



## Relating age at menarche and pelvic pain with occurrence of uterine leiomyomata in South-Eastern Nigeria

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### Abstract

Uterine fibroids affect about 25% of women of reproductive age. This study, therefore, aims to relate Age at Menarche (AAM) and pelvic pain with the occurrence of Uterine Leiomyomata (UL) in South-Eastern Nigeria. The study was carried out in the radiology lab of three hospitals and two diagnostic Centers covering the three senatorial zones in Imo State, Nigeria; Owerri, Orlu and Okigwe. A non-interventional cross-sectional descriptive study with eligible participants (3301) was recruited by convenience sampling method using a structured questionnaire. AAM was found as a significant factor of UL ( $p=0.0001$ ,  $\chi^2=140.64$ ). This indicates that for the menarche age of 11 years or less, the risk of having UL is significantly 6 times more compared to that of the 12-13 years menarche age ( $p<0.0001$ ,  $RR=6.24$ ,  $95\%CI=4.88-7.88$ ), and 7.5 times more compared to risk at not less than 14 years menarche age ( $p<0.0001$ ,  $RR=7.53$ ,  $95\%CI=5.16-11.12$ ). The result of this study demonstrates a significant correlation between age at menarche and the occurrence of uterine fibroids. Early menarche age increases the risk of uterine fibroid incidence, whereas pelvic pain is more likely a gynaecological manifestation of uterine fibroid, rather than a risk factor.

**Keywords:** Age at Menarche, Pelvic pain, Uterine Leiomyomata, Risk factors

### Introduction

Uterine Leiomyomata (UL), also referred to as uterine myomas, leiomyomas, myomas, or simply fibroids are benign soft-tissue tumours that project from uterine smooth muscle tissues (Bulu, 2013; Stewart *et al.*, 2013). First described in 1793 by Matthew Baillie of St George's Hospital, London, they have been described numerously to be hormone-dependent and uterine structure-damaging. UL are a major public health problem among women, occurring more

frequently in women of reproductive age and are associated with diverse symptoms (Laughlin *et al.*, 2010; Marsh *et al.*, 2013). The malignant version of a fibroid is extremely uncommon and termed leiomyosarcoma (Ezeama *et al.*, 2012). UL affects as many as three in four black women at some point in their lives. It is a benign tumour composed of myometrial and connective tissues (Yakasai *et al.*, 2013; Baird *et al.*, 2013). According to Baird *et al.* (2013), risk factors for developing ULs includes age, early age at menarche and the use of oral

contraceptives before 16 years of age have been observed. Factors such as age, age at menarche (Choi & Kim, 2010), and ethnicity cannot be altered or modified. UL risk decreases as the age of menarche increases and increased weight before puberty is strongly linked to early menarche, which can be delayed by exercise. Importantly, the greater UL burden observed in black women declines with increasing age (Qin *et al.*, 2010). UL development enhances with age during the reproductive years (Walker *et al.*, 2015). ULs are mainly premenopausal, decreasing in frequency with menopause. The development of ULs is also statistically associated with early menarche – women who have menarche at an advanced age are affected less frequently (Wise & Laughlin-Tommaso, 2016). This early onset of puberty increases the overall lifetime exposure to estrogen, which increases the risk of UL development and can also lead to adverse health problems later in life, such as depression and obesity. Early Menarche increases the risk of developing ULs and a risk factor for other diseases, such as breast cancers (Khan *et al.*, 2014). Premature menstruation at ages younger than 10 results in an increased risk of UL, however, late menstruation after the age of 16 years old results in a reduced risk of UL. After menopause, when the estrogen level reduces, the number and size of ULs reduce significantly (Dragomir *et al.*, 2010). Most of the older studies has these findings confirmed by newer data. The biological mechanisms are not understood, and they may or may not be the same for the different hormonally mediated conditions (Velez *et al.*, 2013). Risk factors are features related to a condition typically identified by epidemiological studies. Early menarche may swell the number of cell divisions that the myometrium undergoes during the reproductive years, leading to a higher risk for mutations in myometrial proliferation (Ip *et al.*, 2009). UL cell size is significantly smaller in postmenopausal women when endogenous estrogen levels are low (Wise & Laughlin-Tommaso, 2016). The risk of developing ULs increased in women with early menarche (<10 years old) due to longer exposure to ovarian hormones over the years. Therefore, this research work aimed to relate age at menarche (AAM) and pelvic pain with the occurrence of uterine leiomyomata in South-Eastern Nigeria

## Materials and Method

### Study Area

The study was carried out in the radiology, Obstetrics and Gynaecology departments of three hospitals and two diagnostic Centers covering the three senatorial zones, Owerri, Orlu and Okigwe in Imo State, South-eastern Nigeria. Owerri zone consists of Federal Medical Centre Owerri and Ever Right Diagnostic Centre. Okigwe Zone consists of Okigwe General Hospital and Okigwe Medical Centre. Orlu Zone consists of Imo Teaching Hospital Umuna from the period of October 2020-March 2021. These facilities are selected because they serve as referral points for all other smaller hospitals in Imo State.

