

# A 10-year study of endometriosis in an indigenous black African population

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## ABSTRACT

**Background:** Endometriosis is a debilitating disease in women of child-bearing age.

**Objective:** To describe the pattern of presentation, stage of endometriosis and biophysical profile of patients with endometriosis.

**Method:** A retrospective study of 61 consecutive infertile patients between June 2003 and November 2014.

**Results:** The means ( $\pm$ SD) of age (years) and of body mass index (BMI) ( $\text{kg}/\text{m}^2$ ) of the patients were 34.1 (4.3) and 25.8 (5.0), respectively. A relatively high percentage (43, 70.5%) of the women were in the age range of 31-40 years; had normal BMI (27, 44.3%); were nulliparous (53, 86.9%) and were of primary infertility (40, 65.6%). The mean ( $\pm$ SD) age at menarche, of cycle length, of the duration of flow and of years trying to conceive were 12.9 (1.7) years, 29.1 (2.7) days, 4.7 (1.1) days and 5.2 (3.8) years, respectively. A high proportion of them (37, 60.7%) presented with severe endometriosis. The main symptoms at presentation was dysmenorrhea (47, 73.8%). Of the 32 (52.5%) with associated utero-tubal factor, 20 (62.5%) were in severe stage of endometriosis. Among women with endometriosis, those with primary infertility were over three times more likely to present with menorrhagia than those with secondary infertility ( $\chi^2 = 4.70$ ;  $p$  value = 0.03; OR = 3.33; 95% CI = 1.10, 10.12). Only 3 (4.9%) had diagnosis of endometriosis in first-degree relative. Dysmenorrhea was a strong predictor of severe endometriosis.

**Conclusions:** There may be some trends in the biophysical profile of infertile women with endometriosis which may influence diagnosis and management.

**Keywords:** Black African women, Dysmenorrhea, Endometrioma, Endometriosis, Menarche, Nordica Fertility Center

## Introduction

Endometriosis was defined as the existence of endometrial-like tissue (glands and stroma) outside the uterus, which induces a chronic inflammatory reaction, scar tissue, and adhesions that may distort a woman's pelvic anatomy (1). The associated symptoms can impact the patient's general physical, mental, and social well-being. Endometriosis is primarily found in young women, but its occurrence is probably not related to ethnic or social distinctions. Patients with endometriosis mainly complain of pelvic pain, dysmenorrhea, and dyspareunia (2). Endometriosis is a very common debilitating disease found in 6% to 10% of the general female

population though among women who present with pain, infertility or both pain and infertility, the frequency of endometriosis ranges from 35%-50% (3). Earlier observations were that roughly 25% to 50% of infertile women have endometriosis, that 30% to 50% of women with endometriosis are infertile (4) and that young women are more prone to endometriosis, though its incidence may not be linked to ethnicity or social grouping (5).

The frequencies of the more common symptoms remain as dysmenorrhea (60%-80%), chronic pelvic pain (40%-50%), deep dyspareunia (40%-50%), infertility (30%-50%), severe menstrual pain and irregular flow and/or premenstrual spotting (10%-20%), tenesmus (1%-2%), although 2%-25% of patients are asymptomatic (5). Sufferers of endometriosis usually present with symptoms such as pain and a heavy feeling in the lumbo-sacral column and/or legs. Nausea, lethargy, chronic fatigue, any cyclical pain affecting other organs, hemoptysis, scapular or thoracic pain and acute abdomen are also suggestive of endometriosis (5, 6). These symptoms often do not correlate with its laparoscopic appearance (6).

The severity of endometriosis symptoms and the probability of its diagnosis increase with age (7, 8) though the exact

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age group of its peak incidence is still controversial, as some claim a peak among women in their 40s (9) while others claim it is among women in their 30s (10). However, differentiating the diagnosis of pelvic pain due to endometriosis from that due to irritable bowel syndrome (IBS), interstitial cystitis, fibromyalgia, and others may be difficult (11), although the involvement of those visceral structures may be quite common in patients with endometriosis (5). Endometriosis is usually associated with protracted fatigue, severe abdominal pain and with deep-seated pain during sexual intercourse and with painful menstrual periods (12, 13). Most of the organs that are commonly affected by ectopic endometrium are located within the pelvis or are adjacent to it (13, 14). Approximately 70 million women of reproductive age are affected globally (15) and endometriosis, presumably a perplexing and extensively misconstrued disorder, may be branded simply as painful periods.

The current thinking is that endometriosis rarely affects indigenous African women. For example, a study suggested that the prevalence of endometriosis in indigenous African women with infertility seems low, possibly due to a different life style (early pregnancy, increased risk for pelvic inflammatory disease [PID] and blocked Fallopian tubes) and due to lack of laparoscopic facilities and specific training of African gynecologists to diagnose ascites caused by endometriosis (16). About 30 years ago, a facility-based study described a 1.4% prevalence of endometriosis among infertile Nigerian women (17). Around the same time, a case report described massive ascites associated with endometriosis in an indigenous Nigerian woman (18). Later, another case study documented an isolated umbilical endometriosis (19). Five cases of extra-pelvic endometriosis were observed during uterine surgery among Nigeria women with inguino-abdominal nodules, none of which was confirmed with modern laparoscopy but by other methods such as microscopic examination (20). Previous studies have documented various risk factors, such as age, race, body mass index (BMI), alcohol usage, cigarette smoking and menstrual characteristics (length, regularity, intensity of flow and dysmenorrhea) to be associated with endometriosis (21-24).

From records, data on endometriosis among indigenous African population such as Nigerians remain very scanty despite an anecdotal report that approximately 8 million females are afflicted in the country. The majority of previous studies on this disease were undertaken among Caucasians. Almost all earlier studies on endometriosis in Nigeria were spot diagnoses during gynecological surgeries without longitudinal collection of data. Therefore, biophysical, clinical and epidemiological characterization of endometriosis in an African population are very rare. The objective of this study therefore, was to describe the pattern, stages and biophysical profile of patients with endometriosis who presented at our facility between 2003-2014.

## Methodology

A 10-year retrospective cohort study, involving a detailed review and analysis of clinical records, ultrasound findings, laparoscopic results and histological reports of 61 consecu-

tive infertile women was studied. The patients were seen and managed between June 2003 and November 2014. The pre-operative work-up included a detailed history and examination, blood examination and a vaginal ultrasound. The setting was Nordica Fertility Center (NFC) Lagos, Nigeria, a leading private facility for endoscopy and assisted conception.

