

Original Research Article

Correlation of Profiled Sonographic Uterine Fibroids Characteristics with Oestrogen Levels in Reproductive Age Women at Levy Mwanawasa University Teaching Hospital, Lusaka, Zambia

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Received: 05.02.2026

Accepted: 27.03.2026

Published: 30.03.2026

Journal homepage:<https://www.easpublisher.com>**Quick Response Code**

Abstract: Background and Objective: Among Zambian women, uterine fibroids are the most common benign gynaecological tumours, causing significant morbidity and infertility. There is inadequate information demonstrating a link between the sonographic features of uterine fibroids and blood oestrogen levels, despite theories suggesting oestrogen as the main risk factor. The study aimed to explore the relationship between the profiled sonographic characteristics of uterine fibroids and oestrogen hormone levels in women of reproductive age (15-49 years) at Levy Mwanawasa University Teaching Hospital (LMUTH), Lusaka, Zambia. **Methodology:** This was a quantitative, cross-sectional study. One hundred and forty-two reproductive-age women confirmed to have uterine fibroids on ultrasound were recruited. An ultrasound was performed, followed by a laboratory test for oestrogen levels. A questionnaire was also used to obtain participants' demographic, uterine fibroid sonographic characteristics and oestrogen hormone levels. Descriptive and inferential statistics were run for the analysis. **Results:** The median age was 33years (IQR 29-38), and the BMI median was 30 (IQR 24.6-35). The majority of the participants were either overweight or obese (61.1%). Furthermore, the majority were nulliparous (35%) and had a positive family history of fibroids (61%). The prevalence of elevated oestrogen levels among uterine fibroid participants was 61.3% (N=87/142). There was a statistically significant association between the size of UFs and oestrogen level ($r = 0.844, p = 0.001$), statistically significant positive relationship between submucosal UFs and oestrogen hormone level ($r = 0.513, p = 0.001$). There was a significant positive relationship between hypoechoic fibroids and oestrogen hormone level observed ($r=0.290, p = 0.001$), the number of UFs against oestrogen level showed a strong positive relationship ($r=0.710, p= 0.001$). **Conclusion:** The study reviewed that there is a correlation between oestrogen hormone level and sonographic characteristics of uterine fibroids. These research findings have provided insights that could improve the diagnosis and treatment of uterine fibroids in the Zambian population.

Keywords: Correlation, Profiled, Sonographic, Uterine Fibroids, Oestrogen.

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INTRODUCTION

Uterine fibroids (UFs), also known as myomas or leiomyomas, are common benign muscle tumours that develop in the uterine wall (Rachael, 2021). There may be one predominant uterine fibroid or a cluster of many fibroids (Longo and Bulun, 2013). According to Outi *et al.*, (2022), uterine fibroids are the most prevalent benign tumours impacting millions of women globally and have a 75% incidence among reproductive-age women. They

occur at all ages, from menarche to menopause (Stewart, Cookson, Gandolfo *et al.*, 2017; Wise and Laughlin, 2016).

A study done by Wango *et al.*, (2002) on the relationship between uterine fibroid tissue and Oestrogen hormone levels, revealed that UF tissue contained significantly higher levels of oestrogen receptor and progesterone. Lipman (2021) also explained that when oestrogen levels are too high, this can lead to the growth

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of fibroid tumours, and with insufficient progesterone, the body has no way to stop this growth.

Globally, the use of ultrasound to diagnose and monitor the growth of fibroids has been well accepted (Sarkodie *et al.*, 2016a; Khan, Shehmar, and Gupta, 2014). This is the case even in Zambia despite a steady increase in the availability of other imaging modalities like Computed Tomography (Kafwimbi *et al.*, 2021). According to (Sarkodie *et al.*, 2016b; Khan, Shehmar, and Gupta, 2014), uterine fibroids show various echo patterns on ultrasound, such as hypo-echoic, iso-echoic, hyper-echoic, and mixed echo pattern. Uncomplicated fibroids are mostly hypo-echoic, but can be iso-echoic or hyper-echoic compared to normal myometrium, while calcification, which could be associated with a degenerated fibroid, is seen as echogenic foci with shadowing (Sarkodie *et al.*, 2016a; Khan, Shehmar, and Gupta, 2014). Furthermore, the International Federation of Gynaecology and Obstetrics (FIGO) classification system described uterine fibroids as pedunculated, submucosal, intramural, or subserosal (Lalezarian, 2018). Submucous fibroids, which extend into the uterine cavity, tend to be the most disruptive to endometrial integrity as compared with other fibroids.

