

## ASSOCIATION BETWEEN AGE, BMI, AND THE TYPE AND LOCATION OF UTERINE LEIOMYOMA: A UPTH STUDY

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### ABSTRACT

Uterine leiomyoma is the most frequent pelvic mass found in women of child bearing age. They occur in 20-50% of women with increasing incidence as women get older. This study evaluated the association between age, BMI, and the type and location of intrauterine leiomyoma in University of Port Harcourt Teaching Hospital (UPTH), Rivers State, Nigeria over a twelve year period. The study was a retrospective research which utilised clinical records to retrieve subject information as well as anthropological data from women clinically diagnosed with uterine leiomyoma who attended the obstetrics and gynaecological unit of University of Port Harcourt Teaching Hospital from 2007 to 2018. A total of 318 cases were obtained with complete records and the data extracted to excel sheet. Statistical Package for Social Sciences (SPSS, version 23, IBM, Armonk, USA) was used to analyse the data. Chi-Square evaluated the association between categorical variables. Decision Tree using Chi-square Automatic Interaction Detector (CHAID) estimated which subject's characteristics was significantly associated with their clinical presentation. The result showed that age group was not a significant indicator for type (single or multiple) and location of the uterine leiomyoma ( $P > 0.05$ ); however, age group  $\geq 35$  years had the highest incidence (50%). CHAID analysis showed that significantly higher BMI (specific to subserous leiomyomas), in leiomyoma subjects was associated with multiple locations when compared to lower BMI ( $P < 0.05$ ). From the findings, it could be concluded that higher body mass index (BMI) and age was significantly associated with the incidence and location of the different types of the leiomyoma.

**KEYWORDS:** Age, BMI, Women, Incidence, Uterine Leiomyoma, Rivers State.

### INTRODUCTION

Uterine leiomyomas also known as uterine fibroids are the most prevalent mass found in women.<sup>[1]</sup> They are monoclonal tumours that arise from the uterine muscular tissue. This tissue is composed partly of large amounts of extracellular matrix that contains collagen, fibronectin, and proteoglycan.<sup>[2,3]</sup> They occur in 20-50% of women, with an increasing incidence as women get older.<sup>[4]</sup> They are found more commonly, tend to occur at younger age and present with greater number and size in women of African-American descent in comparison to Caucasian, Asian and Hispanic women.<sup>[5]</sup>

There are four common types of uterine leiomyomas. They are identified by their location in the uterus<sup>[6]</sup>: Subserosa leiomyomas develop in the outer portion of the uterus and grow outward. These leiomyomas can be painful if they are large and press on other organs. They usually do not affect a woman's menstrual flow. Submucosal leiomyomas are the least common types and could develop just under the lining of the uterine cavity. Intramural leiomyoma develops and localizes within the

myometrium of the uterus and pedunculated leiomyoma grow on small stalks inside or outside the uterus.

Certain risk factors have been implicated in the aetiology of uterine leiomyomas, even though this is poorly understood, but some studies have suggested multiple risk factors such as age, race (African descent), early age at menarche, reduced fertility, frequent alcohol and caffeine consumption, obesity, consumption of red meat, hypertension, diabetes mellitus, previous pelvic inflammatory disease, genetics and hormonal traits have been associated with the development of leiomyoma.<sup>[7,8]</sup> This study, therefore, evaluated the association between Age, body mass index (BMI), and the type and location of intrauterine leiomyoma in UPTH.

### MATERIALS AND METHODS

The research was designed as a retrospective study involving the use of clinical records and certain anthropological data; obtained from women clinically diagnosed with uterine leiomyoma who attended the gynaecological unit of University of Port Harcourt Teaching Hospital. The study population was drawn

from women within the ages range; 18 to 49 years, who were diagnosed with intrauterine leiomyoma at the gynaecological unit (from January 2007 to December 2018) of UPTH, Port Harcourt, Rivers State, Nigeria. The sample included all the records of women clinically diagnosed with leiomyoma who had complete records at the obstetrics and gynaecology (O&G) unit of university of Port Harcourt. Purposive sampling was used for this study. Women below or above the set age range and those diagnosed with other forms of tumours and pathological conditions were excluded from the study. Secondary data was obtained from medical records of the patients from the O&G Department of University of Port Harcourt Teaching Hospital. The data obtained included; age and body mass index (BMI) which was determined by dividing the Weight in kilograms by the Height in square meters; Education, which was stratified into three levels- primary, secondary and tertiary; Socioeconomic status defined by the average monthly income stratified into greater than 5000 less than 20000, greater than 20000 less than 50000, greater than 50000.

