



## **Endometriosis: A Clinicopathological Study**

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### **Authors' contributions**

*This work was carried out in collaboration between all authors. Author EI designed the study, performed the statistical analysis, wrote the protocol and wrote the first draft of the manuscript. Authors AO and POA acquired the data and managed the analyses of the study. Authors DY and YEN managed the literature searches. All authors read and approved the final manuscript.*

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### **ABSTRACT**

**Background:** Endometriosis is defined by the presence of endometrial like glands and stroma without the endometrium and myometrium. It is an estrogen dependent condition and affects 6-10% of females commonly during their reproductive age. Theories have evolved to explain the mechanism of development of this disease whose etiology is largely unknown. It affects a wide range of organs and could present with symptoms.

**Aims:** The aim of this study is to document the pattern of endometriosis at the Jos University Teaching Hospital in relationship to patient's age, anatomical distribution of lesion, and symptoms (especially infertility).

**Study Design:** This is a hospital based retrospective and descriptive study. The major grouping for data were age, site, and symptoms.

**Place and Duration of Study:** Department of Histopathology, Jos University Teaching Hospital, Jos, Plateau State in North-Central Nigeria between 1st August 2007, and 31st August 2017

**Materials and Methods:** We reviewed all consecutive cases of endometriosis histopathologically

diagnosed at the Histopathology Department of the Jos University Teaching Hospital, Jos, between 1st August 2007, and 31st August 2017. Corresponding patient data such as age, sex, symptoms, and anatomical site of lesion were obtained from case files and surgical pathology records and analyzed. Archived slides and re-cut slides from tissue blocks were reviewed.

**Results:** Thirty-two (32) cases of endometriosis were diagnosed at the Jos University Teaching Hospital during the study period. The age range was 25-58 years and the mean was 38.0 +8.8 years. The ovary recorded 8 cases accounting for 25% of cases, being the commonest anatomical site involved. Thirteen (40.6%) affected women were infertile.

**Conclusion:** Endometriosis in our locality is more frequently located in the ovary and a relatively high percentage of this disease is associated with infertility. We recommend that endometriosis be considered in the management of patients with ovarian disease and infertility in our locality.

*Keywords: Endometrioma; infertility; Jos.*

## 1. INTRODUCTION

The clinico-pathological entity endometriosis is defined by the presence of endometrial like glands and stroma without the endometrium and myometrium [1,2]. It is an estrogen dependent condition and therefore commonly occur within the reproductive age group, thereby presenting in affected women from menarche to menopause [3-8]. It generally affects 6-10% of females [9]. In 2010, an estimated 176 million women were living with the disease globally between the age of 15 and 49 years [10]. It is commoner in women in their thirties and forties [11]. Certain factors increase the risk of development of the disease, and include age, genetic/hereditary, the environmental, and any combination of these [12].

As a chronic inflammatory disease, it invokes fibrosis, a condition that might alter the normal anatomy of organs/tissues with far reaching consequences [2,4,5,6].

Endometriosis and a similar disease adenomyosis share some fundamental characteristics. This has led to the naming of the later "endometriosis interna" since it is domicile within the uterus, and the former "endometriosis externa" owing to its extrauterine location [13]. These shared characteristics include: presence of ectopic endometrial glands and stroma in both pathologies, and the dependence of these heterotropic tissues on estrogen for proliferation with exaggeration in pathophysiological mechanism of tissue injury and healing [14].

Endometriosis could occur almost anywhere, however the pelvis is commonly affected [1]. Anatomical distribution of this ectopic deposit has evolved three distinct clinical forms of the disorder [15]. These include: peritoneal

endometriosis in which the surface of the peritoneum is affected; endometrioma affecting the ovaries; and deeply infiltrating endometriosis in which the lesion is seen in other organs like the bladder, ureters, and bowel [15][16]. To these could be added a fourth group, anterior abdominal endometriosis [17].

Although the etiology of endometriosis is largely unknown, theories have evolved to explain the mechanism of development of the disease [18]. These theories bordering on pathogenesis includes: embryonal theory in which mullerian remnants are believed to evolve into endometriosis; metastatic/migratory theory in which retrograde menstruation leads to regurgitation of endometrial tissues through the fallopian tubes into the pelvis; transplantation theory in which endometrial tissue are thought to reach distant sites via haematogenous/lymphatic embolization; and the iatrogenic theory, where surgical procedure implants endometrial tissues at ectopic sites [19,20]. A role for stem cells has also been demonstrated [20].