Among Zambian women, Uterine fibroids were the most common findings recorded in the 2022 Sonography register at Levy Mwanawasa University Teaching Hospital (LMUTH). Despite the well-known fact that Oestrogen is pronounced as the main contributing factor to uterine fibroid pathogenesis (Outi *et al.*, 2022; Morhason *et al.*, 2022), Oestrogen tests are neither requested nor performed among UF clients presenting for management at the LMUTH. This is because of the scarcity in the laboratory reagents. Furthermore, there are no guidelines to enable clinicians to routinely request oestrogen tests in Zambia.

Evidence showing a relationship between the sonographic profile of UFs and Oestrogen blood levels in the reproductive age group (15-49 years) of Zambian women is largely unknown. This study aimed to establish whether a link exists between profiled sonographic uterine fibroid characteristics and oestrogen hormone levels in women in the reproductive age range of 15–49 years at LMUTH Lusaka, Zambia.

METHODOLOGY

Study Design: This study employed a hospital-based, quantitative cross-sectional study.

Study Site

The study site was the LMUTH Radiology and Laboratory departments. The site was selected because of its centrality and its status as one of the main referral hospitals for the province.

Population and Sample Size

The population in this study was women of reproductive age group between 15 and 49 years confirmed or perceived to have uterine fibroids, who had a request form for pelvic Ultrasound examination and sought medical attention at LMUTH from October 2023 to February 2024. Only women willing to participate in the study were included. The exclusion criteria included: pregnant women, women on contraceptives, and women on hormonal replacement therapy.

A cross-sectional study formula was used to calculate the 142-sample size using the formula

$$n = (Z^2 * p * (1 - p)) / E^2$$

The systematic sampling formula, $K=N/n$, was used.

Data Collection Process

After obtaining consent, a pelvic ultrasound was conducted on women of reproductive age presenting with a clinical history of fibroids, as well as those perceived to have uterine fibroids. The ultrasound was performed in accordance with the standard operating procedure for pelvic examination. The participant was then assisted to complete a questionnaire, which solicited personal details such as age, educational background, marital status, and clinical information related to fibroids. Following the completion of the questionnaire, the patient was sent for laboratory evaluation of oestrogen level. The process flow is illustrated in Figure 1.

Data Management and Analytical Tests

Data collected from each client was coded and double-entered in an Excel spreadsheet to guarantee accuracy before being uploaded to the analytic software. For continuous data, Shapiro Wilk Test was performed to check for data normality (data were not normally distributed [$p < 0.05$]). Median (with associated Interquartile range) and percentage were used to describe the data. Nonparametric correlational analysis (Spearman Rank Correlation) was used to determine the association between uterine fibroid characteristics and oestrogen results. The statistical analytical tools used are Microsoft Excel and Statistical analysis was performed using GraphPad Prism version 8.0.1(244) and Stata version 16.0.

Ethical considerations

The ethical considerations are that; The research was approved at the University of Zambia Post Graduate Proposal forum. Thereafter, study approval was obtained from University of Zambia Research Ethics Committee (UNZABREC REF. NO 4072-2023), ethical clearance was sought from National Health Research Authority (REF. No. NHRA 00012/06/09/2023) and permission to proceed with the study was obtained from Lusaka Provincial Health Office (LSKPHO/101/8/1) and LMUTH Research Committee through authorization letters.