## History taking

All patients were requested to provide gynecological and obstetric, medical and drug history at initial point of service. Family history of endometriosis in a close relative was among the history taken from each of the patients. Some of the patients had to be prompted on the symptomatology of endometriosis for a recall of the disease among family members. Those who had visited other health facilities within or outside the country were advised to produce records of such consultations.

## Menstrual characteristics

Patients were segregated into two groups according to their age at menarche. The first group included those who started menarche at age less than 14 years (early) and the other group included those who started menarche at an older age. Since the length of the menstrual cycle fluctuates significantly among women with a range of 21 to 35 days, we designated 28 days as the average length (25). Duration of menstrual flow was categorized in to <4 days and 4-7 days.

## Imaging and laparoscopy

Ultrasound imaging was done for all patients while laparoscopic surgery was done primarily to ascertain a diagnosis of endometriosis and stage the disease. All surgical procedures were performed under general anesthesia. Standard laparoscopic equipment was used in a laparoscopic theatre in the endoscopy arm of NFC, Lagos. Images were displayed on a high-definition screen and a 3D-chip camera was used. Laparoscopy with multiple-port access was the main surgery performed; diagnosis, staging, retrieval of sample for histological diagnosis, adhesiolysis and ablative surgery were done as required. Two experienced laparoscopic surgeons performed the procedures on each occasion.

## Inclusion criteria

To be enrolled into the study, the patient must have undergone laparoscopic diagnosis and staging of endometriosis.

## Exclusion criteria

Patients who had no laparoscopic diagnosis of endometriosis, those who were severely anemic and those who declined to sign the consent form were excluded from the study.

## Ethics approval

The study was approved by the State Ethics Committee on Health Research

## Patients consent

Participants in the study were contacted and all gave verbal approval for their data to be used in the research. In return, participants were assured of the confidentiality of their data and that the research would not use names of the subjects.

## Data analysis

Participants were grouped and classified according to ASRM classification (26). Age in years was grouped into  $\leq 30$ , 31-40 and 41-50. BMI in  $\text{kg/m}^2$  was classified according to the WHO classification (27):  $<18.5$  (underweight), 18.5-24.9 (normal weight), 25-29.9 (overweight) and  $\geq 30$  (obese). Infertility was classified as primary, if the woman had never been pregnant and secondary if she had ever been pregnant. Parity was also classified as never had a child (nulliparous) or ever had a child. Three data entry clerks were trained by gynecologist (OB) to retrieve data from patients' medical records and enter these into a laptop computer. A pilot data entry was conducted to verify and correct personal, inter- and intra-personal errors. Data entry and cleaning were conducted before statistical analysis was performed using Stata 13 (StataCorp, Texas 77845 USA) software. Chi-square test and Student's test were used to analyze different variables. Multivariate regression analysis was used to determine correlation between dependent and selected independent variables. A  $p$  value of  $<0.05$  was considered statistically significant. Data were presented as Tables and Figures.

## Results

During the period of data collection, 2265 women consulted at our infertility clinic among whom 61 (2.69%) had laparoscopic diagnosis of endometriosis. The mean ( $\pm$ SD) of age, BMI and years trying to conceive of the women with

endometriosis, as shown in Table I, were 34.1 (4.3) years, 25.8 (5.0)  $\text{kg/m}^2$  and 5.2 (3.8) years, respectively, suggesting that black African women with endometriosis are mostly in their fourth decade of life and that they are on the borderline between normal and overweight. Endometriosis was observed to be more common among women with primary infertility (40, 65.6%) than among those with secondary infertility (21, 34.4%) and among nulliparous women (53, 86.9%) than among those with parity of one (8, 13.1%). A significant difference ( $t = -2.79$ ,  $df = 33.11$ ,  $p < 0.005$ ) was observed in the mean BMI ( $\text{kg/m}^2$ ) of those with secondary infertility ( $28.3 \pm 5.5$ ) and those with primary infertility ( $24.5 \pm 4.1$ ) suggesting that, in endometriosis, women with secondary infertility are relatively heavier than those with primary infertility. The highest (43, 70.5%) and the lowest (7, 11.5%) proportions of women with endometriosis were aged 31-40 and 41-50 years, respectively indicating that at age below 30 years and above 40 years, endometriosis is a rare clinical event in a black African woman population.

The mean ( $\pm$ SD) of age at menarche, cycle length and duration of menstrual flow of the patients were 12.8 ( $\pm 1.7$ ) years, 29.1 (2.7) days and 4.7 (1.1) days, respectively (Tab. II). There was no significant difference in the mean age at menarche of those with primary ( $12.7 \pm 1.7$ ) or secondary ( $13.0 \pm 1.8$ ) infertility ( $t = -0.42$ ,  $df = 38.76$ ,  $p = 0.34$ ) or of nulliparous women ( $12.8 \pm 1.5$ ) compared to those with parity of one ( $12.9 \pm 2.7$ ) ( $t = -0.10$ ,  $df = 7.67$ ,  $p = 0.46$ ). Means of age at menarche ( $12.7 \pm 1.9$  years), cycle length ( $28.8 \pm 2.1$  days) and duration of flow ( $4.5 \pm 1.1$  days) were shorter among those with severe endometriosis compared to women with mild endometriosis ( $12.8 \pm 1.3$ ;  $29.5 \pm 3.9$ ;  $5.0 \pm 1.1$ , respectively), though these differences did not approach any level of significance (Fig. 1).

The relative risk of endometriosis was 1.17 among women with primary infertility compared to those with secondary infertility. The risk of endometriosis was 3.15 higher among primarily infertile women whose cycle length was less than

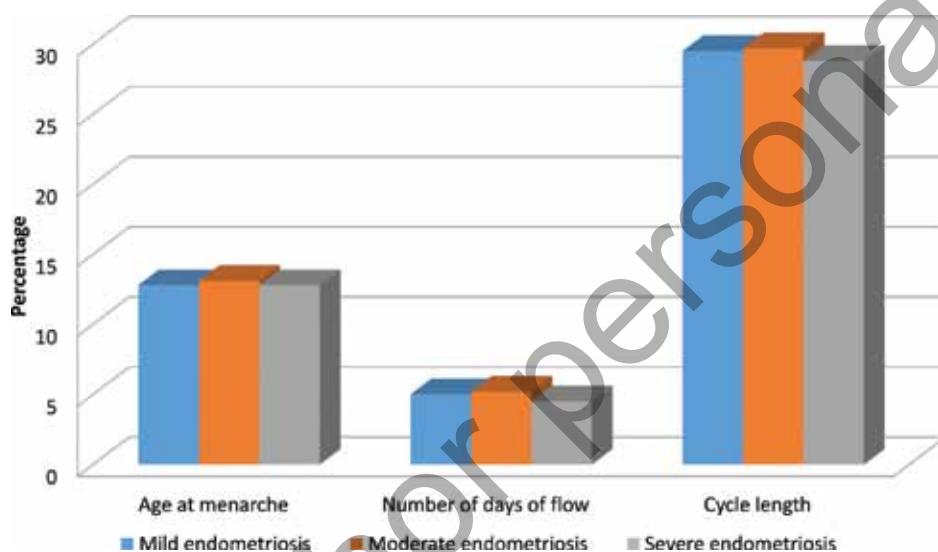
**TABLE I** - Demographic characteristics of infertile women with endometriosis relative to type of fertility and parity