Data Entry was done using Microsoft Office Excel version 10 and Statistical Analysis using the Statistics Package for the Social Sciences (version 23.0). Data was

presented as frequencies and percentages. Chi-Square test was used to describe distribution and determine the relationship between categorical variables. Decision Tree using Chi-Square Automatic Interaction Detector (CHAID) was carried out to determine which of the two (age and BMI) characteristics best explained the patient clinical presentation. Traditionally CHAID splits epidemiological factors into categories (nodes) with approximately equal number of observations, creating all possible cross-tabulations for each category. This process is repeated until the best outcomes are achieved. Confidence level was set at 95%, and  $P < 0.05$  was considered significant.

#### Ethical Considerations

Ethical clearance with reference number UPH/CEREMAD/REC/MM60/062 was obtained from the University Ethics Committee of the Post Graduate School after scrutiny by the Departmental Post Graduate Committee, and the Ethics Committee of University of Port Harcourt Teaching Hospital. Confidentiality was ensured as personal information such as name and address of subjects were not used, however to ensure records obtained were not mixed up, serial/record numbers were assigned to each file.

## RESULTS

**Table 1: Socio-demographic of the patients; stratified by age group.**

Variables	Age group			Total (%)
	15-24 yrs. (%)	25-34 yrs. (%)	≥35 yrs. (%)	
<b>Marital Status</b>				
Single	7 (5.6)	72 (57.1)	47 (37.3)	126 (39.6)
Married	0 (0)	76 (42.2)	104 (57.8)	180 (56.6)
Divorce	0 (0)	2 (33.3)	4 (66.7)	6 (1.9)
Widowed	0 (0)	1 (16.7)	5 (83.3)	6 (1.9)
<b>Education</b>				
Primary	1 (5.9)	7 (41.2)	9 (52.9)	17 (5.30)
Secondary	0 (0)	56 (50.5)	55 (49.5)	111 (34.9)
Tertiary	6 (3.3)	84 (46.4)	91 (50.3)	181 (56.9)
Post grad	0 (0)	4 (44.4)	5 (55.6)	9 (2.8)
<b>Average Monthly Income</b>				
5-20k	2 (1.8)	50 (45.4)	58 (52.7)	110 (34.6)
20-50k	4 (2.8)	69 (47.6)	72 (49.7)	145 (45.6)
>50k	1 (1.6)	32 (50.8)	30 (47.6)	63 (19.8)

In Table 1, married women and singles were observed to be predominant (180; 56.6%) and (126; 39.6%) respectively. The age group 15-24 years and 25-34 years were mostly singles (7; 5.6%) and (72; 57.1%) respectively, while women who were ≥35 years were mostly married (104; 57.8%). Those who were married previously were less than 5% among the total population (12; 3.8%) with the larger proportion of women falling into the age group ≥35 years; divorced (4; 66.7%) and widowed (5; 83.3%). A higher proportion of the study population indicated to have had tertiary and secondary education (181; 56.9% and 111; 34.9% respectively). The level of education attained by the women seemed to be evenly distributed among age groups 25-34 years and

≥35 years. For age group 25-34 years, secondary; 56 (50.5%) and tertiary; 84 (46.4%), while age group ≥35 years, secondary; 55 (49.5%) and tertiary; 91 (50.3%). The predominant average monthly income of the patients was between 20-50k (145; 45.6%), followed by 15-20k (110; 34.6%). The distribution between age group 15-24 years and 25-34 years was similar.

