Original

Relationship between Metabolic Syndrome and Uterine Leiomyoma: A Case Control Study

[1]Olusi AM, [2]Rabiu KA, [3]Oduola-Owoo BB, [4]Rasheed MW, [5]Oduola-Owoo LT, [3]Windapo OB

[1]Royal infirmary Edinburgh, 51 Little France Cres, Old Dalkeith Rd, Edinburgh EH16 4SA
[2]Department of Obstetrics and Gynaecology, Lagos State University College of Medicine, Ikeja, Lagos State, Nigeria.
[3]Department of Obstetrics and Gynaecology, Federal Medical Centre Ebute Metta, Lagos State, Nigeria
[4]Department of Anatomic Pathology, Federal University of Dutse, College of Medicine and Allied Science, Faculty of Clinical Science, Jigawa State, Nigeria
[5]Department of Radiology, Federal Medical Centre, Ebute Metta, Lagos State, Nigeria

Corresponding author: Rasheed Mumini Wemimo, *Department of Anatomic Pathology, Federal University Dutse, College of Medicine and Allied Science, Faculty of Clinical Science, Jigawa State, Nigeria; muminirasheed265@gmail.com; +2347069339824*

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Abstract

Background: Uterine leiomyoma is the most common benign gynaecological tumour of the female reproductive tract. Although, the cause of uterine leiomyoma is still unclear; however, studies have shown that single and multiple components of metabolic syndrome such as hypertension, obesity, elevated triglycerides, and type 2 diabetes may be associated with the prevalence of uterine leiomyoma.

Method: This is a prospective case-control study conducted in the Department of Obstetrics and Gynaecological of the Lagos State University Teaching Hospital from 26th March 2020 to September 28th, 2020. This study aimed to evaluate the associations between metabolic syndrome and uterine leiomyoma. A total of 165 cases were recruited and analysed for both the study population and control. All data was imputed onto a proforma. Statistical analysis was done using the Statistical Package for Social Science (SPSS) version 22. Conditional logistic regression was used to examine the associations between independent variables and uterine leiomyoma.

Result: There was no statistically significant difference in the prevalence of metabolic syndrome between participants in the fibroid and non-fibroid group (3.7% vs1.8%, P=0.315). Prevalence of obesity and hyperglycaemia were significantly higher in the leiomyoma group compared to the control group (77.4% vs 20.2%, P<0.001 and 6.7% vs 1.8%, P=0.028. Regression analysis showed a three-fold risk of uterine fibroids among cases when waist circumference was elevated, (OR=3.876;95% CI,1.759-7.981).

Conclusion: There was no significant association between the prevalence of metabolic syndrome and uterine leiomyomas, however, the prevalence of obesity and hyperglycaemia were significantly associated with uterine leiomyoma.

Keywords: Leiomyoma, Metabolic syndrome (Mets,) Obesity, BMI (Body mass index), Case control study

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Introduction

Uterine leiomyoma is the most common benign tumour in women of reproductive age.[1] Majority of uterine leiomyomas are however asymptomatic with a large proportion being identified on routine ultrasound scans.[2,3] The diagnosis of uterine leiomyoma varied significantly in many parts of Nigeria, a review by Aboyeji et al[4] showed 13.4% of admissions in a tertiary health facility in the southwest while Anate et al reported a prevalence of 9.8% in lokoja[5], and similar 9.8% was reported in Enugu.[6] The diagnosis of uterine leiomyoma accounted for the largest proportion of gynaecological surgeries in Enugu eastern part of Nigeria which accounted for 26.2%.[6] The vast majority of indications for hysterectomy in premenopausal women are due to uterine leiomyoma and annually account for 33.0% of all hysterectomies in the United States with an estimated cost of 1.2 billion dollars on hospital expenditure.[7]

Although this benign tumor is a significant health concern for women, the cause of uterine leiomyomata is unknown.[8] The pathogenesis of uterine leiomyoma growth remains elusive, however, it is believed ovarian hormones: oestrogen, and progesterone, and interaction with their receptors have been reported to play a key role in its growth.[9] Various risk factors both non-modifiable such as age[10], black race[11], family history of uterine leiomyomas[12], early age at menarche[13], hypertension[14], and modifiable risk factors such as obesity[15], diet[16], smoking, and alcohol consumption have been associated with the occurrence of uterine leiomyoma. Some of these risk factors are also seen as the constituents of metabolic syndrome.