In a review, Bamgboye described two types of endometriosis on etiological basis [21]. These are the endometrioid and endometrial types. Endometrial endometriosis consists of live cells originating from uterine endometrial epithelium cells (EECs). These EECs arise before or after menstruation to ectopic sites, but when they do during menstruation, they are not sloughed off necrotic/apoptotic, but live cells. Endometrioid endometriosis consists of cells that have never been residents of the endometrium. These are likely embryonic cells that hitherto did not differentiate into uterine tissue, but remained in ectopic sites. They are hormone depended cells that respond similarly as the endometrium to hormone secreted during the reproductive live of females.

Endometriosis could be asymptomatic [22]. It's commonest symptoms are pain/pelvic-pain (dysmenorrhea, dyspareunia), and infertility [7,18,23,24,25]. Although this condition is not life threatening, it causes significant morbidity, decreasing the quality of life of afflicted women [8,26].

The treatment of the disease is individualized and depends on age or symptoms. It includes medical, surgical, or a combination of both therapies [27]. Ultimately this lifelong treatment is aimed at optimizing medical therapy in a bid to obviate repeated surgery [27].

The objective of this study is to document the pattern of endometriosis at the Jos University Teaching Hospital in relationship to patient's age, anatomical distribution of lesion, and symptoms (especially infertility).

## 2. MATERIALS AND METHODS

The study was a retrospective analysis of consecutive cases of endometriosis seen at the Histopathology Department of the Jos University Teaching Hospital, Jos, between 1st August 2007, and 31st August 2017. The archived slides and paraffin embedded tissue blocks were retrieved for all cases to confirm the diagnosis. All cases of Endometriosis seen within this period were retrieved from the records of patients in the Histopathology Department and the Medical records department. The information retrieved for each case include: age, sex, symptoms, and anatomical site of lesion. The symptoms considered were: mass effect, bleeding per vaginam, pain of any type, and infertility. The data was analyzed using SPSS

statistical software and presented in tables as simple frequencies and percentages.

## 3. RESULTS

During the study period, 32 cases of endometriosis were diagnosed at the Jos University Teaching Hospital. The age range was 25-58 years; the modal class was 30-39 years with 18(56.3%) cases and a mode of 35 years; the mean was 38.0 ±8.8 years; and the median was 31 years. The same is presented in Table 1.

**Table 1. Age distribution of women with endometriosis**

S/no	Age	Frequency	Percentage
1.	20-29	4	12.5
2.	30-39	18	56.3
3.	40-49	5	15.6
4.	50-59	5	15.6
	Total	32	100.0

Ovarian endometriosis was seen in 8 cases accounting for 25% of cases, being the commonest anatomical site involved. The anterior abdominal wall, peri-umbilical region, pelvic cavity, fallopian tubes, cervix, intestine, and perineum recorded decreasing frequencies of 15.6%, 12.5%, 12.5%, 9.4%, 9.4%, 9.4%, and 6.3% respectively. The same is highlighted in Table 2.

Upto 13(40.6%) affected women were infertile. Also 13(40.6%) of cases reported a feeling of a mass (mass effect). The symptoms of bleeding and pain occurred in 9(28.1%) and 18(56.3%) cases respectively. The same is illustrated in Table 2.

**Table 2. Distribution of women with endometriosis according to anatomical site and symptoms**

S/no	Anatomical site	Frequency of cases	Symptoms			
			Mass effect	Bleeding	Pain	Infertility
1.	Ovary	8 (25.0%)	2	-	6	4
2.	Fallopian tubes	3 (9.4%)	-	2	2	2
3.	Cervix	3 (9.4%)	-	3	1	1
4.	Pelvic cavity	4 (12.5%)	2	2	2	2
5.	Perineum	2 (6.3%)	2	-	2	1
6.	Anterior abdominal wall	5 (15.6%)	4	1	2	1
7.	Peri-umbilical region	4 (12.5%)	2	1	2	2
8.	Intestine	3 (9.4%)	1	-	1	-
	Total	32 (100.0%)	13 (40.6%)	9 (28.1%)	18 (56.3%)	13 (40.6%)

#### 4. DISCUSSION

Endometriosis is largely a disease of women [7]. However, it has been reported in men undergoing therapy for prostate cancer with high dose estrogen [28,29]. The absence of male cases in this study might not be unconnected to the choice of therapy for prostate cancer in our locality [30,31]. Ekeke et al. studied 216 cases of prostate cancer in Nigeria, and reported treatment options to include: androgen deprivation therapy in 95% of cases; chemotherapy in 10.2% of cases; radiotherapy in 7.4% of cases; and radical prostatectomy in 2.3% of cases [30]. In this series, no patient was treated with estrogen. This finding was corroborated by Ajape et al., in another Nigerian report where 192 patients were involved [31].

