Original Article

Histopathological Study of Endometrium in Infertility: Experience in A Tertiary Level Hospital

Ahmed M[a], Afroze N[b], Sabiha M[c]

Abstract

Background: *Infertility refers to inability to achieve conception even after one year of unprotected coitus by a couple. It is a global health problem and affects 8-10% couple worldwide. Infertility can be primary or secondary and there are many causes of infertility involving both male and female partner. A wide range of investigations can be done to find out the causes of infertility. Endometrial biopsy or curettage or aspiration followed by histopathological study is a safe procedure. It not only shows the hormonal response of endometrium but also diagnose other endometrial pathology causing infertility. The study was performed to find out the morphological pattern of endometrium in infertile women in a tertiary care hospital to find out the causes of infertility and subsequent treatment of the patients.*

Methods: *It was a cross sectional prospective study, conducted in the Department of Histopathology and Cytopathology in a tertiary care hospital in Dhaka for a period of two years from Jan 2015 to Dec 2016. It included 196 referred cases endometrial curettage or biopsy samples of infertile women, collected between days 21 to 23 of menstrual cycle. The endometrial samples obtained from patients suffering from diseases other than infertility were excluded from the study. Hematoxylin and Eosin (H&E) stained histopathological slides were prepared from the samples and examined under microscope. Reported results and relevant data were recorded in SPSS data collection sheet and statistical analysis was carried out.*

Results: *A total of 196 cases of endometrial biopsy or curettage samples of both primary and secondary infertile women were studied. Age ranged from 20 years to 40 years with a mean age of 29.91±4.32years. 70.92% cases presented with primary infertility and 29.08% cases presented with secondary infertility. Proliferative phase/anovulation (41.33%) was found as the most common morphological pattern of endometrium in infertile women followed by secretory phase (40.30%). Endometrial hyperplasia, inadequate sample, nonspecific ednometritis and tuberculous endometritis were found in 10.72% , 6.12% , 6.12% and 0.51% cases respectively. In primary infertility, proliferative phase / anovulation (43.17%) was also the predominant pattern followed by secretory phase (37.40%) and endometrial hyperplasia (11.52%). Whereas, secretory phase(47.37%) was the most common pattern of endometrium in secondary infertility, followed by proliferative phase (36.37%) and endometrial hyperplasia (8.77%). Primary infertility was most frequently presented in 26-30 years of age, whereas, secondary infertility was more prevalent in later age group.*

Conclusion: *Histopathological study of endometrium gives us valuable information of endometrium in infertility. Morphological pattern of endometrium in our study was quite similar to other studies conducted in different countries with some variations. This study may help other studies in future to find out the cause of infertility.*

Key words: *Histopathology, Infertility, Endometrium*

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Introduction

Infertility refers to inability to achieve conception even after one year of unprotected coitus by a couple.[1] It is a global health problem and affects about 80 million people (8-10% of couple) worldwide.[1,2]

Based on Demographic and Health Surveys from 1990 to 2004, WHO found that, one in every four eligible couples in developing countries was affected by infertility. [3]

It was estimated that the rates of infertility were 4% in Bangladesh, 6% in Nepal, 5% in Pakistan and 4% in Sri Lanka. [4]

Infertility can be primary, where couples have never conceived previously or secondary where couples have had a pregnancy, although not necessary a successful one. [2]

There are many causes of infertility involving both male and female partner. In Bangladesh, a study conducted in another tertiary care hospital found that among infertile couples, 43.63% had female partner problems; 20% were suffering from male partner problems, 21.81% couples had both partner problems and 14.54% couples were suffering from unexplained infertility where no cause was found.[4]

Female infertility can occur due to wide variety of causes, ranging from hormonal imbalance leading to anovulation or improper development of endometrium for implantation to congenital anomalies or infections or other pathologies involving uterus, fallopian tube, external genitalia or error of coitus even. To find out the female cause of infertility a wide range of investigations can be done , ranging from hormone assay to hysteroscopy and laparoscopy.[1]