Metabolic syndrome is a cluster of cardiovascular risk factors that is characterized by central obesity, insulin resistance, atherogenic dyslipidemia, and hypertension.[17] There are different definitions of metabolic syndrome, but the uniform pathophysiology has been postulated as insulin resistance.[18]

Most studies done on the associations between uterine leiomyomas and metabolic syndrome were in the Caucasian and Asian populations with very few studies done in sub–Saharan Africa.

This study therefore aims to determine the association between uterine leiomyomas and metabolic syndrome. Thus, we hypothesized that metabolic risk factors are probably related to uterine leiomyoma among Nigerian women at Lagos State University Teaching Hospital, Ikeja (LASUTH). To investigate this hypothesis, we studied the association between uterine leiomyoma and metabolic risk using a prospective case-control study design.

Method

Study Site

The study was conducted at the Gynaecological Clinic of the Department of Obstetrics and Gynaecology of the Lagos State University Teaching Hospital, Ikeja (LASUTH), Nigeria. LASUTH is a state-owned tertiary healthcare facility. It serves as a referral Centre for peripheral hospitals in Lagos and the surrounding states. The study spanned a total of 7 months, from 26th March 2020 to September 28th 2020.

Study Design

This is a prospective case-control study was carried out among consenting premenopausal women with uterine leiomyoma as the study group and premenopausal women with no uterine leiomyoma, as control.

Study Population

All eligible and consenting patients attending the gynaecology clinic of Lagos State University Teaching Hospital within the study period.

Inclusion Criteria

Eligibility for cases

All consenting premenopausal women between the ages of 18 – 49 with ultrasound diagnosis of uterine leiomyomas.

Eligibility for controls

All consenting premenopausal women between 18 – 49 years with ultrasound scan showing absence of uterine leiomyomas.

Exclusion Criteria

1. Previous history of any cancer in any part of the body.
2. Women with a history of hysterectomy or bilateral oophorectomy.
3. Pregnant and breastfeeding women.
4. Women on Hormone Replacement Therapy or medications that affect ovarian hormone metabolism.

Sampling Method

A non-probability sampling technique (convenience sampling) was used as patients were recruited consecutively until the desired sample size was attained. Cases were identified based on symptomatology (abdominal mass, heavy menstrual bleeding, or prior diagnosis of fibroids) and ultrasound evaluation. Cases and controls were recruited after filling an informed consent form, they subsequently had an ultrasound

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performed by a senior registrar in the radiology department with the investigator in attendance to determine the presence or absence of uterine leiomyoma. Cases and controls were matched for age to reduce confounders. Ultrasound assessment led to the discovery of control patients who became cases (asymptomatic).

Consented women with uterine fibroids were assigned to the case group, while those without uterine fibroids were assigned to the control group.

Sample Size Determination

Sample size estimation

For the difference in proportions: The proposed sample size for the study was calculated using the formula for case-control study.[19]

where n = sample size in the case group

r = ratio of controls to cases = 1

Z_β = desired power of the study at 0.84 (for 80%)

Z_α = level of statistical significance at 1.96

$\bar{p}$ = measure of variability

$(p_1 - p_2)^2$ = effect size (the difference in proportions)

p_2 = proportion of exposed in the control group = prevalence of metabolic syndrome from a previous study in Ogun state = 24.9% (0.25)

p_1 = proportion of cases exposed

Calculating proportion of cases exposed:

$$p_1 = \frac{OR p_2}{p_2(OR-1)+1}$$

Where OR = Odds ratio (study is to detect OR of 2.0 or greater)

$$p_1 = \frac{2.0(0.25)}{(0.25)(2.0-1)+1}$$

p_1=0.40

Average proportion exposed = $\frac{(0.40+0.25)}{2}$ = 0.325

$$n = \left(\frac{1+1}{1}\right)\frac{(0.325)(1-0.325)(0.84+1.96)^2}{(0.40-0.25)^2}$$

Therefore, n = 150 per group (150 cases and 150 controls)[19]

Considering an attrition rate of 10% for both cases and controls, n= 165 per group

Data Collection

Premenopausal women visiting the gynaecology clinic who gave consent were identified and recruited using convenient sampling. The proforma contained both open and closed ended questions and there was provision for multiple responses. The proforma contained questions about socio-demographic details, obstetrics history, menarche, risk factors for metabolic syndrome, family history of uterine fibroids, results of ultrasound, result of lipid profile and fasting blood glucose. The proformas were filled by the researcher and or the assistants.