Variable	Item	Infertility				Parity				All	
		Primary (n = 40; 65.6%)		Secondary (n = 21; 43.4%)		Nil (n = 53; 86.9%)		One (n = 8; 13.1%)		n	Mean ( $\pm$ SD)
		n	Mean ( $\pm$ SD)	n	Mean ( $\pm$ SD)	n	Mean ( $\pm$ SD)	n	Mean ( $\pm$ SD)		
Age (years)	All	40	33.5 (4.5)	21	35.3 (3.8)	53	33.6 (4.2)	8	37.6 (3.8)	61 (100.0)	34.1 (4.3)
	$\leq 30$ (n = 11)	9	28.6 (1.6)	2	28.0 (1.4)	11	28.5 (1.5)	0	0.0 (0.0)		
	31-40 (n = 43)	27	33.7 (2.5)	16	35.1 (2.4)	38	34.1 (2.5)	5	35.4 (3.0)		
	41-50 (n = 7)	4	43.0 (2.7)	3	41.0 (0.0)	5	42.6 (2.5)	2	41.0 (0.0)		
BMI	All	40	24.5 (4.1)	21	28.3 (5.5)	53	25.3 (4.8)	8	28.8 (5.5)	61 (100.0)	25.8 (5.0)
	$<18.5$ (n = 2)	2	17.9 (0.7)	0	0 (0.0)	2	17.9 (0.7)	0	0 (0.0)		
	18.5-24.9 (n = 27)	20	21.6 (1.6)	7	23.6 (0.9)	24	21.9 (1.6)	3	24.3 (0.6)		
	25.0-29.9 (n = 22)	14	27.5 (1.2)	8	27.1 (1.7)	21	27.3 (1.4)	1	28.1 (0.0)		
	$\geq 30$ (n = 10)	4	31.4 (1.9)	6	35.4 (4.9)	7	33.6 (4.3)	3	34.3 (5.2)		
Years trying to conceive (TTC)		40	5.3 (4.3)	21	5.0 (2.6)	54	5.2 (4.0)	7	4.8 (2.3)		5.2 (3.8)

BMI = body mass index; SD = standard deviation.

**TABLE II** - Menstrual characteristics of women with endometriosis according to type of infertility, parity and stage of endometriosis

Variable	Item	Freq.	%	Menstrual characteristics		
				Age at menarche (y)	Cycle length (d)	Duration of menstrual flow (d)
				Mean ( $\pm$ SD)	Mean ( $\pm$ SD)	Mean ( $\pm$ SD)
All		61	100.0	12.8 (1.7)	29.1 (2.7)	4.7 (1.1)
Infertility	Primary	40	65.6	12.7 (1.7)	29.0 (2.8)	4.9 (1.1)
	Secondary	21	34.4	13.0 (1.8)	29.2 (2.6)	4.5 (1.0)
Parity	Nil	53	86.9	12.8 (1.5)	29.2 (2.8)	4.8 (1.1)
	One	8	13.1	12.9 (2.7)	28.4 (2.0)	4.4 (0.9)
Stage of endometriosis	Mild	15	29.4	12.8 (1.3)	29.5 (3.9)	5.0 (1.1)
	Moderate	9	14.8	13.1 (1.5)	29.7 (2.6)	5.2 (0.7)
	Severe	37	60.8	12.7 (1.9)	28.8 (2.1)	4.5 (1.1)
Diagnosis in first degree relative		3	4.9	14.0 (1.0)	26.3 (2.9)	4.8 (1.0)

**Fig. 1** - Menstrual characteristics relative to severity of endometriosis.

28 days compared to secondarily infertile women with endometriosis with cycle length  $<28$  days ( $\chi^2 = 0.59$ ,  $p = 0.44$ ; RR = 3.15, 95% CI = 0.41, 24.47).

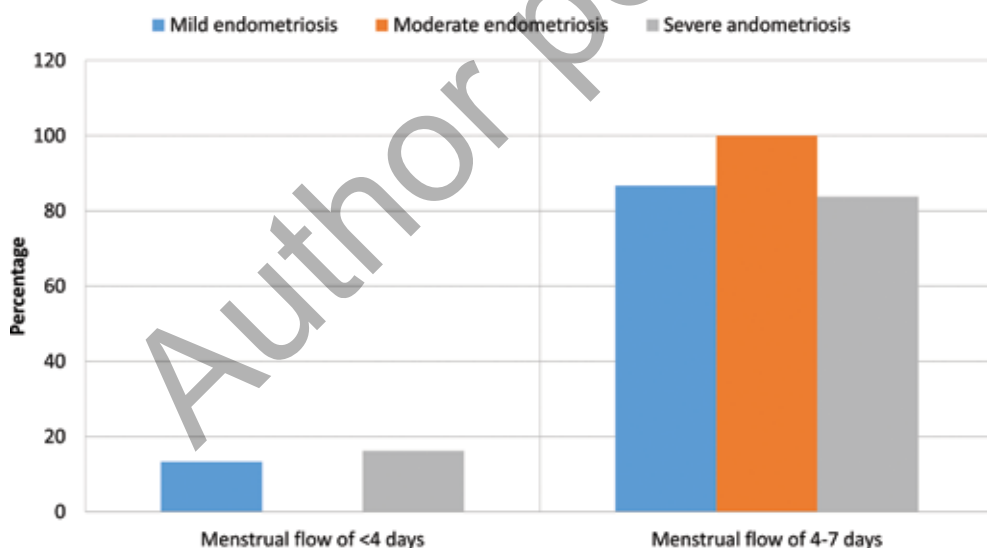
Of the 37 (60.7%) patients who presented with severe form of endometriosis, 17 (46.0%) had normal weight while 2 (5.4%), were underweight and 4 (10.8%) were obese. In all, 27 (73.0%) of these 37 women were aged 31-40 years, including the 2 (7.4%) underweight women (Tab. III). A high proportion (31, 50.8%) of these patients had a duration of infertility of 1.1 and 5 years before presentation, most (18, 48.7%) of whom presented with severe stage of endometriosis. Among these 37 women with severe endometriosis 18 (48.7%) and 3 (8.1%) had been trying to conceive for 1.1-5 years and for more than 10 years, respectively. A high proportion of those with cycle length of  $\geq 28$  days (34, 91.9%) and those with duration of flow between 4-7 days (31, 83.8%) presented with severe stage of endometriosis (Fig. 2).