Informed consent, anonymity, privacy, confidentiality, risks, and participants in the study were

observed. The selection of participants was not based on the personal preferences of the researchers but on the principle of empirical methods. In this study, Informed consent was obtained from the respondents after explaining to them the purpose of the study and how the results would be utilized.

RESULTS

Baseline Participant Characteristics

A total of 142 individuals participated in the study. Although the study inclusion criteria encompassed the reproductive age range of 15 to 49 years, no participants aged 15 - 23 years were recorded. Therefore, in this study, UFs were more common in advanced reproductive age than in younger age. Table 1 below illustrates the baseline characteristics of the study participants.

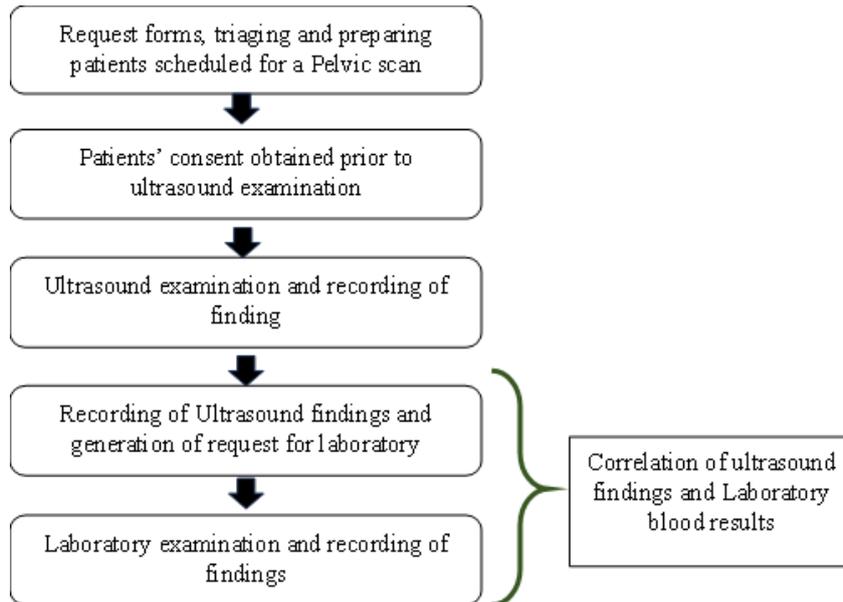


Figure 1: Data collection process

Table 1: Baseline characteristics of study participants

Variable	Category	
BMI (median, IQR)		30 (24.6-35)
BMI categorization (N, %)	Underweight	1(0.7%)
	Normal	54(38%)
	Overweight	19(13.4%)
	Obese	68(47.9%)
Age (median, IQR)		33(29-38)
Employment status (N, %)	Employed	63(44.4%)
	Unemployed	51(35.9%)
	Self employed	28(19.7%)
Educational status (N, %)	Primary School	17(12%)
	Junior High School	10 (7%)
	Senior High School	32(23%)
	Tertially	20 (14%)
	Post graduate	63(44%)
Family history (N, %)	Postive	87 (61%)
	Negative	55(39%)
Number of pregnancies (N, %)	None	50 (35%)
	1	34(24%)
	2	28(20%)
	>/=3	30(21%)

Hormone Level Profile: The majority of the participants had elevated oestrogen levels as depicted in Table 2.

Table 2: Oestrogen level in the different BMI categories

BMI Categorization	Oestrogen level	
	Normal (N=55)	High (N=87)
Underweight	1	
Normal	20	1
Overweight	33	16
Obese	1	70

Sonographic Categorization

Most of the participants had multiple fibroids, and these were in different sites. Furthermore, one individual could have multiple types of fibroids.

Additionally, the size range was very vast (from 0.6cm³ to 527.2 cm³). The sonographic features are summarized in Table 3.