Ultrasound Scan

The ultrasound examination procedures were performed by the researcher using the transabdominal probe, (Philips EPIQ 5 ™ Affinity 70 Ultrasound system) at 3.5 MHz frequency, each patient was asked to lie in a supine position on the ultrasound examination couch after feeling the sensation of a full bladder, the procedure was explained to her in detail, this was followed by application of a water-soluble coupling gel over the abdomen. The curved ultrasound probe was applied to the pelvis using the full bladder as an acoustic window, the uterus was identified, and its orientation was noted, this was followed by identification of adnexal structures. Leiomyomas were identified as hypoechogenic solid masses on and within the uterus. The findings and implications were related to the patient.

Biometric Measurements

Blood pressure (BP) was measured on 2 occasions, 5minutes apart, on the right arm of the patient by an electronic sphygmomanometer (XREXS automatic digital sphygmomanometer Xrexs-C, US Rexs LLC). Both measurements were averaged to the nearest millimeter of mercury and recorded on the patients proforma. Waist circumference (WC) was measured by either the investigator or trained research assistant by taking readings at the midpoint between the lower costal margin and the iliac crest using a tape measure, with values to the nearest centimeter recorded.

Blood Sample Collection

The fasting blood samples were collected by the researcher and the assistant via aseptic technique into bottles contain potassium ethylene diamine tetraacetic acid and fluoride oxalate for lipid profile and fasting glucose levels, respectively. They were sent to the laboratory via a storage cooler with icepacks to keep the samples within 2-6 degrees centigrade. The containers were pre-coded for each woman and for what to assay, the date and time of collection were noted. These samples were taken by the researcher and assistants in the gynaecology clinic.

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Metabolic syndrome was defined using the international diabetes foundation 2006 definition criteria.[20]

***Obesity*:** Waist circumference > 88cm

***Triglyceride*:** TG>150mg/dL or on treatment of lipid abnormality

***High Density Lipoprotein*:** HDL <40mg/dL in males and <50mg/dL in females or on specific treatment for lipid abnormality

***Hypertension*:** SBP >130 or DBP >85 mmHg or treatment of previously diagnosed hypertension

***Hyperglycemia*:** Fasting plasma glucose >100mg/dl or previously diagnosed type 2 diabetes

Laboratory Analysis
Blood samples after an overnight fast of at least 8hrs was collected and put in potassium ethylene diamine tetraacetic acid and fluoride oxalate tube for lipid profile and fasting glucose levels, respectively. The samples were subsequently analyzed at the departments of chemical pathology.

Data Analysis
Data was collated daily, checked for completeness and all errors were identified and corrected immediately. The data was entered and analyzed using a statistical package for social sciences (version 22 IBM SPSS Inc. Rochester, MN, USA). Distribution of continuous variables is expressed as a mean and or standard deviation, and categorical variables as numbers and percentages of proportions. Descriptive statistics, tables, charts, and graphs was used to summarize variables. Continuous variables were compared using the Independent Student T test when normally distributed. Association between categorical variables was assessed using the Chi square test. Binary logistic regression analysis was used to determine associations between independent factors related to uterine leiomyoma. The level of statistical significance will be set <0.05 at 95% confidence interval.

Ethical Considerations
Ethical approval to conduct this study was obtained from the Lagos State University Teaching Hospital (LASUTH) Health Research and ethical review committee with registration number NHREC004/04/2008.

Results

***Recruitment of participants*:** Participants were screened for each group independently. A total of 165 cases were screened, one woman was excluded as she was confirmed to be pregnant on ultrasound leaving 164 participants who were recruited and analysed. One hundred and sixty-five participants were screened as controls for this study, two of these women were excluded from the study as they did not return for blood sample collection. One hundred and sixty-three were women recruited and analysed. Figure 1 shows the flow chart of the participants.