**Table 2: Test of Association between uterine leiomyoma and age groups.**

Variable		15-24 yrs	25-34 yrs	≥35 yrs	Chi-square	df	P-value
Type	Single	5 (2.2)	105 (47.1)	113 (50.7)	0.050	2	0.975
	Multiple	2 (2.1)	46 (48.4)	47 (49.5)			
	Total	7 (2.2)	151 (47.5)	160 (50.3)			
Location	Intramural	1 (1.4)	36 (49.3)	36 (49.3)	4.435	6	0.168
	Submucosal	0 (0)	34 (52.3)	31 (47.7)			
	Subserous	5 (3.20)	72 (46.5)	78 (50.3)			
	Sub/Intra/Sub	1 (4.0)	9 (36.0)	15 (60.0)			
	Total	7 (2.2)	151 (47.5)	160 (50.3)			

In Table 2, the age group 25-34 and ≥35 years were had the most frequency of multiple leiomyomas (46; 48.4%) and (46; 49.5%) respectively, while women who were 15-24 years were the least (2; 2.1%). Leiomyoma located at the subserous was the most observed for all groups;

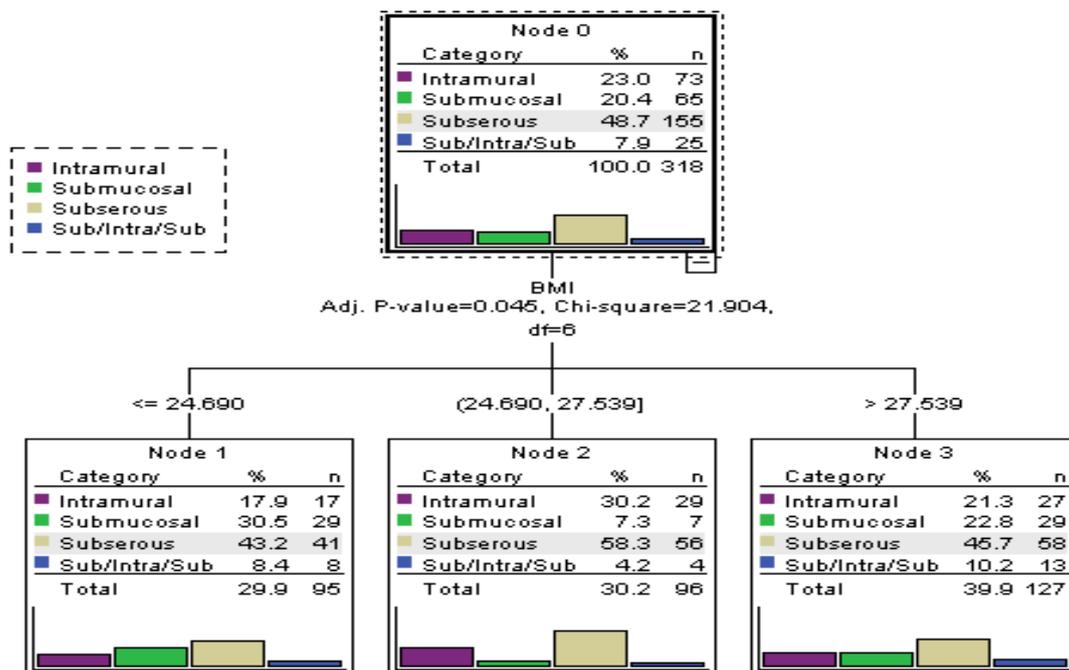
15-24 years (5; 3.20), 25-34 years (72; 46.5%) and ≥35 years (78; 50.3%). The distributional difference among the age groups were not significant for both type ( $\chi^2=0.050$ ,  $P=0.975$ ) and location ( $\chi^2=4.435$ ,  $P=0.168$ ) of uterine leiomyoma.

