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Original research article

Histopathological analysis of the endometrial tissue in women diagnosed with primary infertility

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Abstract

Aim: To determine the endometrial Biopsy In Primary Infertility Patients

Methods: A prospective study was conducted in the Department of obstetrics and gynaecology, VIMS, Pawapuri, Nalanda, Bihar, India, India for 1 year. A total of 100 endometrial samples of patients having primary infertility were taken for histopathological evaluation. The endometrial samples were consisted of 95 endometrial biopsy and 5 curettage material. This was grossly greyish white to greyish brown in color. Material was immediately placed in fixative fallowed by routinely processed and paraffin section of 5 -6 micron, using hematoxylin and eosin were prepared and studied microscopically.

Results: Out of 100 patients, out of which 33 samples (33%) showed proliferative phase, suggestive of an ovulatory cycle where sparse narrow and straight endometrial glands lined by low coloumnar cells embedded in loose stroma of spindle shaped cells in 22 section, while in 3 sections, endometrial glands were more elongated and lined by tall columnar cells, with stromal edema. Remaining 8 sections showed tortuous endometrial glands lined by pseudo stratified epithelium with compact stroma and slightly enlarged stromal cells. Irregular proliferative endometrium was seen in 9 sections (9%) where irregularly shaped enlarged glands interspersed among normal proliferative glands resulting in dyssynchronous development of endometrium. Simple hyperplasia was seen in 5 (5%) cases where section shows cystically dilated proliferating glands of varying size, lined by tall coloumnar cells with many clear cells, while stroma was dense and compact with stromal cells having scant cytoplasm.

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.

Keywords: infertility, endometrium, nonspecific infections

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 an ovulatory (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 an ovulatory 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]

Materials and methods

A prospective study was conducted in the Department of obstetrics and gynaecology, VIMS, Pawapuri, Nalanda, Bihar, India, India for 1 year. after taking the approval of the protocol review committee and institutional ethics committee.

Methodology

A total of 100 endometrial samples of patients having primary infertility were taken for histopathological evaluation. A detailed relevant clinical history were recorded regarding age group, duration of infertility, result of any previous evaluation and treatment, menstrual history (age at menarche, cycle length, onset or severity of dysmenorrhoea), previous method of contraception, coital frequency and sexual dysfunction, any history of thyroid disease, pelvic or abdominal pain and dyspareunia were recorded. Family history of birth defect, mental retardation, early menopause, occupation and use of tobacco and alcohol were noted. The endometrial samples were consisted of 95 endometrial biopsy and 5 curettage material. This was grossly greyish white to greyish brown in colour. Material was immediately placed in fixative fallowed by routinely processed and paraffin section of 5-6 micron, using hematoxylin and eosin were prepared and studied microscopically.

Results

Out of 100 patients, 100 endometrial sample sectionswere taken, out of which 33 samples (33%) showed proliferative phase, suggestive of an ovulatory cycle where sparse narrow and straight endometrial glands lined by low coloumnar cells embedded in loose stroma of spindle shaped cells in 22 section, while in 3 sections, endometrial glands were more elongated and lined by tall coloumnar cells, with stromaledema. Remaining 8 sections showed tortuous endometrial glands lined by pseudo stratified epithelium with compact stroma and slightly enlarged stromal cells.

Irregular proliferative endometrium was seen in 9 sections (9%) where irregularly shaped enlarged glands interspersed among normal proliferative glands resulting in dyssynchronous development of endometrium. The gland were lined by pseudo stratified epithelium at places, ciliated epithelium was seen in all these cases. Thestroma was mitotically active proliferative type. Simple hyperplasia was seen in 5 (5%) cases where section shows cystically dilated proliferating glands of varying size, lined by tall coloumnar cells with many clear cells, while stroma was dense and compact with stromal cells having scant cytoplasm.

Adequate secretory phase seen in 35 cases (35%) showing sub nuclear vacuolation in morethan 50% gland (16 days), in 3 cases uniform sub nuclear vacuolation pushing nuclei towards apex (17 days), in 2 cases nuclei return to base with secretion at tip of epithelial cells give frayed appearance (18 days), in 4 cases secretion at free margin seen as a globular cap (19 days) ,in 2 case dilatation of glands filled with secretion (20 days), in 5 cases beginning of stromal edema, stromal cells appear as naked nuclei (21 days), in 2 cases maximal stromal edema (22 days), in 3 cases prominent spiral arterioles (23 days), in 8 cases predecidualization of periarterial stromal cells (24 days), in 2 cases predecidualization of upper compact layer with appearance of endometrial granulocytes (25 days), in 2 cases predecidualization of entire compacta layer, predominant endometrial granulocytes (26days), in 2 cases saw toothed shaped glands, very dense predecidual stroma (27 days).