Presenting symptoms of endometriosis could be singular or synergistic. The data presented in Table IV look at the

presenting symptoms individually. Painful menstruation (dysmenorrhea) was the commonest (47, 77.0%) complaint, especially among those whose age at menarche was  $<14$  years (33, 70.2%), whose cycle length was  $\geq 28$  days (41, 87.2%), whose duration of flow was 4-7 days (41, 87.2%) and among those in the severe stage of endometriosis (32, 68.1%). Dyspareunia (10, 16.4%) was also observed more when age at menarche was  $<14$  years (7, 70.0%), at cycle length  $\geq 28$  days (8, 80.0%) and duration of flow of 4-7 days (8, 80.0%). Menorrhagia (32, 52.5%) also followed this pattern as it was observed more at age of menarche  $<14$  years, at cycle length  $\geq 28$  days and at longer duration of flow. All these symptoms were observed more among women with severe form of endometriosis. Further analysis (data not displayed) indicated that women with primary infertility were over 1½ times more likely to present with dysmenorrhea than women with secondary infertility ( $\chi^2 = 0.57$ ;  $p = 0.45$ ; OR = 1.60; 95% CI = 0.47, 5.44) and nulliparous women were over two times more likely to present with dysmenorrhea than uniparous women ( $\chi^2 = 0.36$ ;  $p = 0.55$ ;

**TABLE III** - Frequency distribution of age in years, BMI (kg/m<sup>2</sup>), years trying to conceive, type of infertility, age at menarche, cycle length and duration of flow by stages of endometriosis

Variable	Item	All		Stage of endometriosis					
				Mild		Moderate		Severe	
		Freq.	(%)	Freq.	(%)	Freq.	(%)	Freq.	(%)
Age (y)	All	61	100.0	15	24.6	9	14.7	37	60.7
	≤30	11	18.0	3	20.0	2	22.2	6	16.2
	31-40	43	70.5	9	60.0	7	77.8	27	73.0
	41-50	7	11.5	3	20.0	0	0.0	4	10.8
BMI (kg/m <sup>2</sup> )	<18.5	2	3.3	0	0.0	0	0.0	2	5.4
	18.5-24.9	27	44.3	7	46.7	3	33.3	17	46.0
	25.0-29.9	22	36.1	5	33.3	3	33.3	14	37.8
	≥30	10	16.4	3	20.0	3	33.3	4	10.8
Years trying to conceive	≤1	7	11.5	3	20.0	1	11.1	3	8.1
	1.1-5	31	50.8	9	60.0	4	44.4	18	48.7
	5.1-10	18	29.5	2	13.3	3	33.3	13	35.1
	>10	5	8.2	1	24.6	1	11.1	3	8.1
Type of infertility	Primary	40	65.6	7	46.7	7	77.8	26	70.3
	Secondary	21	34.4	8	53.3	2	22.2	11	29.7
Age at menarche (y)	<14	42	68.9	11	73.3	7	77.8	24	64.9
	≥14	19	31.1	4	26.7	2	22.2	13	35.1
Cycle length (d)	<28	7	11.5	3	20.0	1	11.1	3	8.1
	≥28	54	88.5	12	80.0	8	88.9	34	91.9
Duration of flow (d)	<4	8	13.1	2	25.0	0	0.0	6	75.0
	4-7	53	86.9	13	24.5	9	17.0	31	58.5

**Fig. 2** - Frequency distribution of days of menstrual flow relative to severity of endometriosis.

OR = 2.29; 95% CI = 0.47, 11.10). It was also observed that patients with primary infertility were over three times more likely to present with menorrhagia than those with secondary infertility ( $\chi^2 = 4.70$ ;  $p = 0.03$ ; OR = 3.33; 95% CI = 1.10, 10.12). Nulliparous women with endometriosis were about twice as likely to present with menorrhagia than those with parity of one ( $\chi^2 = 0.28$ ;  $p = 0.60$ ; OR = 2.01; 95% CI = 0.44, 9.30).

Utero-tubal factor (32, 52.5%), the most common co-morbidity presented by patients in this study, included bilateral tubal blockage (BTB) (16, 50.0%) and unilateral tubal blockage (UTB) (10, 31.3%), as shown in Table V. Utero-tubal factors were observed mostly in the severe stage of endometriosis. Ultrasound finding of endometrioma was observed in 14 (23.0%) patients, all in the severe stage of endometriosis.

**TABLE IV** - Common presenting symptoms of endometriosis seen at Nordica Fertility Center relative to type of fertility, parity, years trying to conceive, age at menarche, cycle length and duration of flow

Symptom	Severity of endometriosis			Menstrual characteristics					
	Mild	Moderate	Severe	Age at menarche (y)		Cycle length		Duration of flow	
	Freq. (%)	Freq. (%)	Freq. (%)	<14	≥14	<28	≥28	<4	4-7
				Freq. (%)	Freq. (%)	Freq. (%)	Freq. (%)	Freq. (%)	Freq. (%)
Dysmenorrhea	8 (17.0)	7 (14.9)	32 (68.1)	33 (70.2)	14 (29.8)	6 (12.8)	41 (87.2)	6 (12.8)	41 (87.2)
Painful intercourse	2 (20.0)	1 (10.0)	7 (70.0)	7 (70.0)	3 (30.0)	2 (20.0)	8 (80.0)	2 (20.0)	8 (80.0)
Bleeding from other site	0 (0.0)	0 (0.0)	1 (100.0)	1 (100.0)	0 (0.0)	0 (0.0)	1 (100.0)	0 (0.0)	1 (100.0)
Menorrhagia	5 (15.6)	5 (15.6)	22 (68.8)	20 (62.5)	12 (37.5)	5 (15.6)	27 (84.4)	2 (6.3)	30 (93.7)

