Uterine leiomyoma in an infertile population in Kinshasa (DR Congo)

Léiomyome utérin dans une population infertile à Kinshasa (RD Congo)

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Résumé

Objectif. Déterminer les caractéristiques épidémiologiques et cliniques des patientes infertiles avec léiomyomes utérins (LMU) dans 2 institutions sanitaires de Kinshasa. ***Méthodes***. C'est une étude transversale sur les LMU chez les patientes infertiles aux Cliniques universitaires de Kinshasa et au Centre Médical Edith sur une période de 12 ans. Elles étaient réparties en deux groupes selon qu'elles étaient (les cas) ou non (contrôles) porteuses des LMU. Les caractéristiques sociodémographiques et cliniques étaient ont été comparées entre les deux groupes, à l'aide des tests t de Student, le χ^2 ou la régression logistique, selon le cas, avec la signification fixé à $p<0.05$. ***Résultats***. Sur 2631 patientes, 775 (29,4%) avaient des LMU. Cette fréquence avait augmenté avec l'âge : 5,6% à moins de 26 ans ; à 42,1% au-delà de 35 ans. La parité moyenne était faible chez les cas. Le risque de trouver des LMU était 6 et 12 fois plus élevé, entre 26 à 35 ans et au-delà de 35 ans respectivement, par rapport aux moins de 26 ans. Après ajustement, ce risque était monté à 9 et 27 fois respectivement. La durée moyenne d'infertilité était plus longue ($p< 0.0001$) chez les cas (5,0± 3.9 ans) que chez les témoins (4,2 ± 3,4 ans). Le risque d'avoir les LMU était double chez les nullipares comparées aux multipares. ***Conclusion***. Le LMU touche 1 femme sur trois parmi les infertiles. L'âge demeure le principal facteur de risque des LMU et la parité apparaît comme un facteur protecteur.

Mots-clés : Léiomyome utérin, infertilité, Age, Kinshasa
Historique de l'article
Reçu le 6 juin 2017 ; Accepté le 2 septembre 2017

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Summary

Objective. Assessment of epidemiological and clinical characteristics of patients with Uterine Leiomyoma (ULM) in an infertile population from 2 medical institutions in Kinshasa. ***Methods***. A cross-sectional study on ULM in infertile patients, seeking care from January 1st, 2001 to December 31st, 2012 in the Teaching Hospital (University clinic of Kinshasa) and a private clinic (Centre Medical Edith). Two groups were compared: the 1st of patients with ULM (case group) and the second of patients without the disease (control group). Socio-demographic and clinical characteristics were recorded. Student t, χ^2, and logistic regression tests were used for analysis as appropriate. A p value ≤ 0.05 was considered significant. ***Results***. Out of the 2631 infertile patients, 775 (29.4%) had ULM. The prevalence increased with age: 5.6% below 26 to 42.1% above 35 years. The average parity was lower in the case group, where the nulliparous were predominant. The risk of having ULM was 6 and 12 times higher in patients of 26-35 years age group and above 35, respectively in comparison with those aged under 26 years. Adjusted to other predictors, the risk increased to 9 and 27 times respectively. The average duration of infertility was longer in case group. Compared to multiparous, nulliparous had twice the risk of having a ULM (OR: 1.55 (1.1 - 2.2). ***Conclusion***. ULM was present in a third of infertile patients. The age stands as the main risk factor of ULM and the parity seems to be protective.

Key-words: Uterine leiomyoma, infertility, age, Kinshasa
Article information
Received: June 6th 2017 Accepted: September 2nd 2017

Introduction

Uterine leiomyoma (ULM) is a benign tumour of the myometrium, and the most frequent gynaecological tumour of reproductive age (1, 2). Its prevalence is related to some environmental and socio-demographic features (1) like: age, parity, ethnicity and Body Mass Index (BMI). It is responsible for some significant disorders in women's life (3, 4). Until now its aetiology remains unclear (5).