'Dating' the endometrium is possible by its histological examination. It is often used clinically to assess hormonal status or document ovulation. Endometrium changes from proliferative to secretary phase after ovulation. Endometrial proliferation occurs under the influence of estrogen. Whereas, secretory activity and decidual reaction are brought about by progesterone in the presence of oestrogen. [1] Therefore, histopathological examination of premenstrual endometrium can determine ovulation/ anovulation by assessing its phase.[5]

Infertility is either anovulatory (absence of ovulation) or ovulatory (with normal ovulation). Secretory phase of endometrium in premenstrual biopsies indicates that the ovulation has occurred and therefore the cause of infertility is other than anovulation. Whereas, proliferative

phase in premenstrual biopsies indicate anovulation and this is a major cause of infertility. Main causes of anovulatory cycles are polycystic ovary syndrome, ovarian neoplasms, enzyme deficiency, gonadal dysgenesis, autoimmune reactions, luteinized unruptured follicle syndrome. Depending on the level of estrogen hormone, endometrium can be resting, atrophic, irregularly proliferative or hyperplastic. In ovulatory infertility absolute or deficient progesterone deficiency may result in deficient secretory phase with delayed maturation of glands and stroma.[6] Moreover, histopathological examination of endometrium can diagnose other pathology which is associated with infertility, such as tuberculosis, endometritis, hyperplasia etc.[7]

Endometrial aspiration or biopsy is a safe, reproducible procedure and adequate mean of

providing histological evidence of normal endometrial development as well to find out other endometrial pathology. For this, endometrial aspiration or biopsy taken in premenstrual period is still one of the initial investigations done in developing countries.[1]

The present study aimed at evaluating the histological patterns of endometrium in infertile women in an attempt to find out the cause of infertility and subsequent management of the patients.

Methods

This was a cross sectional study, conducted in the Department of Histopathology and Cytopathology, in a tertiary care hospital in Dhaka for a period of two years from January 2015 to December 2016. This study included 196 referred cases of endometrial curettage or biopsy samples received in 10% formalin in the Department of Pathology for histopathological evaluation. Patients suffering from either primary or secondary infertility were included in the study. Endometrial samples were collected between days 21 to 23 of menstrual cycle of each patient. The endometrial samples obtained from patients suffering from diseases other than infertility such as DUB or postmenopausal bleeding were excluded from the study. Gross examinations of the samples were done following the guideline described by standard textbook of surgical pathology. Paraffin blocks were made; Hematoxylin and Eosin (H&E) stained histological slides were prepared and examined under microscope.

During microscopic examination, evaluation of morphological features, such as cyclical phase, presence of hyperplasia, non specific endometritis or tuberculous endometritis were made. Secretory phase is further subdivided into early, mid and late secretory phase depending on its morphological pattern.

Reported results and relevant data were recorded in SPSS data collection sheet and statistical analysis was carried out using SPSS version 17. For statistical analysis, patients were divided into four age groups, as follows: 20-25 years, 26-30 years, 31-35 years, 36-40 years and percentages (frequencies) of various parameters were calculated.

Results

A total of 196 cases of endometrial biopsy or curettage samples of infertile women were studied. Age ranged from 20 years to 40 years with a mean age of 29.91±4.32years. Majority of them belonged to 26-30 years age group and majority of the patients (70.92%) presented with primary infertility. Figure 1

Proliferative phase/anovulation was found as the most common morphological pattern of endometrium in infertile women followed by secretory phase. Among the secretory phase late secretory phase was most common (25% cases). Table I.

Proliferative phase / anovulation was also the predominant pattern of endometrium in primary infertility. It was found in 60 (43.17%) cases in primary infertility. Whereas, secretory phase (including its different stages) was the most common pattern of endometrium in secondary infertility. Other types of endometrial pathology were found in both types of infertility with slight variation of their incidences. Table II.