**Table 3: Test of Association between uterine leiomyoma and weight categorization of subjects.**

Variable		Normal	Overweight	Obese	Chi-square	df	P-value
Type	Single	70 (31.4)	112 (50.2)	41 (18.4)	0.593	2	0.743
	Multiple	34 (35.8)	45 (47.4)	16 (16.8)			
	Total	104 (23.7)	157 (49.4)	57 (17.9)			
Location	Intramural	19 (26.0)	41 (56.2)	13 (17.8)	13.031	6	0.043
	Submucosal	31 (47.7)	21 (32.3)	13 (20.0)			
	Subserous	45 (29.0)	85 (54.8)	25 (16.1)			
	Sub/Intra/Sub	9 (36.0)	10 (40.0)	6 (24.0)			
	Total	104 (23.7)	157 (49.4)	57 (17.9)			

In Table 3, overweight women had the highest frequency of both single and multiple leiomyomas (112; 50.2%) and (45; 47.4%) respectively, while obese women had the least frequencies of single (41; 18.4%) and multiple (16; 16.8%) leiomyoma. Overweight women were mostly observed with subserous (85; 54.8) and intramural (41;

56.2%), while submucosal were observed with normal women (31; 47.7%). BMI association with type was not significant ( $\chi^2=0.593$ ,  $P=0.743$ ); however, there was an association with location ( $\chi^2=13.031$ ,  $P=0.043$ ) of uterine leiomyoma.



**Fig. I: Decision tree for explaining the relationship between the studied epidemiological factors (age & BMI) and the location of the uterine leiomyoma.**

In Figure 1, BMI was the only significant explanatory variable ( $\chi^2=27.662$ ,  $P=0.045$ ). When BMI was  $\leq 24.69 \text{ kgm}^{-2}$  (node 1), it seemed to be associated with submucosal (43.2%), when compared to  $>24.69 \text{ kgm}^{-2}$  to  $27.54 \text{ kgm}^{-2}$  (node 4) that explained more of subserous (58.3%) and intramural (30.2%) leiomyoma. At BMI  $> 27.54 \text{ kgm}^{-2}$ , multiple of the location (13; 10.2%) was evident.

## DISCUSSION

In this study, subjects in the age group of  $\geq 35$  years had higher incidence of uterine leiomyoma followed by the age group of 24–34 years, which happened to be around the female reproductive years. Reports have shown that the risk of leiomyoma development increases with age.<sup>[9,10]</sup> The findings in this study is consistent with findings of<sup>[9,11,12]</sup> among Nigerians and<sup>[13]</sup> among Ghanaians, as they reported a near zero prevalence of uterine leiomyomas among ages less than twenty years, but the greatest prevalence from the age groups of 30 to 40 years (29.8%). It is believed that the prevalence and incidence of uterine leiomyoma is greatest at the late age because the symptoms are usually milder and tend to go unnoticed at early ages but become severe at the older ages, which then prompts the need to seek medical intervention.<sup>[9,14]</sup> Studies by<sup>[15,16,17,18]</sup> showed that women in ages 20-25 and 30-40 are the most often diagnosed with uterine leiomyoma, when compared to women who are older than 40 years. However, this may not be consistently correct as this study and studies by<sup>[9,10,11,12,13]</sup>, found that reproductive aged women (from ages 24 and above until menopause) were the most likely to be afflicted with uterine leiomyoma. Clinical incidence of uterine leiomyomas, in terms of asymptomatic diseases that eventually require some form of treatment and/or surgery have been reported to be the most frequent in perimenopause, but after menopause there is a sharp decline.<sup>[19]</sup>

Additionally, it should be noted that it is usually uncommon for leiomyomas to appear before puberty and also when women attain menopause, their frequency decreases greatly<sup>[2,20]</sup> and this have been reported by Edwards and Katali.<sup>[21]</sup>

The relationship between obesity and leiomyoma development has been inconsistent in empirical studies.<sup>[16,22]</sup> In some epidemiological studies<sup>[2,9,16,22,23]</sup> it was found that increased risk of leiomyoma development was associated with greater than normal BMI and the findings were consistent with the results of the prediction model of the decision tree in this study. It is believed that the influence of insulin resistance, together with elevated IGF-I and androgen levels is responsible for leiomyoma risk in obese women.<sup>[16,24]</sup>