Deficient secretory phase or luteal phase deficiency was seen in 13 (13%) cases. There were 8 cases (61.54%) of deficient secretory phase with apparent delay and 5 cases (38.46%) of deficient secretory phase with dissociated delay.

Deficient secretory phase with dissociated delay was seen in 7 cases showing widely spaced poorlyconvoluted glands with variation in development of glands and stroma, with glandular epitheliallining having dense hyperchromatic nucleus, decreased luminal secretion, subnuclear vacuolation, spindle shaped stromal cells with decreased stromal differentiation.

Arias stella reaction was seen in 2 case (2%) showing star shaped glands lined by epithelial cells having grotesquely shaped nucleus with dense chromatin and abundant clear cytoplasm, spindle shaped stromal cells with scant cytoplasm.Tuberculous endometritis was seen in 3 cases (3%) showing proliferating endometrial glands comprising granulomas with central caseation surrounded by radiating epitheloid cells andlymphocytes.

Table 1: Age of patients

Age(years)	Number of patients	Percentage
Below 20	19	19
20-25	45	45
25-30	31	31
30-35	3	3
Above 35	2	2
Total	100	100

Table 2: Duration of infertility

Duration of Marriage (Infertility) In years.	Number of patients	Percentage
2-3	43	43
4-5	23	23
6-7	16	16
8-9	9	9
10-11	6	6
12	3	3
Total	100	100

Table 3: Histopathological Finding of Endometrial Biopsy Tissue

Histopathological Finding of Endometrial Biopsy	Number of patients	Percentage
Proliferative phase	33	33
Irregular proliferative endometrium	9	9
Simple hyperplasia	5	5
Adequate secretory phase	35	35
Luteal phase deficiency (Deficient secretory)	13	13
Tuberculous endometritis	3	3
Arias Stella reaction	2	2

Discussion

Primary infertility is one of the common conditionfor which married women seeks medical advice.In India there are an estimated 10.2 million infertile couple. Female infertility may occur due to disturbances of genital system or part of central nervous system that control the ovaries hormonally.

In present study, mean age of the patient was 27.5 years and age ranged from 18 -40 years. Similar findings were also found in Pakistan in a study done by Kafeel et al.[8] 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.[9] Whereas, in Algeria women presented in more older age. Mean age was 33 years and age ranged from 23- 43 years.[10] The reason may be that overall women literacy and employment rate is higher in Algeria.[11,12]

This study is in accordance with the findings of Ramesh Kumar and Thomas (1991),[13] while the duration of infertility ranged from 2 -12 yrs with a mean of 7.5 years which are in accordance with findings of Usha ks(1989)[14] having a mean of 6.5 yrs.

Out of 100 patients, out of which 33 samples (33%) showed proliferative phase, suggestive of anovulatory cycle where sparse narrow and straight endometrial glands lined by low coloumnar cells embedded in loose stroma of spindle shaped cells in 22 section, while in 3 sections, endometrial glands were more elongated and lined by tall coloumnar cells, with stromaledema. Remaining 8 sections showed tortuous endometrial glands lined by pseudo stratified epithelium with compact stroma and slightlyenlarged stromal cells. Similar results was found by other author.[15-18]

Majority of cases 70 (70%) had regular menstrual pattern, irregular history was noted in 30 cases (30%) of which 25 cases (83.33%) were found to have uterine and or ovarian pathology

similar tostudies done by Gupta a Anatal (1989)[15], MP Zawar(2003)[16], Girish C1 (2006) and Kajal (2008).[17,18]

In a developing country like India where complex expensive immunological and hormonal assay procedure are not easily available in small cityand in rural areas, endometrial biopsy is avaluable investigation for Primary infertility Proper correlation, clinical data and dating of endometrium helps to diagnose functional abnormalities of the endometrium, as well as intrinsic abnormalities, most of who are otherwise asymptomatic in patients of infertility. In spite of certain limitation in dating of endometrium and itsaccuracy, endometrial biopsy still remains the most accepted and widely studied parameter providing sufficient information about the hormonal status of the endometrium. However in 35% of cases no cause can be found for infertility. The entire reproductive process iscontrolled by brain, so in today fast paced world factors like chronic stress, high pressure work,emotional distress and even life style take a toll onthe reproductive process.

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.

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