### Research Design

The study was a non-interventional cross-sectional descriptive study with eligible participants recruited by convenience sampling method. Four hundred and thirty-four women were calculated for the minimum sample size using Cochran's sample size formula for cross-sectional studies. The study population were all presenting women of reproductive age (15-49) that reside in the 3 senatorial zones who met the selection criteria within the period of study. Before being considered for study entry, each potential subject has a complete gynecologic evaluation by a study physician to exclude women with concomitant issues. All women who attended Gynecology OPD with complaints of menstrual disorders, with anaemia or abdominopelvic mass with pain and feeling heaviness in the abdomen were also registered for the study. At the beginning of each day's gynaecological clinic, patients who visited the clinic to seek care for UL were assembled and addressed and then those that consented to be part of the study were recruited. For those who accept to participate in this study, informed written consent was obtained from each participant. All consenting women presenting for a pelvic ultrasound between the ages of 16 and 50 years were included in the study. Women who declined consent, women below the age of 16 years, and women above the age of 50 years were excluded from the study. Recruitment for participants ceased on observation of theoretical saturation of data. Eligible women were recruited for this study from the selected facilities in the 3 senatorial zones of Imo State consecutively until the desired sample size was attained. This study lasted from October 2020-March 2021, 6 months.

## Sampling Procedure

Each participant completed a single interview. All interviews took place in a private consultation room at each of the facilities. The patients were interviewed to elicit important relevant history and to ensure that they fulfill the set inclusion criteria for the study. A semi-structured interview guide was utilized to elicit conversation about pertinent topics while allowing for patients to share their experiences. Here qualitative data were collected to provide elaboration, clarification, and explanation for the quantitative results. To collect data, a routine demographic computerized file was kept for every patient and pelvic transabdominal ultrasonography was performed. We retrieved from each patient their age at the time of consultation, weight, height, history of pelvic pain and age of menarche, Through the ultrasound examination, we recorded the presence of uterine myomas. On recruitment into the study, a structured questionnaire was administered to the respondents. The questionnaire was used to collect data regarding their socio-demographic details, age at menarche, use of oral contraceptives, associated comorbidities. The mode of data collection was face-to-face interviews based on a standardized questionnaire. A structured and a pretested interviewer-administered

questionnaire containing both open and closed-ended questions was administered to each consenting respondent. The independent variables in this study were menarche age and pelvic pain. The dependent variables were uterine fibroid. The data collected were analysed and the results were presented in tables.

## Results

A total of 3301 eligible women attended the gynaecological section at the clinics of study within the study period (October 2020 to March 2021). The women who consented to the study were 2965 (90%) in all and they were all included in the study.

Table 1 represents the socio-demographic and gynaecological characteristics of the women. Based on the study conducted at selected facilities across the 3 senatorial zones of Imo state in 2020 - 2021, the following results were obtained: For the majority of the women (84.2%) the age at menarche was 12 -13 years, while up to 91 (3.1%) responded that their age at menarche is unknown to them. The majority (68.6%) indicated that they experience irregular menstrual cycles and a similar proportion (67%) number experience pelvic pain.

**Table 1: Gynaecological characteristics of respondents (2965) across selected facilities (2020-2021)**

Characteristics	Frequency (n)	Percent (%)
<b>Age at Menarche (years)</b>		
≤11	132	4.4
12 – 13	2497	84.2
>14	246	8.3
Unknown	91	3.1
<b>Type of Menstrual Cycle</b>		
Normal	937	31.6
Irregular	2033	68.6
<b>Pelvic pain</b>		
Yes	1987	67.0
No	978	33.0

Age at Menarche was also found as a significant factor of UL ( $p=0.0001$ ,  $\chi^2=140.64$ ). Women who observed their first menstrual cycle on or before 11 years of age were found to be at greater risk compared to others (Table 2). The rate of UL was found to be 62.1% on the studied women menarche age of 11 years old or less while it was approximately 18% among the

women whose age at menarche were at least 14 years old. For the menarche age of 11 years or less, the risk of having UL is significantly 6 times more compared to that of the 12-13 years menarche age ( $p<0.0001$ ,  $RR=6.24$ ,  $95\%CI=4.88-7.88$ ), and 7.5 times more compared to risk at not less than 14 years menarche age ( $p<0.0001$ ,  $RR=7.53$ ,  $95\%CI=5.16-11.12$ ).