**TABLE V** - Factors associated with various stages of endometriosis in Nigeria

Factor		Total		Stage of endometriosis					
				Mild		Moderate		Severe	
		Freq.	%	Freq.	%	Freq.	%	Freq.	%
Utero-tubal									
• All		32	52.5	9	28.1	3	9.4	20	62.5
• Unilateral tubal blockage		10	31.2	2	20.0	2	20.0	6	60.0
• Bilateral tubal blockage		16	50.0	3	18.8	1	6.2	12	75.0
• Right hydrosalpinx		1	3.1	1	100.0	0	0.0	0	0.0
• Bilateral hydrosalpinx		3	9.4	2	66.7	0	0.0	1	33.3
• Adhesion		2	6.3	1	50.0	0	0.0	1	50.0
• Age at menarche (y)	<14	19	59.4	8	42.1	1	5.3	10	52.6
	≥14	13	40.6	1	7.7	2	15.4	10	76.9
• Cycle length (d)	<28	5	15.6	2	40.0	1	20.0	2	40.0
	≥28	27	84.4	7	25.9	2	7.4	18	66.7
• Duration of flow (d)	<4	4	12.5	1	25.0	0	0.0	3	75.0
	4-7	28	87.5	8	28.6	3	10.7	17	54.8
Ultrasound finding of endometrioma									
• All		14	23.0	0	0.0	0	0.0	14	100.0
• Age at menarche (y)	<14	11	78.6	0	0.0	0	0.0	11	100.0
	≥14	3	21.4	0	0.0	0	0.0	3	100.0
• Cycle length (d)	<28	2	14.3	0	0.0	0	0.0	2	100.0
	≥28	12	85.7	0	0.0	0	0.0	12	100.0
• Duration of flow (d)	<4	1	7.1	0	0.0	0	0.0	1	100.0
	4-7	13	92.9	0	0.0	0	0.0	13	100.0
How long to diagnosis (y)									
<1		4	6.6	2	13.3	1	11.1	1	2.7
1-5		19	31.1	6	40.0	4	44.4	9	24.3
5.1-10		6	9.8	1	6.7	1	11.1	4	10.8
>10		4	6.6	1	6.7	0	0.0	3	8.1
At presentation		28	45.9	5	33.3	3	33.3	20	54.1

**TABLE VI** - Multivariate regression analysis for association between stages of endometriosis as dependent variable and some independent variables

Equation	Observed	R <sup>2</sup>	F	p value	
Stage of endometriosis	61	0.3608	2.82	0.007	
Independent variable	Dependent variable = stages of endometriosis				
	Coef. (r)	SE	t	p value	95% CI
Dysmenorrhea	-0.62	0.24	-2.54	0.014	-1.10, -0.13
Dyspareunia	-0.02	0.28	-0.06	0.95	-0.57, 0.53
Menarche	0.37	0.22	1.66	0.10	-0.08, 0.82
Duration of flow (d)	-0.16	0.09	-1.74	0.09	-0.35, 0.03
Cycle length (d)	-0.03	0.04	-0.68	0.50	-0.11, 0.05
Menorrhagia	-0.14	0.22	-0.65	0.52	-0.57, 0.29
Diagnosis in first relatives	0.74	0.49	1.52	0.13	-0.24, 1.73
Utero-tubal factors	0.37	0.21	1.74	0.08	-0.06, 0.80
Constant	4.84	1.41	3.43	0.001	2.00, 7.67

SE = standard error; CI = confidence interval.

Among these 14 women, 11 (78.6%), had their menarche at age <14 years, 12 (85.7%) had a cycle length of  $\geq 28$  days and 13 (92.9%) had longer duration of menstrual flow. In all, endometriosis was diagnosed at presentation in 28 (45.9%) women while the disease was diagnosed in 33 (54.1%) women <1 year to >10 years earlier.

Multivariate regression analysis was computed, with stages of endometriosis as dependent variable and nine other independent variables – dysmenorrhea, dyspareunia, age at menarche, duration of flow, cycle length, menorrhagia, diagnosis in first relatives, presence of endometrioma and incidence of utero-tubal factors (Tab. VI). These independent variables combined to explain a significant 36.1% of the stages of endometriosis ( $R^2 = 0.3608$ ,  $F = 2.82$ ,  $p < 0.007$ ). A strong negative correlation was observed between dysmenorrhea and stages of endometriosis ( $r = -0.62$ , standard error [SE] = 0.24,  $t = -2.54$ ,  $p = 0.014$ , 95% CI = -1.10, -0.13).

## Discussion

Endometriosis is typically found in the peak period of reproduction, especially among women in their 30s and 40s pursuing their careers and trying to form their own nuclear families. The low prevalence of endometriosis found in our study may not reflect the true picture of this condition in this part of the world. A family history of endometriosis in a close relative is difficult to get in this part of the world as most women are not even aware of the symptomatology of endometriosis. In most cases, diagnosis of endometriosis could not be ascertained due to low availability of laparoscopy and lack of high index of suspicion even among medical practitioners. Most cases of menstrual pain are waved aside as usual and are dealt with using over-the-counter medication and

not further evaluated. One of the key findings of our study is that African women diagnosed with endometriosis were in their peak period of reproduction, in their fourth decade of life and at the borderline of normal weight and overweight. That endometriosis is found in the fourth decade of life, as reported in this study is consistent with what Hediger et al (28) documented but does not agree with the findings of Arruda et al (29) and of Vessey and his colleagues (30).

Our study is the first to report the link between BMI and endometriosis in a black African women population. Some authors have tried to explain a relationship between BMI and endometriosis elsewhere. Hediger et al (28), for example, reported that a unit increase in BMI in  $\text{kg/m}^2$  led to a 12%-14% decrease in likelihood of developing endometriosis. Our findings suggest that indigenous black African women with endometriosis are heavier than their Caucasian counterparts, which is in line with what Hemmings et al (31) documented and what Shah et al (32) suggested as an inverse relationship between endometriosis and BMI among Caucasians. This disparity may be due to some African cultures that engage in a tradition of “fattening” for a woman prior to marriage or an apparent sedentary way of life compared to their Caucasian counterparts. It should be said, nevertheless, that the two underweight women in our study, aged 35 and 36 years, respectively, presented with severe endometriosis. This may signal a high prevalence of the disease in underweight women in their fourth decade of life. More studies will be beneficial in elucidating why African women with endometriosis appear to be heavier than their Caucasian counterparts.

The mean age at menarche among women in our study was 12.8 years. Early age at menarche is often cited as a risk factor for endometriosis (33, 34) as this increases a woman's

exposure to menstruation during her reproductive life. Several observational studies and a meta-analysis have provided some evidence that early age at menarche increases the risk of endometriosis (35, 36). Separately, Hediger et al (28) in 2005 and Treloar et al (37) in 2013 demonstrated that menarche at or after 14 years greatly reduces the risk of endometriosis. In our study, the proportion of women with endometriosis who had their menarche before age 14 years (42, 68.9%) was higher than those who had their menarche after that age (19, 31.1%), especially among those with primary infertility and among nulliparous women. This finding accords with the observation of a study that 'never been pregnant' (primary infertility) is a recognized associated risk factor for endometriosis and it was noted that women with endometriosis were more likely (OR = 1.5, 95% CI 1.0-2.0) to have never conceived (28).