Table 3: Sonographic features

Feature	Detail	N	%
Number of fibroid locations per participant (N, %)	One site	24	17
	Two sites	71	50
	three or more sites	47	33
Overall distribution	Anterior	97	32
	Posterior	112	37
	Fundal	88	29
	Lower uterine segment	9	3
Number of fibroid types per individual	1	26	18
	2	84	59
	3	31	22
	4	1	1
Types of uterine fibroid	intracavitoy	6	2
	Intramural	120	41
	Submucosal	55	19
	Subserosal	92	32
	Pedunculated	10	3
Uterine fibroid size and echogenicity	Cervical	9	3
	hypoechoic	132	89
	hyperechoic	12	8
Fibroid size (median, IQR)	isoechoic	5	3
		78.55(3.3-156)	

Correlation of Sonographic Characteristics of Uterine Fibroids with Oestrogen Biological Reference Level/Interval

The results indicated a statistically significant positive correlation between the size of uterine fibroids and oestrogen hormone using the biological reference level. The findings implied that the higher the oestrogen level, the larger the uterine fibroid size among participants. In terms of the type of fibroids, only submucosal fibroids were associated with elevated oestrogen levels.

When the echo pattern was evaluated, hypoechoic fibroids were found to be associated with an increase in oestrogen hormone. Iso-echoic echogenicity had a weak negative correlation with oestrogen hormone levels. Furthermore, an increase in the number of fibroids an individual had was also associated with an increased oestrogen level. The profiled sonographic characteristics correlation of uterine fibroids with oestrogen hormone level using the oestrogen biological reference level has been summarized below in Table 4.

Table 4: Shows the profiled sonographic characteristics correlation of uterine fibroids with the oestrogen hormone biological reference range

No	Ultrasound Characterization	Spearman r	p-value	Confidence interval	
1.	Uterine fibroid size (cm ²)	0.844	0.001	0.7868 to 0.8865	
2	Location of uterine fibroid	Intramural	-0.061	0.472	-0.2279 to 0.1099
		Intracavitary	0.095	0.260	-0.07558 to 0.2604
		Submucosal	0.513	0.001	0.3768 to 0.6283
		Subserosal	0.171	0.042	0.001043 to 0.3305
		Pedunculated	0.106	0.210	-0.06483 to 0.2705
	Cervical	0.147	0.080	-0.02257 to 0.3093	

3.	Echogenicity	Hypoechoic	0.290	0.001	0.1264 to 0.4377
		Isoechoic	-0.240	0.004	-0.3937 to -0.07377
		Hyperechoic	-0.226	0.007	-0.3811 to -0.05895
4.	Number of fibroids		0.710	0.001	0.7868 to 0.8865

DISCUSSION

Studies have identified age and obesity as risk factors for the development of fibroids. In this study, uterine fibroids were more prominent in older women than in young age as no participants between 15-23 years were recorded. The findings are consistent with studies by Sabry *et al.*, (2012), Sarkodie *et al.*, (2016a), who established that uterine fibroids are mainly associated with women in the older reproductive age group rather than the younger age categories.

Obesity has been linked to an increased likelihood of developing uterine fibroids. Studies suggest that increased adipose tissue may promote fibroid development because of increased adipose tissue's metabolic processes (Botia *et al.*, 2017; Adawe *et al.*, 2022). In this study, most participants were classified as being obese. This finding is in keeping with several studies that associate high BMI with the presence of fibroids (Sarkodie *et al.*, 2016b; Ciebiera *et al.*, 2016; Sun *et al.*, 2019).

Another factor associated with fibroids is the elevated levels of oestrogen. Borahay *et al.*, (2017); Morhason *et al.*, (2022); Sarkodie *et al.*, (2016b), and Longo and Bulun (2013) acknowledge oestrogen hormone as one of the main factors contributing to the risk and pathogenesis of uterine fibroids. This is due to its pronounced effect on various gene expressions involved in the control of cell growth and apoptosis. Our study findings also reflect the association between increased oestrogen and fibroids, with 61.3 % of those with fibroids having laboratory results showing elevated levels of oestrogen.