Uterine leiomyoma develops from one myocyte that undergoes progressive transformations to abnormal shape. The modified myocyte, escapes the normal regulatory mechanisms, and multiply abnormally to form a tumour, known as myoma or leiomyoma (2,6,7).

ULM develops on a particular genetic background (8, 9) with influence of steroid hormones: Oestrogens & Progesterone (10, 11) and multiple growth factors (Epidermal growth factor, Insulin-like growth factor, cytokines like Transforming growth factor (TGF) β (12, 13).

It is the most frequent benign tumour of the myometrium; affecting approximately 20 – 25% of women aged between 30 – 40 years old and as high as 40% of the ones above 40 years (2, 6). Black women are 2 to 3 times more likely to develop ULM than Caucasians (14, 15). From the clinical perspective, it is reported that 7.8% to 15.2% of women seeking care for infertility are affected by ULM (16, 17). It is said that this prevalence climbs above 70% after postoperative systematic histological analysis (18, 19).

ULM is responsible for some important gynaecological disorders such as: menstrual cycle abnormalities (menorrhagia, menometrorrhagia), iron deficiency anaemia, mass syndrome and infertility (3, 7, 20). ULM is the most frequent indication of hysterectomy in France (3), USA (21) and in our area (22). It constitutes one of the big expenditure of many insurance organisations. In USA, 19,000 hysterectomies for ULM were performed, costing 2 billion US dollars (21). In our setting, hysterectomy for ULM represented 42% of the major surgeries (22) with an average cost of 1,260 US dollars (23). Therefore, ULM is a real worldwide public health problem, and especially in sub-Saharan Africa.

Globally, it is reported that advanced age, obesity, black ethnicity and family history of ULM are the main risk factors (20, 24, 25); whereas parity and smoking are protective (26). While several studies have shown an increase in the prevalence of obesity (27) and infertility in sub-Saharan setting (25), ULM is expected to be more prevalent in our milieu. A most recent study about ULM in the Democratic Republic of Congo (DRC) aimed to check its risk factors among patients seeking care for any gynaecological issues. The main risk factors of ULM found were age and parity (28). This study aims to determine epidemiological and clinical characteristics of ULM within a specific population, of infertile patients for whom ULM is considered both as aetiology and consequence.

Methods

A retrospective study including patients seeking care for infertility at the University Hospital of Kinshasa and Edith Medical Centre, from January 1st, 2001 to December 31st, 2012 (12 years). The two health institutions are specialized in taking care of infertile patients. A total of 2631 patients were divided into two groups: the case group, made of 775 patients with ULM and the control group, 1846 patients without ULM. The diagnosis of ULM was suspected clinically and confirmed by ultrasound.

The data were drawn from the Access 2003 databases of the two health institutions, and completed with the patients' records. The variables of interest were: patients age, parity, marital status, menarche, duration of infertility, duration of menstrual cycle, body mass index (BMI), duration of menstrual, haemoglobin level, endometrial biopsy findings, and hysterosalpingogram and ultrasounds findings. In this study, the age was considered from the birth date to the diagnosis of ULM date; the marital status: referred to the civilian status (married or single); the parity: the number of viable pregnancies the patient had carried; menarche: age at the first occurrence of menstruation; the duration of infertility: the time from the desire of motherhood to the moment of ULM diagnosis; Haemoglobin: the level of haemoglobin; endometrial biopsy: endometrial biopsy was previously taken at the middle luteal phase of menstrual cycle for ovarian hormonal secretion checking and mainly for infectious status of endometrium, body mass index : the ratio of weight in kilogram and height in square meter. Related to the BMI, patients were categorized according to the WHO classification (29).

Statistical analysis

Statistical analyses were performed using Stata IC 12 software. Quantitative data were summarized as mean and standards deviation, and categorical data as frequencies. The Student t test was used to compare quantitative variables and Chi2 test for qualitative variables. The strength of the association between predictors among them and between predictors and ULM was appreciated by univariate and multivariate logistic regression. The Odds ratio (OR) and 95% confidence interval (CI) were determined. A p value ≤ 0.05 was considered statistically significant. The research proposal received approval from the ethical board of the Department of Obstetrics and Gynaecology of the University Hospital of Kinshasa.

