number of the risk factor while ferritin recorded no significant ($p > 0.05$) variation with increase in the number of risk factors.

Table 4: Effect of increasing number of risk factors of MS on the mean level of the biochemical parameters measured.

Variables	0 (n=17)	1-2 (n=142)	≥ 3 (n= 65)	P value
TAG (mmol/L)	0.85± 0.07	1.12± 0.03	1.39± 0.06	P <0.05
HDLC (mmol/L)	1.67± 0.09	1.52± 0.03	1.23± 0.04	P < 0.05
FPG (mmol/L)	4.41± 0.07	4.85± 0.12	6.41± 0.32	P < 0.05
Ferritin (µg/l)	70.41± 6.60	96.18± 6.32	96.57± 8.38	P > 0.05

Variables are expressed as mean±standard error of mean.

Serum ferritin was correlated with the risk factors of MS and the result in Table 5 showed that values of serum ferritin showed significant weak correlation with only WHR ($r = 0.174$) and FPG ($r = 0.175$).

Table 5: Correlation of serum ferritin and risk factors of MS.

Variables	r value	P value
WC (cm)	0.084	P >0.05
WHR	0.174	P <0.05
BMI (kg/m²)	0.008	P >0.05
SBP (mmHg)	-0.062	P >0.05
DBP (mmHg)	-0.084	P >0.05
TAG (mmol/L)	0.064	P >0.05
HDLC (mmol/L)	0.080	P >0.05
FPG (mmol/L)	0.175	P <0.05

(r) Spearman correlation coefficient.

DISCUSSION

In this study, it was observed that the most frequent risk factor in this population was central obesity measured as high WC. This agrees with the result of the study conducted among the postmenopausal women in Brazil and Tehran but disagrees with the study conducted among POMW in Gorgan Iran in which low HDLC was reported as the most frequent. Although WHR and BMI were relatively high in this study, they were not as sensitive as WC in detecting central obesity.¹⁷⁻¹⁹

However, BMI may be more specific in identifying individual with MS as greater percentage of subjects with high BMI had MS. Increase in intra-abdominal fat is a common disorder associated with women in their menopausal stage and occurs in approximately 65% of all women.²⁰ This is as a result of cellular changes that include increased lipoprotein lipase activity and decreased lipolysis those results from oestrogen deficiency and increased androgenicity.²¹

Also, variation in socio-demographic factor, genetic predisposition and diet, may have contributed to the variation in the frequency of these risk factors. This can explain why this present work and that of Ulasi *et al* which was done in Enugu Eastern Nigeria recorded high WC as most frequent risk factor while the works of Adediran, Alebiosu and Odusan, Nwegbu and Jaiyesimi conducted in South western part of Nigeria recorded HBP as the most frequent risk factor.²²⁻²⁵ The most common cluster of risk factors (high WC, HBP and low HDLC) recorded in this study, is a common feature of most studies in Nigeria and some parts of Africa.^{22,25-29} However, studies in Saudi, recorded low HDLC, TAG, and WC as the most frequent cluster with HBP and FPG being the least frequent while among the Mexican-American, WC, TAG and FPG was the most frequent cluster.^{30,31} High fasting plasma glucose and TAG which were the least occurring risk factors in this study showed a higher specificity in identifying subjects with MS. The presence of high WC and low HDLC in the predominant cluster of risk factor among this group studied conforms to the fact that low oestrogen seen in postmenopausal women favours atherogenic dyslipidaemia (low HDLC) and preferential deposition of fat in the abdominal region. Some researchers in the Western world have associated high serum ferritin to the prevalence of MS and some of its risk factors like insulin resistance, hypertension, obesity, high FPG but in this study, ferritin recorded a very weak association with FPG and WHR and there was no significant difference in the mean values of ferritin of POMW+MS and POMW-MS. The research conducted among postmenopausal women in US and Korea reported a significantly higher level of ferritin among those with MS and demonstrated that ferritin level may predict MS.^{8,32}

The prevalence of MS (29%) recorded in this study is low compared to 31%, 31%, 32.6%, 33.7%, 41.5%, and 54.6% reported among POWM in Iran, Canada, China, Austria and Korea respectively.^{18,33-36} Decreasing oestrogen level and alteration of its ratio with testosterone has been implicated as a causal factor for the emergence of MS at menopausal transition.³⁷ This results to preferential increase in intra-abdominal fat and atherogenic lipoprotein- lipid profile (low level of HDLC and high TAG) and these were very high risk for MS and consequently, type 2 diabetes, premature aging, cardiovascular diseases and some forms of cancer.

CONCLUSION

This study has determined that central obesity measured as WC was the most common risk factor of MS among POMW in Enugu urban and that the predominant cluster of risk factors for MS in this group is high WC, HBP and low HDLC. Although serum ferritin is slightly associated with FPG and WHR, it may not be used as diagnostic tool for MS in the group studied.

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