Furthermore, the findings are similar to those of Borahay *et al.*, (2017) on oestrogen receptors and signalling in Fibroid Pathobiology. Clinical and laboratory studies support the essential role of oestrogen in the development and growth of fibroids. In the study, it was established that although plasma oestrogen levels are similar in women with and without fibroids, tissue levels are higher in women with fibroids. The study findings are also similar to Wango *et al.*'s (2002) study, which found that uterine fibroid tissue contained significantly higher levels of oestrogen receptor (28.2 ± 1.6 vs 19.1 ± 0.4 fm/mg protein) and progesterone receptor (16.8 ± 0.7 vs 9.4 ± 0.2 fm/mg protein) compared to normal myometrial tissue.

Studies have investigated the sonographic features of uterine fibroids (Sarkodie *et al.*, 2016) and the association of oestrogen levels with uterine fibroid myometrial tissue and non-fibroid myometrial tissue

(Wango *et al.*, 2002; Alsudairi, 2021; and Outi *et al.*, 2022). Our study sought to characterize sonographic features with oestrogen levels. The characteristics considered were the size, type, echogenicity, and number of fibroids.

Bivariate association revealed a statistically significant positive relationship between the size of uterine fibroids and the biological reference level (BRL) / interval of oestrogen hormone among the participants. Although the study focused on sonographic characteristics of uterine fibroids in relation to oestrogen hormone levels and not on uterine fibroids in general, the results align with studies (Ofori *et al.*, 2012; Sarkodie *et al.*, 2016a; Sefah *et al.*, 2023) which expressed that oestrogen plays a significant role in the development and growth of uterine fibroids, with high levels of this hormone often leading to increased fibroid size and associated symptoms.

In terms of the relationship between sonographic type characterization and oestrogen level, our study revealed that the submucosal type of fibroids showed a statistically significant positive correlation with oestrogen level. In tissue analysis, Marugo *et al.*, (1989) also observed that oestrogen was significantly more in submucosal than in subserosal myomas, both in proliferative and in the secretory phase of the cycle.

Our study indicated a statistically significant positive relationship between hypoechoic fibroids and oestrogen hormone levels. Isoechoic echogenicity demonstrated a significant negative relationship with oestrogen, while hyperechoic fibroids also showed a negative relationship with oestrogen hormone level using Spearman's correlation. Hyperechoic fibroids and oestrogen hormone levels showed a negative association. These findings are similar to Lipman (2021), who explained that uterine blood vessels supply the all-important nutrients that keep fibroids alive. With rapid growth, the centre of the fibroid gets further away from where the nutrients are coming from, and these areas can become ischemic and often die. This degeneration process can lead to thin, eggshell-like calcification in the fibroid (Lipman, 2021).

The number of uterine fibroids and oestrogen level using Spearman Correlation showed a very strong positive relationship in line with Lipman's (2021) study, which explained that when oestrogen levels are too high, this can lead to the growth of fibroid tumors, and with insufficient progesterone, the body has no way to stop this growth.

CONCLUSION

Ultrasound plays a crucial role in diagnosing and managing fibroids. Recognising the variations and patterns in their ultrasound appearance and correlating with oestrogen hormone levels is vital for accurate assessment and treatment planning. The bivariate analysis revealed significant findings regarding the association of independent variables (age, BMI, size, number, hypoechoic, and type [specific submucosa]) with increased levels of oestrogen.

This has offered insight into the use of ultrasound as a proxy for determining the likelihood of elevated oestrogen levels. This information can assist in the management of fibroids, especially in environments that have inadequate laboratory infrastructure to perform routine evaluation of oestrogen.

Study Limitation

The limited number of participants makes generalization of the findings to the larger population problematic. The increased number would also have significantly strengthened the study outcome in terms of model development for prediction.

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Cite This Article: Alice Mbewe, Oliver Sutherland, Stefan Kafwimbi, Phanny Nankonde, Nchimunya Gwaba, James Sichone (2026). Correlation of Profiled Sonographic Uterine Fibroids Characteristics with Oestrogen Levels in Reproductive Age Women at Levy Mwanawasa University Teaching Hospital, Lusaka, Zambia. *EAS J Radiol Imaging Technol*, 8(2), 48-54.