The significantly higher BMI in leiomyoma subjects was associated with subserous leiomyomas, and multiple locations when compared with lower BMI. Luoto<sup>[25]</sup> in their study reported that women with higher BMI were

most predisposed to uterine leiomyomas. The possible explanation for this is that increased levels of circulating oestrogens is induced by the presence of aromatized androgens in peripheral fatty tissues of obese women.<sup>[24]</sup> But an inconsistency to this theory is that a large proportion of circulating oestrogens is derived from the ovaries in premenopausal women.<sup>[9]</sup> Certainly, the closest explanation to the possible predisposition of obese women to leiomyomas is reduced hepatic secretion of sex hormone binding globulin (SHBG), which causes and increase in available oestrogens and androgens.<sup>[9,16,24]</sup>

He<sup>[26]</sup> found out that in premenopausal Asian women with a high BMI, there was increased risk of leiomyomas. However, according to<sup>[27]</sup>, there was no association between BMI and the risk of leiomyomas among Italian women.

Obesity is presumed to be significant for the racial differences in the risk of leiomyoma, because in US, it is most prevalent among blacks, and this has produced complex non-linear relationship between BMI and leiomyoma risk.<sup>[28]</sup> Other cofounding variables such as parity, extent of obesity, and bias in detection has also widened the possibility of any linear relationship. Wise<sup>[9]</sup> had also reported a positive association between weight gain at adulthood and leiomyoma risk and the relationship between BMI and leiomyoma risk was most significant in surgically confirmed cases.<sup>[9,28]</sup>

## CONCLUSION

From the findings, it could be concluded that higher body mass index (BMI) and age was significantly associated with the incidence and location of the different types of the leiomyoma. This revealed that women located around the region of the study should see that they remain within the normal weight range. And also women who seem to be advancing in age probably due to pursuit of career or other things should endeavour to go for periodic medical check-up so as to start early treatment if uterine leiomyoma is suspected.

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## REFERENCES

1. Wallach, E.E. and Vlahos, N.F. (Uterine myomas: an overview of development, clinical features, and management). *Obstetrics and Gynaecology*, 2004; 104(2): 393–406.
2. Parker, W.H. (Etiology, symptomatology, and diagnosis of uterine myomas). *Fertility and Sterility*. 2007; 87(4): 725–736.
3. Sankaran, S. and Manyonda, I.T. (Medical management of fibroids). *Best Practice Research*