Results

Characteristics of patients with ULM

Patients with ULM represented third (29.4%) of 2631 patients included in the study.

As shown on Table I, individuals in case group were older (35.3 ± 4.9 years old) than in controls group (32.2 ± 5.6 years) (p<0.0001). The frequency of patients with ULM increased steadily with age: 5.6% below 26 to 42.1% above 35 years (p=0,000). The parity was lower in case group (0.52 ± 0.03) than in the control (0.66 ± 0.82) (p=0,004), with predominance of nulliparous (68.25%). The two groups were comparable for menarche (p=0.4) and BMI (0.09).

The average duration of infertility was significantly higher (p=0.0001) in patients with ULM (5.0 ± 3.9 years) compared to controls (4.2± 3.4 years). The proportion of the patients with ULM increased with the duration of infertility: 11.3% at the first year to 42.1% between 11 and 25 Years. Most of them (42.1%) had infertility duration above 10 years. The average duration of the cycle is shorter in the case group (28±3.09 days) than (p<0.0001) in controls (28.9 ± 4.1). In contrary the average duration of menstruation in ULM group (4.12 ± 1.14 days) was higher (p<0.005) compared to controls (3.9±1.2 days). Their average haemoglobin level (11.2±1.5 g/l) was lower (p<0.0001) than the controls (11.5 ± 1.6). More hysterosalpingogram abnormalities were found among patients in the case group (86.1%) than (p<0.0001) the controls (60%).

Determinants of ULM

The table II shows that, in univariate logistic regression, the age was significantly (p<0.0001) associated to the presence of ULM. In comparison with younger patients (≤ 25 years old), the risk of finding ULM in patients within 26-35 years age group and above 35 years was 6 and 12 times higher, respectively. In contrary, the parity was inversely associated with the presence of ULM: the higher the parity, the lower the risk of having ULM. A nulliparous had a 1.6 times greater risk of having ULM than the grand multiparous. The chance of finding a patient with ULM with haemoglobin normal (> 12 g %) is reduced by half (OR=0.6) in the case group.

The risk of tubal occlusion and endometriosis in case group was respectively two and three times higher compared to controls. In multivariate logistic regression, adjusted to other predictors, the age and parity remained strongly associated with the presence of ULM. The risk of having ULM increased to 9 and 27 times for patients in 26-35 years age group and above 35 years old, respectively, compared to younger patients (≤25 years old). In contrast, patients whose parity was three or more had twice lesser risk of developing ULM than the nulliparous.

Discussion

Prevalence of ULM

In current study, infertile patients with ULM represented a third of all included patients (29.4%). That frequency is close to the ones (30.6% and 40%) respectively reported by Marshall *et al* (30) and Baird *et al* (15) among African-American women in USA. Bassot *et al*

(31) found ULM among 25 – 30% of infertile patients. That high frequency is consistent with the well-known finding that ULM is the most frequent benign tumour among women at reproductive age in general, and especially in black and infertile (7, 14). In contrary, our frequency was superior to the ones reported, in Africa, by Laghzaoui *et al* (32) in Morocco, Adama-Hongegal *et al* (33) in Togo, Okogbo *et al* (25) in Nigeria and Pither *et al* (34) in Libreville, respectively: 15.2%; 12.9%; 9.3% and 8.5%. Those frequencies were lower; because they took into account, not only infertile patients but all the patients with gynaecological problems.

Furthermore, the frequency of ULM is affected by several factors, among which the access to providing care facilities, the availability of diagnostic equipment, and the ULM symptomatology (most of ULM are asymptomatic) are the common. Therefore, our prevalence seems to be underestimated, especially when it is reported that with systematic histological analysis of surgical specimens, the frequency of ULM increased up to 77% of the patients operated for gynaecological pathologies (14, 18, 19).