**Table 2: Occurrence of Uterine Leiomyomata pertaining to Menarche age in the Study Area**

Factor	Total	Number	%	UL: Yes		RR (95% CI)	p
				Number	%		
12 - 13	2497	520	20.8	1977	79.2	6.24 (4.88 – 7.88)	<0.0001
≥14	246	44	17.9	202	82.1	7.53 (5.16 -11.12)	<0.0001
Unknown	90	6	6.7	84	93.3	23.0 (10.11-4.38)	<0.0001
Total	2965	652	22.0	2313	78.0		<0.0001 ( $\chi^2=140.6$ )

## Discussion

There was a clear relationship between age at menarche and fibroid development as confirmed by other studies and implies a stronger relationship for women with multiple fibroids and shows a stronger inclination for early-onset disease (Table 4.4). Additionally, respondents with age at menarche ( 11 years) were most at risk of having multiple fibroids in comparison with those with a mean age of menarche of 12–13. These outcomes are regular with past studies that have implied that early menarche age is strongly related to developing ULs (Velez *et al.*, 2013, Wise & Laughlin-Tommaso, 2016). The outcomes reflect early age at menarche related to fibroids across all 3 fibroid types assessed. This is consistent with the Uterine Fibroid study findings, in which similar findings were seen across fibroid types (Yu *et al.*, 2018). According to Radin *et al.* (2010) findings from the Black Women’s Health Study cohort, early menarche at or before the age of 11 years was associated with a 25 percent increase in risk compared with menarche at the ages of 12 and 13 years, the same magnitude of the effect was reported for women in the Nurses’ Health Study cohort (Radin *et al.*, 2010; Wise *et al.*, 2013). In both studies, the risk also continued to decrease as the age of menarche increased. Increased prepubertal weight was opined to be a strong risk factor for early menarche (Collective, 2010) and exercise can delay it. Perhaps childhood obesity or exercise is also related to fibroid development. Girls who have early menarche have been reported to move through the stages of puberty faster than girls with later menarche (Velez *et al.*, 2013). This difference may reflect enhanced tissue sensitivity to hormones and/or suppressed feedback controls of steroid production. Low birth weight or small-gestational-age birth weight has been associated with early menarche (Ezeoma *et al.*, 2012). In past

studies assessing the association between early age at menarche and fibroids, there have been speculations on biological nuances and the role of hormones in fibroid risk. The explanation proffered for the observed associations includes an additional year of hormonal cycles confers additional risk for developing ULs (Aissani, *et al.*, 2015) therefore ULs enhance an estrogen-enriched environment and react actively than normal myometrium to estrogens. Age at menarche (AAM) has been proffered as a risk factor for UL (Velez *et al.*, 2013; Terry *et al.*, 2010; Wise and Laughlin-Tommaso, 2016). Women with an early AAM have, typically, a longer period of menstrual periods in their life including more exposure to estrogens, promoting the growth of UL.

## Conclusion

Our study indicates that irregular menstrual cycles and earlier menarche are risk factors for Uterine Leiomyomata, based on this study results, we can conclude that the majority of patients with uterine fibroid had menarche at < 11 years old. For the menarche age of 11 years or less, the risk of having UL is significantly 6 times more compared to that of the 12-13 years menarche age ( $p < 0.0001$ , RR=6.24, 95%CI = 4.88 – 7.88) and 7.5 times more compared to risk at not less than 14 years menarche age. Irregular menstrual cycle in women with uterine fibroid is more likely an expression of this disease, rather than the risk factor for the occurrence of Uterine Leiomyomata. The result of this study calls for yearly ultrasound scans for screening of fibroids commencing from earlier ages to achieve the goal of early diagnosis, effective awareness/screening strategy be adopted in line with efforts to meet the millennium development goals on maternal mortality and morbidity.

## Authors contribution:

Author Eze Chinwe Catherine designed the study, performed the statistical analysis, wrote the protocol, wrote the first draft of the manuscript, finalized the paper, made critical revisions and supervised editing. Authors Okemadu Obioma Christian, Obiora Onuabuchi Udochi and Ezenwata Ifeoma Susan contributed to writing of the manuscript, Onyemeka Regland Michael did the editing, revised and assisted in reformatting the manuscript and conclusions. Nelson Okwudiri Chibundu reviewed and contributed to the writing of the manuscript. All authors read and approved of the final manuscript.

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## Conflicting interests

The authors declare that there are no conflicting interests.

## Ethics approval

Consent was obtained or waived by all participants in this study.

## Disclosure

This study was independently self-funded by the researcher.

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