- and *Clinical Obstetrics and Gynaecology*, 2008; 22(4): 655–676.
4. Ryan, G.L., Syrop, C.H., Van Voorhis B.J. (Role, epidemiology, and natural history of benign uterine mass lesions). *Clinical Obstetrics and Gynaecology*, 2005; 48: 312–324.
  5. Day, B.D., Dunson, D.B., Hill, M.C., Cousins, D., and Schectman, J.M. (High cumulative incidence of uterine leiomyoma in black and white women: ultrasound evidence). *American Journal of Obstetrics and Gynaecology*, 2003; 188(1): 100–107.
  6. Govan; Macfarlane, Callander. *Pathology Illustrated*. 2<sup>nd</sup> ed. Churchill Living Stone, 2002; 687- 694.
  7. Evans, P. and Brunsell, S. (Uterine fibroid tumors: Diagnosis and treatment). *American Family Physician*, 2007; 75(10): 1503-1508.
  8. Catherino, W.H., Eltoukhi, H.M., and Al-Hendy, A. (Racial and ethnic differences in the pathogenesis and clinical manifestations of uterine leiomyoma). *Seminars in Reproductive Medicine*, 2013; 31(5): 370-379.
  9. Wise, L.A., and Laughlin-Tommaso, S.K. Uterine leiomyomata. In: Goldman MB, Troisi R, Rexrode KM, editors. *Women and Health*. San Diego: Academic Press, 2013; 285–306.
  10. Lawal, Y., Yaro, I.B., Rabi, A., and Emmanuel, R. (Prevalence and sonographic patterns of uterine fibroids in Northern Nigeria). *New Nigeria Journal of Clinical Research*, 2019; 8: 24-29.
  11. Okogbo, F.O., Ezechi, O.C., Loto, O.M., Ezeobi, P.M. (Uterine leiomyomata in south western Nigeria: A clinical study of presentations and management outcome). *African Health Sciences*, 2011; 11: 271-278.
  12. Omole-Ohonsi, A., and Belga, F. (Surgical management of uterine fibroids at Aminu Kano teaching hospital). *Obstetrics and Gynaecology International*, 2012: 702325.
  13. Sarkodie, B.D., Botwe, B.O., Adjei DN, and Ofori, E. (Factors associated with uterine fibroid in Ghanaian women undergoing pelvic scans with suspected uterine fibroid). *Fertility Research Practice*, 2016; 2: 9.
  14. Garba, I., Ayyuba, R., Adewale, T.M., Abubakar, I.S. (Surgical management of uterine fibroids at Aminu Kano teaching hospital). *Nigerian Journal Basic Clinical Sciences*, 2016; 13: 50-54.
  15. Fleischer, R., Weston, G.C., Vollenhoven, B.J., Rogers, P.A. (Pathophysiology of fibroid disease: angiogenesis and regulation of smooth muscle proliferation). *Best Practice and Research Clinical Obstetrics and Gynaecology*, 2008; 22(4): 603-614.
  16. Okolo, S. (Incidence, aetiology and epidemiology of uterine fibroids). *Best Practice Research and Clinical Obstetrics and Gynaecology*, 2008; 22: 571–88.
  17. Duhan, N. (Current and emerging treatments for uterine myoma - an update). *International Journal of Womens Health*, 2011; 3: 231–241.
  18. Sparic, R. (Uterine myomas in pregnancy, childbirth and the puerperium). *Srpski Arhiv za Celokupno Lekarstvo*, 2014; 142(1-2): 118–124.
  19. Gupta, S., Jose, J., and Manyonda, I. (Clinical presentation of fibroids). *Best Practice and Research Clinical Obstetrics and Gynaecology*, 2008; 22(4): 615–626.
  20. Othman, E.E., and Al-Hendy, A. (Molecular genetics and racial disparities of uterine leiomyomas). *Best Practice and Research Clinical Obstetrics and Gynaecology*, 2008; 22(4): 589–601.
  21. Edwards, J., and Katali, H. (A Novel Case of Fibroids after Menopause). *Case Reports in Obstetrics and Gynaecology*, 2018; Article ID: 9104719, 2 pages.
  22. Wise, L.A., Palmer, J.R., Spiegelman, D., Harlow, B.L., Stewart, E.A., Adams-Campbell, L.L., and Rosenberg, L. (Influence of body size and body fat distribution on risk of uterine leiomyomata in U.S. black women). *Epidemiology*, 2005; 16(3): 346-354.
  23. Lethaby, A.E., and Vollenhoven, B.J. (Fibroids uterine myometosis, leiomyomas). *BMJ Clinical Evidence*, 2007; 0814–0814.
  24. He, Y., Zeng, Q., Li, X., Liu, B., and Wang, P. (The association between subclinical atherosclerosis and uterine fibroids). *Public Library of Science (PLoS) One*, 2013; 8(2): e57089–e57089.
  25. Luoto, R., Kaprio, J., Rutanen, E.M., Taipale, P., Perola, M., Koskenvuo, M. (Heritability and risk factors of uterine fibroids--the Finnish Twin Cohort study). *Maturitas*, 2000; 37(1): 15–26.
  26. He, Y., Zeng, Q., Dong, S., Qin, L., Li, G., and Wang, P. (Associations between uterine fibroids and lifestyles including diet, physical activity and stress: a case control study in China). *Asia Pacific Journal of Clinical Nutrition*, 2013; 22(1): 109–117.
  27. Chiaffarino, F., Parazzini, F., La Vecchia, C., Chatenoud, L., Di Cintio, E., & Marsico, S. (Diet and uterine myomas). *Obstetrics and Gynecology*, 1999; 94(3): 395–398.
  28. Uimari, O., Suomalainen-Konig, S., Sakkinen, N., Santala, M., Nieminen, P., and Ryyanen M. (Natural history of familial myomas). *European Journal of Obstetrics Gynecology and Reproductive Biology*, 2006; 125(2): 255–258.