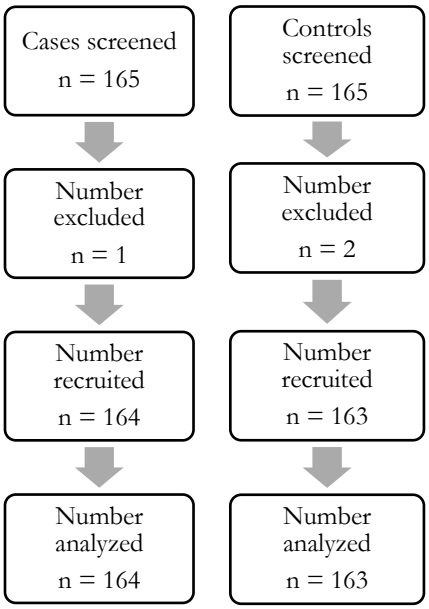

Figure 1: Flow chart of recruited participants

Basic Sociodemographic characteristics of Participants
The mean age of the study population was 33.35±5.5 years and about one-third (32.1% n= 105) of participants were in the age group 36 – 40 years. The majority were of the Yoruba ethnic group (n= 280, 85.6%) and more than half were married (n= 202, 61.8%) or had tertiary education (n=174, 53.2%). Age distribution of the two groups was comparable (p=0.573). No significant difference in marital status distribution of subjects with uterine myomas and those without myomas (p=0.451). There was no statistical difference among both groups in terms of educational level(p=0.4). Other socio-demographic variables are highlighted in Table 1

Obstetric characteristics of Participants

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Table 2 shows the obstetric characteristics of patients. Age of menarche was not statistically significant among both groups (p=0.151), with 70.6% of all patients attaining menarche between age 11-13yrs. The number of pregnancies irrespective of outcome was not statistically different in both groups (p=0.113), however number of life births was statistically different with women without uterine myomas having more parous experiences compared with women with uterine myomas (59.8% vs 51%, p=0.001)

Lifestyle and Clinical characteristics

Table 3 shows the lifestyle and clinical characteristics of both the cases and controls. None of the participants in the study had smoked cigarettes, used lipid-lowering drugs or Insulin. Alcohol consumption was similar in both groups (6.7% vs6.1%, P=0.833), the use of antihypertensives was also similar in both groups (3.7% vs 2.5%, P=0.527). There were no current users of oral contraceptive pills, however, 5.5% of participants in the fibroid arm and 2.5% in the non-fibroid arm had used oral contraceptives in the past. Two participants in the fibroid group were on treatment for diabetes while one patient in the non-fibroid arm was on treatment using oral hypoglycemic drugs for diabetes. Family history of uterine fibroids was a significant finding among the fibroid group when compared to the non-fibroid group (47.6% vs 19%, P= <0.001)

Figure 2 is a bar chart showing the prevalence of metabolic syndrome in cases and controls. The prevalence of metabolic syndrome in the myoma group was 3.7% vs 1.8% in the control group, however there was no statistical difference between both groups (p=0.315) in terms of metabolic syndrome.

Mean comparison of individual components of Metabolic syndrome

Table 4 shows the mean comparison between individual components of metabolic syndrome amongst cases and controls. With regards to the individual components of metabolic syndrome, women with uterine myomas had a larger waist circumference, as compared to women without myomas (90.54±6.4 vs 78.83±9.2, p= 0.001). There was a significant difference between both groups with regards to low density lipoprotein, with the control group having higher values (87.11±13.8 vs 81.02±15.1, p<0.001). Systolic blood pressure in both groups did not show a statistical difference, however there was a statistical difference of the diastolic blood pressures between both groups, with the non-fibroid group having a higher diastolic blood pressure (73.16±4.8 vs 74.36±9.2, p= 0.032). Mean triglyceride levels, fasting plasma glucose and high-density lipoprotein levels were similar in both groups.

Prevalence of the individual components of metabolic syndrome

Table 5 shows the prevalence of the individual components of metabolic syndrome among women with myomas and women without myomas. Difference in waist circumference and fasting plasma glucose was statistically significant (77.4% vs 20.2%, P<0.001 and 6.7% vs1.8%, P=0.028). All other components of metabolic syndrome showed no statistically significant difference.

Logistic Regression of Independent Risk Factors for Fibroids

Table 6 shows Binary logistic regression of the independent predictors of uterine fibroids. It shows that elevated waist circumference (OR=3.876;95% CI,1.759-7.981), a proxy for central obesity, is significantly associated with increased risk for uterine leiomyoma. There was no statistical association between Metabolic syndrome and uterine leiomyoma.