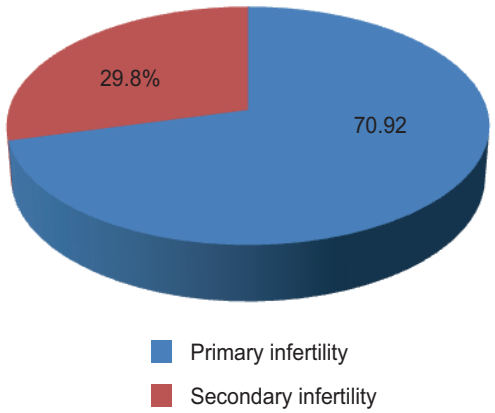

Figure 1. *Distribution of primary and secondary infertility*

Table I. Histological pattern in endometrium in infertile women (n= 196)

Pattern of endometrium		No of cases	Percentages (%)
Proliferative phase		81	41.33
Secretory phase		79	40.30
	Early secretory	*15*	*7.65*
	Mid- secretory phase	15	7.65
	Late secretory phase	49	25.00
Simple endometrial hyperplasia		21	10.72
Inadequate sample		12	6.12
Non-specific endometritis		02	1.02
Tuberculous endometritis		01	0.51
Total		196	100%

Table II. Histological pattern in endometrium in different types of infertility

Pattern of endometrium		Primary infertility	Secondary infertility
Proliferative phase		60 (43.17%)	21(36.85%)
Secretory phase		52(37.40%)	27 (47.37%)
	Early secretory	*06 (4.31%)*	*09(15.79%)*
	Mid- secretory phase	11(7.91%)	04 (7.02%)
	Late secretory phase	35(25.18%)	14 (24.56%)
Simple endometrial hyperplasia		16(11.52%)	05(8.77%)
Inadequate sample		09(6.47%)	03(5.26%)
Nonspecific endometritis		02(1.44%)	-
Tuberculous endometritis		-	01 (1.75%)
Total		139(100.00%)	57 (100.00%)

Table III. Relative frequencies of endometrial findings in our study with other studies.

	Endometrial pathologyPercentage (%) of cases in different studies						
	Girish et al, India	Kafeel et al, Pakistan	Kaur P et al, India	Cheleb N Algeria	Zawar MP India	Ikeme ACC, Nigeria	Present study Bangladesh
Proliferative phase/anovulation	56.70	25.0	23.0	31.3	50.0	56.7	41.33
Secretory phase	32.30	56.6	66.0	50.0	28.2	16.6	40.30
Endometrial hyperplasia	5.5	14.1	-	10.9	1.7	20.0	10.72
Nonspecific endometritis	2.2	3.3	-	-	-	1.7	1.02
Tuberculous endometritis	2.2	0.83	3.0	-	2.6	-	0.51

Primary infertility was most frequently presented in 26-30 years of age, whereas, secondary infertility was more in older age group (31-35 years age group). Figure 2.