Another key finding in our study is that endometriosis occurred more among women with primary infertility than among those with secondary infertility. That endometriosis is associated with infertility has been well debated over the years (38-44). Many studies have reported the association between infertility and endometriosis but extremely few have associated endometriosis specifically with primary infertility, less so among indigenous black African women. Ectopic endometrial tissue may attach itself to, and invade, pelvic organs such as the ovaries and bring about irritation in the pelvis leading to pain and infertility. We can only speculate that complete attachment and invasion of pelvic organs by ectopic endometrial tissue before first pregnancy is probably responsible for primary infertility while incomplete attachment and invasion is probably responsible for secondary infertility.

Menstrual cycle characteristics affecting the frequency of exposure to menstruation may be related to the incidence of endometriosis (45). Our study found longer cycle length of 28 days or more and longer duration of flow of 4-7 days among a high proportion of women with severe endometriosis similar to the findings of Treloar et al (37) and Sangi-Haghighi et al (46) but discordant with what others reported (47-50).

Dysmenorrhea, dyspareunia, and menorrhagia were observed more among those with longer cycle length of  $\geq 28$  days than among those with shorter cycle length. In addition, severe form of endometriosis was noted in all women with longer cycle length. This may be a point of departure in the expression of symptomatology of endometriosis in indigenous black African women compared to their Caucasian counterparts. In contradiction to our finding, a previous study reported that women with menstrual cycle lengths  $\leq 27$  days were at an increased risk of developing endometriosis and those with menstrual cycle lengths  $\geq 29$  days were at an approximately 32% lower risk of endometriosis (48).

Menorrhagia or abnormal uterine bleeding (AUB) and primary infertility are recognized associated symptoms of endometriosis. Their strong coexistence in this study is understandable. We report an incidence of 52.5% (32/61) of menorrhagia among women with endometriosis in our study, which is far below the 75% reported elsewhere (<http://gynaeonline.com/signs.htm>). We wondered if menorrhagia in endometriosis could be a marker of more severe or aggressive disease and hence resulting in primary infertility rather than secondary infertility. A study reported that, using visual

chart, women with endometriosis recorded heavy menstrual flow (51). However, endometriosis is not the only cause of menorrhagia. Other causes of this abnormal uterine bleeding may include stress and lifestyle factors, use of birth control pills or other contraceptives, uterine polyps or fibroids, pelvic inflammatory disease, polycystic ovarian syndrome (PCOS), and premature ovarian insufficiency. Our findings suggest that menorrhagia may be of shorter duration among black indigenous Africans with endometriosis than among their Caucasian counterparts, though this needs further investigation.

Dysmenorrhea was the leading complaint among our patients, recorded in approximately 77% of these women, mostly among those with early menarche and among those with longer cycle length. These findings accord with what others (5, 52, 53) earlier documented though it is higher than the 40%-62% reported by Belleli et al (10) and by Alborzi et al (54). The pathology of dysmenorrhea in endometriotic women is not yet conclusive. This condition may be associated with spasms of uterine blood vessels or with cytokines as described in other studies (55-57).

Dyspareunia was reported in approximately 16% of our patients, a prevalence lower than the almost 55% reported elsewhere (10). Painful intercourse could be regarded as a valuable pointer to deep infiltrating disease, with likely involvement of the retro-cervical region or rectovaginal fascia (58).

Endometrioma, a marker of severe endometriosis was found in about a quarter of our patients, which is consistent with the 17%-44% earlier documented (54). It is supposedly formed by progressive invagination of the ovarian cortex after accumulation of menstrual debris that has derived from the shedding of superficial endometriotic active implant (59, 60). Endometrioma may cause more damage to the ovary and its surrounding tissues thus contributing significantly to infertility. Enlarging endometrioma is a risk factor for ovarian torsion (61) and the possibility of ovarian cancer (62).

Women with moderate-severe endometriosis were more likely to be younger, have primary infertility, dysmenorrhea, menorrhagia and dyspareunia than those with minimal-mild endometriosis. Even though pain symptoms have been shown to correlate poorly with stage of endometriosis, infertility is more likely with advanced stages. These findings were however not statistically significant. The major predictor of severity of endometriosis in our study was dysmenorrhea.

## Conclusion

Our study contributes to elucidating the biophysical profile, menstrual characteristics, and gynecological outline of indigenous black African women suffering from endometriosis. These women present an array of characteristics that may be divergent from the presentation of endometriosis in the developed world. Culture, ethnicity, living standards and geographical location may be relevant in "typing" patients with endometriosis. Indigenous black African women with endometriosis are apparently heavier than their Caucasian counterparts and mostly present in the fourth decade of life, with a high proportion of them starting their menarche early and also suffering from primary infertility. Clinicians in Africa should have a high index of suspicion of endometriosis when an indigenous black African woman with primary infertility



and in her fourth decade of life consults with the main symptoms of dysmenorrhea, dyspareunia and probably menorrhagia as well as endoscopic findings of endometrioma and associated utero-tubal factors. Results of our study also have implications for better management of these patients.

### Study limitations and strength

This study has several limitations worth mentioning. The first was the lack of a control group which made it difficult to adequately access the exact odds ratio between cases and control. However, our main focus was to study the pattern and stages of endometriosis and determine the clinico-pathological and biophysical profiles of these women. Granted though, having a control group might have improved the robustness of the study. Another limitation of this study was that it was a facility-based study and our data may not reflect accurately the statistics of the disease in the general African population or be representative of the women population there. To ascertain this, a wider and bigger study is needed. Third, the study design included extraction of secondary data and any flaws in initial recording of these data would not have been amended or modified during data entry and analysis. Since the data were recorded by specialists, we were of the opinion that any intra-personal error would have been minimal. The strength of this study lies in the fact that it was conducted by top gynecologists and in one of the most modern facilities for assisted reproductive treatment (ART) in Africa with conducive environment for patients, assured confidentiality and well-motivated staff.