Table 1: Socio-demographic characteristics of Participants

	Fibroid Group (n=164) Case n(%)	Non-Fibroid Group (n=163) n(%) Control	Total n=327	X^2	p-value
Age group (Years)					
≤25	13(7.9)	13(8)	26(8)	0.237	0.994
26-30	46(28)	44(27)	90(27.5)		
31-35	39(23.8)	37(22.7)	76(23.2)		
36-40	52(31.7)	53(32.5)	105(32.1)		
>40	14(8.5)	16(9.8)	30(9.2)		
Mean ± SD	33.18±5.6	33.53±5.7		0.564	0.573
Marital status					
Single	66(40.2)	59(36.2)	125(38.2)	0.567	0.451

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Married	98(59.8)	104(63.8)	202(61.8)		
Educational level					
Primary	8(4.9)	12(7.4)	20(6.1)	1.560	0.458
Secondary	64(39.0)	69(42.3)	33(40.7)		
Tertiary	92(56.1)	82(50.3)	174(53.2)		
Ethic group					
Yoruba	138(84.1)	142(87.1)	280(85.6)	2.658	0.447
Igbo	17(10.4)	11(6.7)	28(8.6)		
Hausa	4(2.4)	7(4.3)	11(3.4)		
Others	5(3)	3(1.8)	8(2.4)		

Table 2: Obstetrics characteristics of Participants

	Fibroid Group(n=164)	**Non-Fibroid group(n=163)**	**Total**	**X^2**	**p-value**
Age at menarche (Years)					
≤10	25(15.3)	35(21.5)	60(18.4)	3.780	0.151
11-13	123(75.5)	107(65.6)	230(70.6)		
>13	15(9.2)	21(12.9)	36(11)		
Mean ± SD	11.74±1.2	11.77±1.5			
Gravida					
0	53(32.3)	62(38)	115(35.2)	7.473	0.113
1	15(9.1)	26(16)	41(12.5)		
2	53(32.3)	39(23.9)	92(28.1)		
3	25(15.2)	25(15.3)	50(15.3)		
≥4	18(11)	11(6.7)	29(8.9)		
Parity					
0	80(49.1)	66(40.2)	146(44.6)	18.207	**0.001***
1	28(17.2)	9(5.5)	37(11.3)		
2-4	56(34.1)	88(54.0)	144(44.0)		

Table 3: Lifestyle and clinical characteristics of Participants

	Fibroid group (n=164)	**Non-fibroid group (n=163)**	**Total**	**X^2**	**p-value**
Alcohol consumption					
Yes	11(6.7)	10(6.1)	21(6.4)	0.045	0.833
No	153(93.3)	153(93.9)	306(93.6)		
Oral contraceptive					
Nonusers	155(94.5)	159(97.5)	314(96.0)	1.971	0.160
Former users	9(5.5)	4(2.5)	13(4.0)		
On Antihypertensive					
Yes	6(3.7)	4(2.5)	10(3.1)	0.400	0.527
No	158(96.3)	159(97.5)	317(96.9)		
Use of oral hypoglycemic drugs					
Yes	2(1.2)	1(0.6)	3(0.9)	0.330	0.565
No	162(98.8)	162(99.4)	324(99.1)		
Family history of fibroid					
Yes	78(47.6)	31(19.0)	109(33.3)	29.970	<0.001*
No	86(52.4)	132(81.0)	218(66.7)		

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Table 4: Mean comparison of component of metabolic syndrome among women with leiomyomas and without

	Fibroid group (n=164) Mean ± SD	Non-Fibroid group (n=163) Mean ± SD	t-value	p-value
Waist circumference (cm)	90.54±6.4	78.83±9.2	13.338	**<0.001***
Systolic blood pressure(mmHg)	117.98±8.4	118.78±9.6	-0.815	0.416
Diastolic blood pressure	73.16±4.8	74.36±5.3	-2.157	**0.032***
Triglyceride(mmHg)	109.41±29.1	109.41±20.2	-0.630	0.529
High density lipoprotein (mmol/L)	76.96±13.7	77.81±10.5	-0.630	0.529
Low density lipoprotein(mmol/L)	81.02±15.1	87.11±13.8	-3.795	**<0.001***
Fasting blood sugar (mg/dl)	84.25±8.6	85.44±9.5	-1.181	0.238