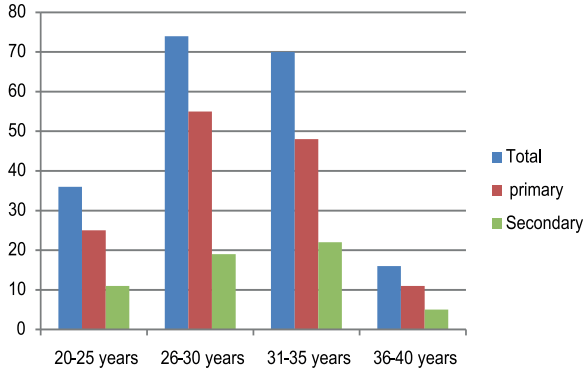

Figure 2. *Age distribution of primary and secondary infertility.*

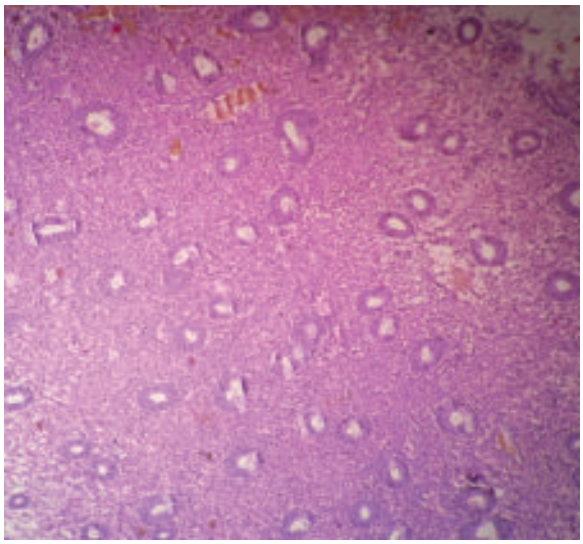

Figure 3. *Proliferative phase of endometrium 100X (H&E Stain)*

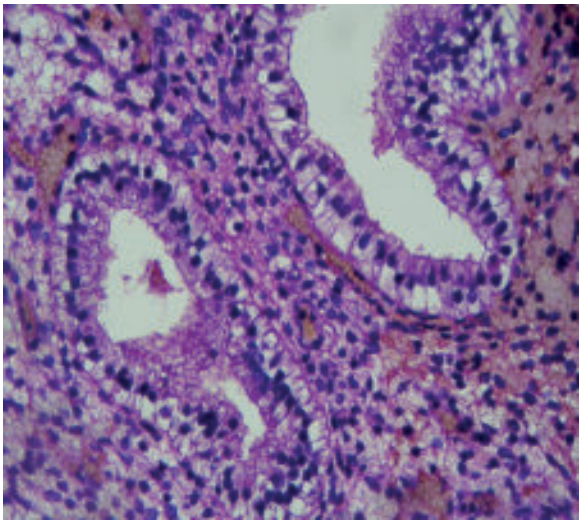

Figure 4. *Early secretary phase of endometrium 400X (H&E Stain)*

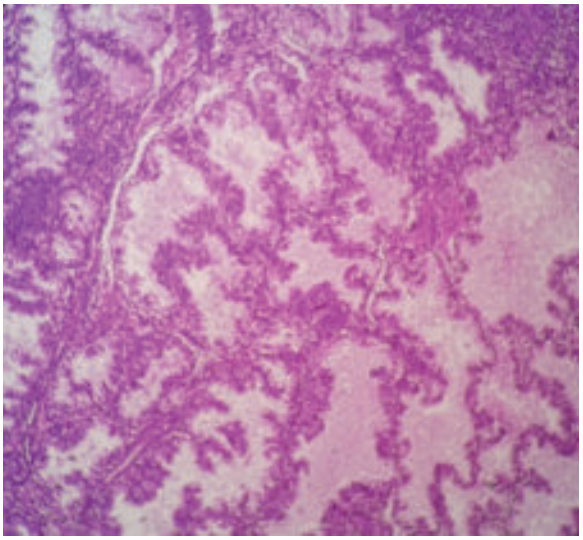

Figure 5. *Late secretory phase of endometrium 100X (H&E Stain)*

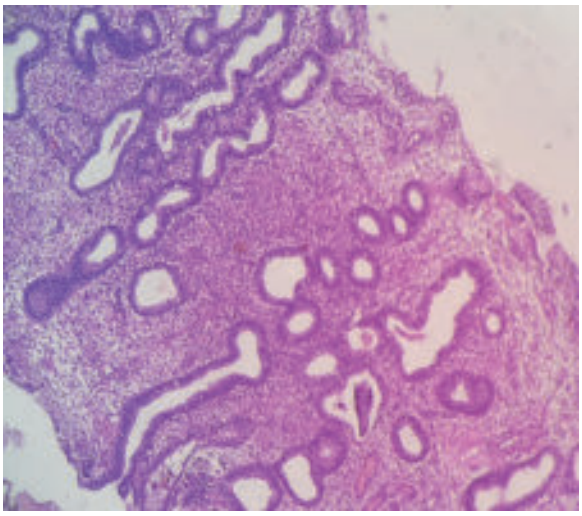

Figure 6. *Simple hyperplasia of endometrium 100X (H&E Stain)*

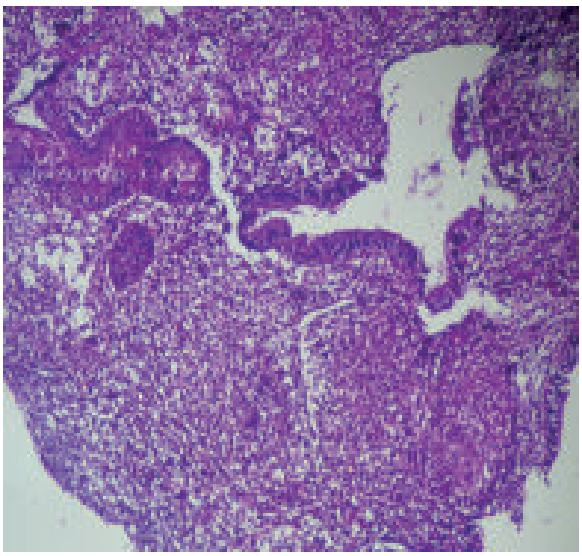

Figure 7. *Tuberculous endometritis 100X (H&E Stain)*

Discussion

In our study it was found that infertile women presented more with primary infertility (70.92%). Similar findings were also observed in the studies conducted by Kaur et al [8] in India and Chelab et al in Algeria.[9] Where they found women presented with primary infertility in 77.14% and 71.90 % cases respectively. Whereas, in Nigeria secondary infertility (61.7%) occurred more than primary infertility (38.3%).[10]

In present study, mean age of the patient was 29.91years and age ranged from 20 -40 years. Similar findings were also found in Pakistan in a study done by Kafeel et al. [11] Where he found mean age was 29 years, and age ranged from 21-37 years. The mean age of infertility in Nigerian women was 31.7 years. [10] Whereas, in Algeria women presented in more older age. Mean age was 33 years and age ranged from 23- 43 years. [9] The reason may be that overall women literacy and employment rate is higher in Algeria. [12, 13]

In our study, we found that proliferative phase/ anovulation was the most common cause of infertility followed by secretory phase. Similar findings were also observed by Girish et al , [14] in India and Ikene et al in Nigeria [10] and Cheleb et al in Algeria.[9] However, other studies conducted in India and Pakistan, found secretory phase was the most common cause of infertility followed by proliferative phase. [8, 11, 15]

Among the secretory phase we found late secretory phase was most frequent (25% cases). Our finding varies with the findings of Kafeel et al, [11] where he found early secretory phase (37.5% cases) was most common followed by mid secretory phase (14.1% cases) and late secretory phase (5.0% cases). Incidences of other endometrial pathology in our study also varied slightly with other studies. Table 3