Researchers have consistently reported the estrogen dependence of endometriosis. Hence the disease is commoner within the reproductive age group, afflicting women from menarche to menopause [3-8]. The mean age at menarche in our locality is 13.5 years while that of menopause ranges from 44-56 years [32,33]. Menopause is associated with a decline in ovarian function-the major source of estrogen [34]. From the foregoing, it follows that more than 68.8% of patients in this study are within the reproductive age group. This mirrors the dependence of endometriosis on estrogen.

The source of estrogen necessary to sustain the endometriotic tissue has been thought largely to be an endocrine phenomenon in which the hormone is delivered via the blood stream [35]. Advancements in this field has however demonstrated a significant role for autocrine/paracrine signaling. The endometriotic implant has been demonstrated to have the capability of establishing a concentrated estrogenic milieu by producing high levels of estrogen [36-39]. In post-menopausal women, the high level of estrogen is as a result of local production and/or replacement therapy for the hormone [40]. Takayama et al., successfully treated endometriosis in a 57 years old post-menopausal woman with Anastrozole, an inhibitor of Aromatase, an enzyme responsible for the local production of estrogen. This was documented as the first ever report in this regard [41].

Lee and Co-researchers studied endometriosis in 1,350 women with endometriosis that went through 1,376 surgeries, with 1,376 pathology

results, at the Seoul National University Bundang Hospital over an eight year period, and found a mean age of of 36.3±7.5 years and an age range of 15 to 71 years [42]. This is similar to the mean age of 38.0 ±8.8 years in this study, but with a comparatively narrower age range (25-58 years). Both studies however have a population of women in a stage of their lives where estrogen is most active, thereby steering the course of this disease.

The ovary was the predominant site of occurrence of endometriosis in this study. This is consistent with a report by Jenkins et al. in which 54.9% of endometriosis was located in the ovary [43]. This is however a higher figure to the 25% seen in this study. A large nationwide hospital based study in France found out that up to 40-50% of endometriosis cases were endometriomas thereby comprising the majority of cases [18]. Similarly, Santos et al, in a retrospective analysis of 310 women with histologically confirmed endometriosis after surgery found ovarian endometriosis consisting of 63.4% of cases [44]. A staggering figure of 96.4% for endometriomas was reported by Lee et al, in 1,350 women with confirmed endometriosis [42]. Although any of the theories of the pathogenesis of endometriosis could lead to endometriomas, the reason behind the predominance of this site over others has not been elucidated. The sequence for other anatomical sites in the distribution of distribution of endometriosis shows variation in our study and other literature reviewed [18, 42, 43, 44]. Lee et al, found endometriosis in soft tissues (2.8%), gastrointestinal tract (0.3%), and the urinary tract (0.2%) [42]. Santos et al, reported endometriosis in the peritoneum (27.9%), abdominal wall (9.9%), uterosacral ligament (8.4%), fallopian tube (8.0%), rectovaginal septum and retrocervical (6.5%), and the bowel (4.2%) [44].

Endometriosis is asymptomatic in about 25% of cases [27]. Therefore it is an under-reported disease [45]. However, infertility has been identified as a consistent risk factor of this clinic-pathologic entity [45]. As much as 25-50% of women with endometriosis are infertile [46-50]. Conversely, about 25-50% of infertile women have endometriosis [50]. Also infertile women are 6 to 10 times more likely to have endometriosis than fertile women [51]. A low fecundity rate has also been associated with endometriosis [52,53]. Furthermore, women with the disease have been reported to have lower live birth rate [54]. The finding of 40.6% in this study for cases of

endometriosis presenting with infertility is consistent with these reports. A lower prevalence of 27.1% for infertile women in 310 women with endometriosis confirmed by surgery and histology was reported by Santos et al. [44]. This however falls within the 25-50% range alluded to earlier [46-50]. Possible mechanisms linking endometriosis with infertility have been reported. These include chronic inflammatory-adhesive reproductive organ distortion and secretion of soluble substances (hormones/cytokines) that negatively affects ovarian/endometrial cellular functions [27]. Also cells from endometriotic sites have been shown to migrate to the eutopic endometrium where they affect embryo implantation [3].

Pain was seen in 56.3% of women in this study. The study however did not categorize pain into the myriads of its presentation. Santos et al, found dysmenorrhea (82.8), dyspareunia (48.5), acyclic pain (38.5), and pericatricial pain (7.6), manifesting as symptoms in patients with endometriosis [44]. Also in a cross-sectional study of 239 women with gynaecological indications in Ibadan, Nigeria, 115 (48.1%) of these were found to have endometriosis, and dysmenorrhea and pelvic pain were commoner in women with the disease [55].

## 5. CONCLUSION

Endometriosis in our locality is more frequently of the endometrioma subtype, and a relatively high rate of this disease is associated with infertility. We recommend that endometriosis be considered in the management of patients with ovarian disease and infertility in our locality.

## COMPETING INTERESTS

Authors have declared that no competing interests exist.

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