Table 5: Prevalence of individual components of metabolic syndrome among Participants within fibroid and non-fibroid groups

	Fibroid group (n=164)	Non-fibroid group(n=163)	Total	Odd ratio	95%CI	X^2	p-value
Waist circumference							
Elevated	127(77.4)	33(20.2)	160(48.9)	13.52	7.97-22.95	107.013	**<0.001***
Normal	37(22.6)	130(79.8)	130(79.8)				
Triglyceride							
Elevated	9(5.5)	3(1.8)	12(3.7)	3.097	0.82-11.65	3.076	0.074
Normal	155(94.5)	160(98.2)	315(96.3)				
High density lipoprotein							
Low	11(6.7)	4(2.5)	15(4.6)	2.858	0.89-9.17	3.379	0.066
Normal	153(93.3)	159(97.5)	312(95.4)				
Low density lipoprotein							
Elevated	6(3.7)	3(1.8)	9(2.8)	2.025	0.49-8.23	1.010	0.315
Normal	158(96.3)	160(98.2)	318(97.2)				
Systolic BP							
Elevated	16(9.8)	10(6.1)	26(8.0)	1.654	0.75-3.89	1.465	0.226
Normal	148(90.2)	153(93.9)	301(92.0)				
Diastolic BP							
Elevated	21(12.8)	11(6.7)	32(9.8)	2.029	0.945-4.36	3.397	0.065
Normal	143(87.2)	152(93.3)	295(90.2)				
Blood pressure							
High	20(12.2)	10(6.1)	30(9.2)	2.125	0.96-4.69	3.603	0.058
Normal	144(87.8)	153(93.9)	297(90.8)				
Fasting blood sugar							
High	12(6.7)	2(1.8)	14(4.3)	6.355	1.40-28.86	4.827	**0.028***
Normal	152(93.3)	161(98.2)	313(95.7)				

Table 6: Multivariate Binary logistic showing independent predictor of fibroid

Variable	Adjusted Odd ratio	95% CI	p-value
Waist circumference			
Normal	1		
Elevated	3.876	1.759-7.981	**<0.001***
Systolic blood pressure			
Normal	1		
Elevated	1.793	0.795-4.044	0.795

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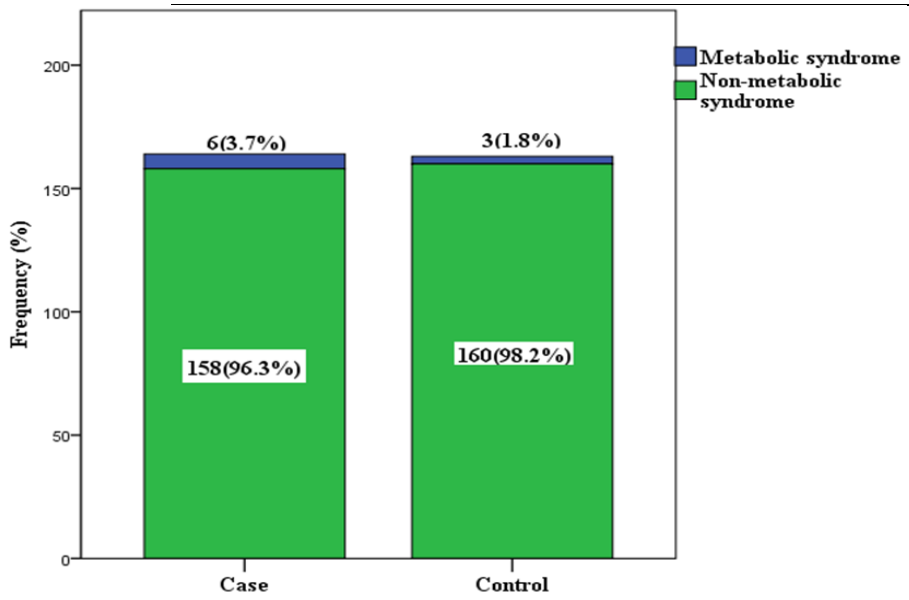
Variable	Adjusted Odd ratio	95% CI	p-value
Diastolic blood pressure			
Normal	1		
Elevated	2.125	0.798-5.659	0.131
Triglyceride			
Elevated	1		
Normal	3.097	0.823-11.653	0.095
Low density lipoprotein			
Normal	1		
Elevated	1.372	0.243-7.732	0.720
Fasting blood sugar			
Normal	1		
Elevated	2.184	0.475-10.032	0.315
Metabolic syndrome			
Absent	1		
Present	2.025	0.498-8.240	0.324
Parity			
None	1		
1	0.990	0.172-1.883	0.748
2-4	0.732	0.290-1.339	0.283



X^2=1.010, p=0.315

Figure 1: Prevalence of metabolic syndrome metabolic syndrome among women with leiomyomas and without.