Endometrial hyperplasia was found in 10.72% cases in our study. It was also found higher (14.1%) in Pakistan [11] and highest in Nigerian women (20.0%).[10] But, in India, its incidence was much lower.[8, 14, 15]

Tuberculous endometritis is still a major cause of infertility in developing countries and any woman with unexplained infertility should be investigated for tuberculosis.[16] 0.8% cases of tuberuclous endometritis was observed in Pakistan.[11] Its incidence was found more in different studies conducted in India, reaching 3.9% cases in a study done by Punyashetty et al. [17] But, in our study, we found only 0.51% cases with tuberculous endometritis. Table 3.

The reason may be that our Hospital is a tertiary level non-government Hospital, so patients attended here belonged to a higher socio-economic class rather than poor socio-economic group, where tuberculosis is more common as an infectious disease.

Present study found primary infertility was most frequently presented in 26-30 years of age, whereas

secondary infertility was more in older age group, similar things were also observed in a study conducted in Pakistan.[11]

In present study it was found that proliferative phase / anovulation was the predominant pattern of endometrium in primary infertility and secretory phase was the most common in secondary infertility. Other varieties of endometrial pathology were found in both types of infertility with slight variation of their incidences. Table III.

Conclusion

In infertility, histomorphological study of endometrium not only shows the hormonal response of endometrium but also gives additional information about the local factors of endometrium concerning atrophy, hyperplasia, specific or nonspecific infections and malignancy. Morphological pattern of endometrium in our study was quite similar to other studies conducted in different countries with some variations. The study was conducted in one tertiary level hospital only. To find out the female cause of infertility in our country a bigger study is needed. This study may help other studies in future to find out the cause of infertility.

Conflict of interest: Nothing to declare.

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