Population characteristics

The two groups of the present study were comparable for menarche, menstrual cycle, body mass index (BMI) and endometrial biopsy findings, but different for age, parity and the duration of infertility. Patients with ULM were older ($p<0.001$) than the ones without it (35.3 ± 4.9 vs 32.2 ± 5 years old). Their mean age (35,3 ± 4.9 years) was similar to the findings of Cham et al (34.5 ± 7.5 years) in South Eastern population of DRCongo (28); Bang et al (34.9 ± 5.3 years) in Gabon (35); Okogbo et al (39.4 ± 7.3 years) and in Nigeria (25). Those findings are consistent with the thesis that ULM is a pathology of women of reproductive and advanced age who consult late, often when ULM become symptomatic (7). While it concerned women seeking care for infertility, it is known worldwide that; nowadays, ladies get married more and more late (36). They are exposed largely to Oestrogen effect for a long time, susceptible to trigger ULM development (2, 32). In the current study, the frequencies of patients with ULM increased steadily with age: 5.6% in fewer than 25 years old to 42.1% over 35 years. Findings consistent with Baird et al (15): the incidence of new cases of ULM increased proportionally with age: 30-40% in 35-39 years age group and around 50% above 40 years. In comparison with young women under 25 years, with univariate logistic regression analysis, the ones within 26-35 years old and over 36 years had respectively 6 and 12 times high risk of having ULM ($p<0.0001$). Nevertheless, with multivariate logistic regression, that risk increased to 9 and 27 times, respectively ($p=0.03$ and $p=0.002$). Obviously, the age is the main factor associated with ULM development, as known in the literature (20).

The mean parity in the case group was lower (0.52± 0.03) than ($p=0.004$) in the control (0.66± 0.03). Nevertheless, the proportion of nulliparous in the case group was higher than in the control group in comparison with other groups. In univariate logistic regression analysis, the risk of having ULM is almost twice (OR: 1.55; 95%IC {1.1 – 2.2}; $p=0.022$) for nulliparous than multiparous. Even if this trend was not well-emphasized in multivariate logistic regression analysis (OR: 0.11; 95%IC {0.12 – 1.04}; $p=0.05$), these findings support the existing literature that stressed the protective role of parity for ULM (20).

The duration of infertility was significantly ($p=0.0001$) higher in the group with ULM (5.04 ± 3.9 years) than in the control (4.2± 3.4 years). In addition, the proportion of patients with ULM increased with the duration of the infertility: 11.3% at a year up to 42.1% in 11-25 years age group. As reported worldwide (36), more and more patients start seeking care for infertility late in our setting: 29.5±4.6 years in 1996 (37) and 33.7±5.2 years old in 2011(38). As the infertility is culturally considered mainly of

spiritual origins or related to curse, most patients began by consulting alternative medicine (traditional, religious healers) before going to modern medicine (38). These two aspects stand as determinant factors increasing the prevalence of ULM among infertile patients in our setting. In conclusion, ULM is present in a third of patients seeking care for infertility in a sub-Saharan African area. The majority sought care at modern facilities at an advanced age, which remains the main determinant factor of ULM.

Conflict of interest

The author declared no competing interests

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Table I: Socio-demographic, clinic and paraclinic characteristics of the patients

Variables	LMU (n=775)	Controls (n=1846)	p
Age (years)			
≤ 25	5.6	94.3	< 0.0001
26 – 35	25.5	74.4	
>35	42.1	57.8	
Average age	35.3±4,9	32.2±5.6	<0.00001
Marital status			
Maried	55.7	71.0	**0.01**
Single	44.2	28.9	
Parity			
0	68.3	61.0	**0.004**
1	18.9	23.8	
2	8.5	8.3	
3 – 8	5.4	7.0	
Average parity	0.52 ± 0.03	0.66 ± 0.03	
Menarche (years)			
8 – 16	70.6	70.4	0.94
17 – 22	29.3	29.3	
Average menarche	13.7 ± 2	13.8 ± 1.7	0.13
BMI			0.092
< 16,49	11.1	88.8	
16,5 – 18,49	23.6	76.3	
18,5 – 24,9	31.8	68.1	
25 – 29,9	36.7	63.2	
30 – 34,9	27.1	72.8	