Discussion

In this study, the prevalence of metabolic syndrome in the uterine myomas group did not differ statistically from the prevalence in the non-fibroid group. Similarly, Tak et al[21] from Japan and Moon et al[22] from South Korea also found no statistically significant difference in

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the prevalence of metabolic syndrome (Mets) among participants with or without fibroid. On the other hand, the prevalence of metabolic syndrome was found to be higher among women with Uterine fibroids when compared to patients without fibroids in a retrospective case control study that was conducted by Takeda et al[23], in Japan. The difference in findings between Takeda et al [23] in Japan and this index study may be related to the population studied. Indeed, Takeda et al [23] restricted their study population to only women who had a hysterectomy and thus did not include asymptomatic women with uterine fibroids. However, this study recruited participants with both symptomatic and asymptomatic uterine fibroid that was diagnosed via transabdominal ultrasound. Moreover, this study diagnosed MetS based on BMI, not waist circumference which is the proxy for obesity. Additionally, the mean age among the cohort of women from the Japanese study was higher than the mean age if recruited women of this study (44 years vs. 33 years). The difference in age between our study and that of Takeda et al [23] may cause a difference in conclusions as MetS is associated to increase age.[24] The occurrence of uterine fibroids is multi-factorial and could be potentiated by some individual components of metabolic syndrome may be deranged but not statistically significant.[20,25]

Furthermore, waist circumference has been used as an index for central obesity was found to be significantly higher amongst women with leiomyomas in this study as compared to the non-myoma group. Similarly, Tak et al [21] also reported a significant association between waist circumference and uterine leiomyoma. Although this study as well as that from Tak et al [21] used waist circumference as the proxy for obesity, however, a larger waist circumference (88cm) was used in this study due to the racial differences in assessing central obesity, while 80cm was used for the Asian population. In a review by Uimari et al[22] in a large Cohort Study of uterine myoma and cardiovascular risk involving the Northern Finland Birth Cohort 1966 (NFBC1966) also observed an increased prevalence of myomas for every 1cm increase in waist circumference and every unit increase in waist circumference in women with significant cardiovascular risk. Babah et al however did not find a statistically significant correlation between obesity and uterine myoma in their retrospective study looking at the body mass index of women who had fibroid surgery in Lagos University Teaching Hospital in southwest Nigeria.[26]

In addition, obesity has been described as a major contributor to metabolic dysfunction.[27] This occurs through multiple pathways, oestrogen production and insulin resistance, which influence uterine leiomyoma growth and worsens metabolic syndrome. The elevated waist circumference is directly correlated to central adiposity and body fat, which is associated with a decreased level of sex hormone binding globulin and an increase in the peripheral conversion of circulating androgens. Reduced level of sex-hormone binding globulin leads to an elevated level of circulating oestrogen and physiologically active forms of this oestrogen. Notably, various studies have shown that increased fat levels have led to an increase in the growth of leiomyoma by stimulating insulin resistance.[25,27,28] This assumption asserts the fact that insulin has been shown to stimulate the growth of smooth muscle cells in leiomyoma through insulin-like growth factor receptors. Since our study found an association between myoma and elevated waist circumference with three-fold odds this tends to support a relationship between obesity and myoma growth which may be through abnormal insulin metabolism. Thus, further research may be conducted to evaluate an alternative preventive intervention and management for uterine myoma.

This study identified a significant relationship between the prevalence of hyperglycemia and uterine myomas. A similar finding was described by Tak et al[21] in Pusan, South Korea. Next, insulin resistance has been proposed as the central pathophysiology underlying the relationship between uterine leiomyoma and MetS.