### Abbreviations

ART	Assisted Reproductive Technique
ASRM	American Society of Reproductive Medicine
AUB	Abnormal Uterine Bleeding
BMI	Body Mass Index
BH	Bilateral Hydrosalpinx
BTB	Bilateral Tubal Blockage
CI	Confidence Interval
GnRHa	Gonadotropin-release hormone agonist
IBS	Irritable Bowel Syndrome
OR	Odds ratio
IVF	In-vitro Fertilization
NFC	Nordica Fertility Center
PID	Pelvic Inflammatory Disease
PCOS	Polycystic Ovarian Syndrome
UTB	Unilateral Tubal Blockage
WHO	World Health Organization

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### References

- Kennedy S, Bergqvist A, Chapron C, et al; ESHRE Special Interest Group for Endometriosis and Endometrium Guide-

line Development Group. ESHRE guideline for the diagnosis and treatment of endometriosis. *Hum Reprod.* 2005;20(10):2698-2704.

- Rock JA, Markham SM. Pathogenesis of endometriosis. *Lancet.* 1992;340(8830):1264-1267.
- Giudice LC, Kao LC. Endometriosis. *Lancet.* 2004;364(9447):1789-1799.
- Macer ML, Taylor HS. Endometriosis and infertility: a review of the pathogenesis and treatment of endometriosis-associated infertility. *Obstet Gynecol Clin North Am.* 2012;39(4):535-549.
- Bullett C, Coccia ME, Battistoni S, Borini A. Endometriosis and infertility. *J Assist Reprod Genet.* 2010;27(8):441-447.
- Vercellini P, Trespidi L, De Giorgi O, Cortesi I, Parazzini F, Crosignani PG. Endometriosis and pelvic pain: relation to disease stage and localization. *Fertil Steril.* 1996;65(2):299-304.
- Gruppo italiano per lo studio dell'endometriosi. Prevalence and anatomical distribution of endometriosis in women with selected gynecological conditions: results from a multi-centric Italian study. *Hum Reprod.* 1994;9(6):1158-1162.
- Bérubé S, Marcoux S, Maheux R; Canadian Collaborative Group on Endometriosis. Characteristics related to the prevalence of minimal or mild endometriosis in infertile women. *Epidemiology.* 1998;9(5):504-510.
- Vessey MP, Villard-Mackintosh L, Painter R. Epidemiology of endometriosis in women attending family planning clinics. *BMJ.* 1993;306(6871):182-184.
- Belleis P, Dias JA Jr, Podgaec S, Gonzales M, Baracat EC, Abrão MS. Epidemiological and clinical aspects of pelvic endometriosis—a case series. *Rev Assoc Med Bras (1992).* 2010;56(4):467-471.
- ACOG Committee on Practice Bulletins Gynecology. ACOG Practice Bulletin No. 51. Chronic pelvic pain. *Obstet Gynecol.* 2004;103(3):589-605.
- Somigliana E, Vigano P, Parazzini F, Stoppelli S, Giambattista E, Vercellini P. Association between endometriosis and cancer: a comprehensive review and a critical analysis of clinical and epidemiological evidence. *Gynecol Oncol.* 2006;101(2):331-341.
- Bulun SE. Endometriosis. *N Engl J Med.* 2009;360(3):268-279.
- Giudice LC. Clinical practice. Endometriosis. *N Engl J Med.* 2010;362(25):2389-2398.
- Vinatier D, Orazi G, Cosson M, Dufour P. Theories of endometriosis. *Eur J Obstet Gynecol Reprod Biol.* 2001;96(1):21-34.
- Kyama MC, DHooghe TM, Debrock S, Machoki J, Chai DC, Mwenda JM. The prevalence of endometriosis among African-American and African-indigenous women. *Gynecol Obstet Invest.* 2004;57(1):40-42.
- Otolorin EO, Ojengbede O, Falase AO. Laparoscopic evaluation of the tuboperitoneal factor in infertile Nigerian women. *Int J Gynaecol Obstet.* 1987;25(1):47-52.
- Olubuyide IO, Adebajo AO, Adeleye JA, Solanke TF. Massive ascites associated with endometriosis in a Nigerian African. *Int J Gynaecol Obstet.* 1988;27(3):439-441.
- Okunlola MA, Adekunle AO, Arowojolu AO, Oluwasola AO. Isolated umbilical endometriosis a rare finding. *Afr J Med Med Sci.* 2002;31(3):281-282.
- Thacher TD, Nwana EJ, Karshima JA. Extrapelvic endometriosis in Nigeria. *Int J Gynaecol Obstet.* 1997;59(1):57-58.
- Guo SW, Wang Y. Sources of heterogeneities in estimating the prevalence of endometriosis in infertile and previously fertile women. *Fertil Steril.* 2006;86(6):1584-1595.
- Missmer SA, Hankinson SE, Spiegelman D, Barbieri RL, Marshall LM, Hunter DJ. Incidence of laparoscopically confirmed endometriosis by demographic, anthropometric, and lifestyle factors. *Am J Epidemiol.* 2004;160(8):784-796.
- Calhaz-Jorge C, Mol BW, Nunes J, Costa AP. Clinical predictive factors for endometriosis in a Portuguese infertile population. *Hum Reprod.* 2004;19(9):2126-2131.