Variables	LMU (n=775)	Controls (n=1846)	p
35 – 39,9	35.4	64.5	
≥ 40	20	80	
Average BMI	26.7 ± 4.6	26.5 ± 5.3	0.62
Infertility duration			< 0.0001
1	11.3	88.3	
2	29	71	
3 – 6	33.6	66.3	
7 – 10	35.3	64.6	
11 – 25	42.1	57.8	
Average infertillity duration	5.04±3.9	4.2 ± 3.4	< 0.0001
Menstrual cycle			
Regular	31.1	68.8	0.01
Irregular	22.1	77.8	
Mixte	32.3	67.6	
Cycle duration			
Average cycle duration	28±3.09	28.9±4.1	0.0001
Menstruation duration (days)			
Average menstrual duration	4.12±1.14	3.9±1.2	0.005
Hemoglobin (g %)			< 0.0001
6 – 8	1.16	0.6	
9 – 12	37.3	28.5	
>12	61.6	70.9	
Mean Hb	11.2±1.5	11.2±1.5	< 0.0001
HSG			**< 0.0001**
Normal	23.8	39.8	
TO+adhesions	54.2	44.4	
Synechiae	5.4	6.7	
Others lesions	16.6	9.1	

Cycle duration in days; TO= tubal occlusion

Table II: Univariate logistic regression of predictors and ULM

Variables	OR	IC 95%	P
Age			
≤ 25	1	-	
26 – 35	5.7	(3.1 – 10.3)	**0.0001**
>35	12	(6.6 – 21.9)	**0.0001**
Parity			
≥ 3	1	-	
2	1.32	(0.8 – 2.1)	0.237
1	1.10	(0.7 – 1.6)	0.644
0	1.55	(1.1 – 2.2)	**0.022**
Type of cycle			
Regular	1	-	
Irregular	0.7	(0.5 – 0.9)	0.22
Cycle duration			
Normal	1	-	
Short	1.5	(0.5 – 3.9)	0.4
Long	0.6	(0.2 – 0.7)	**0.003**
Haemoglobin			
9 – 12	1	-	
6 – 8	1.5	(0.5 – 4.2)	0.42
≥13	0,6	(0.5 – 0.8)	**0.0001**

Variables	OR	IC95%	P
Hysterosalpngogram			
Normal	1	-	
TO+adhesions	2.03	(1.5 – 2.6)	**0.0001**
Synechiae	1.3	(0.7 – 2.2)	0.280
Others lesions	3.0	(2.0 – 4.5)	**0.0001**

TO= tubal occlusion

Table III: Multivariate logistic regression of predictors and ULM

Variables	Z	ES	OR	IC95%	P
Age					
26 -35	2.08	9.951	9.27	(1.13 – 75.9)	**0.03**
>35	3.05	29.73	27.41	(3.27 – 229.6)	**0.002**
Parity					
1	-1,46	0.225	0.54	(0.24 – 1.22)	0.144
2	0,22	0.882	1.18	(0.27 – 5.10)	0.822
≥3	-1,92	0.129	0.11	(0.12 – 1.04)	0.05
Cycle duration					
Short	0.60	3.591	2.427	(0.13 – 44.1)	0.54
Long	-0,57	0.474	0.667	(0.16 – 2.68)	0.57
Hb	0.20	0.332	1.065	(0.57 – 1.96)	1.96
HSG					
TO+adhesions	1.42	0.51	1.59	(0.83 – 3.01)	3.01
Synechiae	0.45	1.11	1.41	(0.30 – 6.59)	6.59
Others	0.11	0.55	1.06	(0.37 – 2.96)	2.96
Endometrium biopsy					
Offset endometrium	-1.91	0.18	0.455	(0.20 – 1.02)	1.02
Metaplasia	-0.34	0.51	0.800	(0.22 – 2.84)	2.84