Hyperglycemia induces hyperinsulinemia which changes the expression of growth factors such as insulin-like growth factor, vascular endothelial growth factor, and signaling pathways. Changes in these pathways and receptors by hyperinsulinemia leads to tumor growth propagated by either anti-apoptotic or proliferative mechanisms or both. Hyperinsulinemia also alters the ovarian hormonal levels by reducing transport globulin production in the liver, freeing up circulating oestrogen and progesterone leading to myoma smooth muscle proliferation and deposition of extracellular matrix.[29] Nonetheless, Sadlonova et al[30], Faerstein et al [29] and Baird et al [28] also found no association between hyperglycemia or and uterine leiomyoma.

More importantly, family history of uterine fibroids is a known risk for uterine fibroids and in this study, a positive family history of UL among participants in the fibroid group was significantly associated with the

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prevalence of uterine fibroids. Similarly, another have shown 2-fold risk for UL among participants with uterine fibroids in the United States of America.[31]

Although, nulliparity has been documented to be associated with uterine leiomyoma, however in this study, there was no significant association noted. Nulliparity however is associated with continuous cyclical production of oestrogen and progesterone, both of which have been proposed to augment fibroid growth. Pregnancy and breastfeeding reduce this exposure which leads to a proposed reduction in fibroid growth and prevention of fibroid formation.[32] Indeed, Marshal et al found that higher parity was inversely proportional to the risk of developing uterine fibroids.[10] The relationship between hypertension and uterine myomas has been investigated with conflicting results.[33,34,35] This study did not find any significant statistical difference between the prevalence of elevated systolic blood pressure among participants in the fibroid group. The lack of association between the prevalence of elevated blood pressure among women with fibroids in this study could be explained by the relatively young age of the participants (mean age of fibroid group 33.18±5.6).

This result was like that reported by Uimari et al[25] in a large prospective cohort study to determine the relationship between uterine myomas and cardiovascular risk. The study population was the Northern Finland Birth Cohort 1966 (NFBC1966). Blood pressure measured at 46years did not show an association with uterine myoma risk in both medicated and un-medicated hypertensives. Interestingly, in the largest prospective study of hypertension and risk of uterine leiomyoma to date the authors reported that after adjusting for covariates, it was noted that for every 10-mmHg rise in diastolic blood pressure, the risk of uterine leiomyomas increased by 8% amongst participants not on antihypertensives and 10% amongst participants on anti-hypertensives.

Abnormal lipid metabolism has been associated with myoma growth and metabolic syndrome. This study found reduced levels of HDL-C and elevated levels of triglyceride among the myoma group, although values were not statistically significant. Contrary to the findings in the study, Seram et al reported elevated levels of HDL-C in their case-control study comparing us lipid profile of patients with uterine fibroids with control.[35]

In a study showing the atherogenic hypothesis of uterine fibroids in Chinese women, He et al[34] reported both HDL-C and LDL-C were found to be reduced in patients with uterine myomas. Elevated triglyceride levels however did correlate directly with the presence of uterine myoma; however, this finding was not corroborated in this study.

Conclusion

This study found that there was no significant difference in the prevalence of MetS between premenopausal women with UL and those without. However, there was a significant association between the prevalence of elevated waist circumference of participants, used as a proxy for obesity, and uterine fibroids even after adjusting for confounders. The prevalence of hyperglycemia and therefore hyperinsulinemia was significantly associated with UL. This study provides some evidence that obesity and hyperinsulinemia may stimulate fibroid growth. This study provides a template for future research in the management and prevention of uterine leiomyomas.

Strengths and Limitations of the Study

One of the strengths of the study was the screening of participants via ultrasound scan. This enabled the identification of both symptomatic and asymptomatic participants and precise classification into fibroid and non-fibroid groups. Secondly, metabolic syndrome was diagnosed based on laboratory results, unlike other similar studies where a recall system was used. This reduced recall bias amongst the participants. In addition, vitamin D deficiency, food addictive consumption, use of soya beans, and others that could serve as cofounder in the evaluation of metabolic syndrome could not be accounted for.

Declarations

Ethical consideration: Ethical approval to conduct this study was obtained from the Lagos State University Teaching Hospital (LASUTH) Health Research and ethical review committee with registration number NHREC004/04/2008.

Authors' contribution:

All the authors made a significant contribution to this study. All the authors have read and approved the final version of the manuscript.

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Abbreviation:
Mets- Metabolic syndrome
UL- Uterine leiomyoma
HDL-C- High density lipoprotein
LDL-C- Low density lipoprotein
BMI-Body mass index

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