24. Parazzini F, Cipriani S, Bravi F, et al. A metaanalysis on alcohol consumption and risk of endometriosis. *Am J Obstet Gynecol*. 2013;209(2):106.e1-106.e10.
25. Tolossa FW, Bekele ML. Prevalence, impacts and medical managements of premenstrual syndrome among female students: cross-sectional study in College of Health Sciences, Mekelle University, Mekelle, northern Ethiopia. *BMC Womens Health*. 2014;14(1):52.
26. American Society for Reproductive Medicine (ASRM). Endometriosis: a guide for patients. Available from [https://www.asrm.org/BOOKLET\\_Endometriosis/](https://www.asrm.org/BOOKLET_Endometriosis/). Accessed Nov 23, 2016.
27. WHO. BMI classification. Available from [http://apps.who.int/bmi/index.jsp?introPage=intro\\_3.html](http://apps.who.int/bmi/index.jsp?introPage=intro_3.html). Accessed Nov 23, 2016.
28. Hediger ML, Hartnett HJ, Louis GM. Association of endometriosis with body size and figure. *Fertil Steril*. 2005;84(5):1366-1374.
29. Arruda MS, Petta CA, Abrão MS, Benetti-Pinto CL. Time elapsed from onset of symptoms to diagnosis of endometriosis in a cohort study of Brazilian women. *Hum Reprod*. 2003;18(4):756-759.
30. Vessey MP, Villard-Mackintosh L, Painter R. Epidemiology of endometriosis in women attending family planning clinics. *BMJ*. 1993;306(6871):182-184.
31. Hemmings R, Rivard M, Olive DL, et al. Evaluation of risk factors associated with endometriosis. *Fertil Steril*. 2004;81(6):1513-1521.
32. Shah DK, Correia KF, Vitonis AF, Missmer SA. Body size and endometriosis: results from 20 years of follow-up within the Nurses Health Study II prospective cohort. *Hum Reprod*. 2013;28(7):1783-1792.
33. Viganò P, Parazzini F, Somigliana E, Vercellini P. Endometriosis: epidemiology and aetiological factors. *Best Pract Res Clin Obstet Gynaecol*. 2004;18(2):177-200.
34. Batt RE, Mitwally MFM. Endometriosis from thelarche to mid-teens: pathogenesis and prognosis, prevention and pedagogy. *J Pediatr Adolesc Gynecol*. 2003;16(6):337-347.
35. Buck Louis GM, Hediger ML, Peña JB. Intrauterine exposures and risk of endometriosis. *Hum Reprod*. 2007;22(12):3232-3236.
36. Nnoaham KE, Webster P, Kumbang J, Kennedy SH, Zondervan KT. Is early age at menarche a risk factor for endometriosis? A systematic review and meta-analysis of case-control studies. *Fertil Steril*. 2012;98(3):702-712.e6.
37. Treloar SA, Bell TA, Nagle CM, Purdie DM, Green AC. Early menstrual characteristics associated with subsequent diagnosis of endometriosis. *Am J Obstet Gynecol*. 2010;202(6):534.e1-534.e6.
38. Garcia-Velasco JA, Somigliana E. Management of endometriomas in women requiring IVF: to touch or not to touch. *Hum Reprod*. 2009;24(3):496-501. Published online December 4, 2008.
39. Macer ML, Taylor HS. Endometriosis and infertility: a review of the pathogenesis and treatment of endometriosis-associated infertility. *Obstet Gynecol Clin North Am*. 2012;39(4):535-549.
40. Barri PN, Coroleu B, Tur R, Barri-Soldevila PN, Rodríguez I. Endometriosis-associated infertility: surgery and IVF, a comprehensive therapeutic approach. *Reprod Biomed Online*. 2010;21(2):179-185.
41. Lessey BA. Medical management of endometriosis and infertility. *Fertil Steril*. 2000;73(6):1089-1096.
42. Paskulin DD, Cunha-Filho JS, Souza CA, Bortolini MC, Hainaut P, Ashton-Prolla P. TP53 PIN3 and PEX4 polymorphisms and infertility associated with endometriosis or with post-in vitro fertilization implantation failure. *Cell Death Dis*. 2012;3(9):e392.
43. Opøien HK, Fedorcsak P, Omland AK, et al. In vitro fertilization is a successful treatment in endometriosis-associated infertility. *Fertil Steril*. 2012;97(4):912-918.
44. Dong X, Liao X, Wang R, Zhang H. The impact of endometriosis on IVF/ICSI outcomes. *Int J Clin Exp Pathol*. 2013;6(9):1911-1918.
45. Matalliotakis IM, Cakmak H, Fragouli YG, Goumenou AG, Mahutte NG, Arici A. Epidemiological characteristics in women with and without endometriosis in the Yale series. *Arch Gynecol Obstet*. 2008;277(5):389-393.
46. Sangi-Hagheykar H, Poindexter AN III. Epidemiology of endometriosis among parous women. *Obstet Gynecol*. 1995;85(6):983-992.
47. Arumugam K, Lim JM. Menstrual characteristics associated with endometriosis. *Br J Obstet Gynaecol*. 1997;104(8):948-950.
48. Wei M, Cheng Y, Bu H, Zhao Y, Zhao W. Length of Menstrual Cycle and Risk of Endometriosis: A Meta-Analysis of 11 Case-Control Studies. *Medicine (Baltimore)*. 2016;95(9):e2922.
49. Moini A, Malekzadeh F, Amirchaghmaghi E, et al. Risk factors associated with endometriosis among infertile Iranian women. *Arch Med Sci*. 2013;9(3):506-514.
50. Cramer DW, Wilson E, Stillman RJ, et al. The relation of endometriosis to menstrual characteristics, smoking, and exercise. *JAMA*. 1986;255(14):1904-1908.
51. Vercellini P, De Giorgi O, Aimi G, Panazza S, Uglietti A, Crosignani PG. Menstrual characteristics in women with and without endometriosis. *Obstet Gynecol*. 1997;90(2):264-268.
52. Donnez J, Van Langendonck A, Casanas-Roux F, et al. Current thinking on the pathogenesis of endometriosis. *Gynecol Obstet Invest*. 2002;54(Suppl 1):52-58, discussion 59-62.
53. Zondervan KT, Cardon LR, Kennedy SH. The genetic basis of endometriosis. *Curr Opin Obstet Gynecol*. 2001;13(3):309-314.
54. Alborzi A, Zarei A, Alborzi S, alborzi M. Management of Ovarian Endometrioma Clinical Obstetrics and Gynecology. 2006;49(3):480-491.
55. Harada T, Iwabe T, Terakawa N. Role of cytokines in endometriosis. *Fertil Steril*. 2001;76(1):1-10. Published online July 05, 2001.
56. Lebovic DI, Mueller MD, Taylor RN. Immunobiology of endometriosis. *Fertil Steril*. 2001;75(1):1-10. Published online February 13, 2001.
57. Witz CA. Interleukin-6: another piece of the endometriosis-cytokine puzzle. *Fertil Steril*. 2000;73(2):212-214. Published online February 24, 2000.
58. Remorgida V, Ferrero S, Fulcheri E, Ragni N, Martin DC. Bowel endometriosis: presentation, diagnosis, and treatment. *Obstet Gynecol Surv*. 2007;62(7):461-470.
59. Hughesdon PE. The structure of endometrial cysts of the ovary. *J Obstet Gynaecol Br Emp*. 1957;64(4):481-487.
60. Brosens IA, Puttemans PJ, Deprest J. The endoscopic localization of endometrial implants in the ovarian chocolate cyst. *Fertil Steril*. 1994;61(6):1034-1038.
61. Lee EJ, Kwon HC, Joo HJ, Suh JH, Fleischer AC. Diagnosis of ovarian torsion with color Doppler sonography: depiction of twisted vascular pedicle. *J Ultrasound Med*. 1998;17(2):83-89.
62. Wentzensen N, Poole EM, Trabert B, et al. Ovarian cancer risk factors by histologic subtype: an analysis from the ovarian cancer cohort consortium. *J Clin Oncol*. 2016;34(24):2888-2898.