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Original Research Article

Histopathological Evaluation of Endometrial Biopsy Tissue of the Patients, Suffering From Primary Infertility, Attending In Tertiary Care Hospital, at Muzaffarpur, Bihar

Authors
Dr Manoj Kumar[1], Dr Manoj Kumar[2], Dr O.P. Dwivedy[3*], Dr Manju Geeta Mishra[4] Dr Satyendu Sagar[5]
[1]Tutor, Department of Pathology, Sri Krishna Medical College, Muzaffarpur
[2]Professor and HOD, Department of Pathology, Sri Krishna Medical College, Muzaffarpur
[3]Associate Professor, Department of Pathology, Nalanda Medical College, Patna
[4]Director, M.G.M. Hospital, Patna
[5]Assistant Professor, Department of Microbiology, Nalanda Medical College, Patna
*Corresponding Author
Dr O.P. Dwivedy
Associate Professor, Department of Pathology, Nalanda Medical College, Patna, India

Abstract
Objective: *The aim of present study was to histopathological evaluation of endometrial tissue in the cases of primary infertility.*
Material and Methods: *A total of 92 female patients with 18 to 36 years of age group and 2-12 years of duration of infertility were attending in GOPD with the presenting complains of infertility, were included in the study. After detailed history, clinical examination and relevant investigation endometrial biopsy were taken. From all the patients' informed consent were taken. Out of 92 patients 88 endometrial biopsy materials were taken and from 4 patient's 4 curettage samples were collected. All the biopsy materials were fixed and send to our department for processing and histopathological evaluation. All the relevant data were noted.*
Results: *Out of 92 patients, maximum 42 (45.65%) patients were in the 21-25 years of age, followed by 28 (30.43%) patients was in 18-20 years of age. 40 (43.48%) patients comes after 2-3 years of durations of infertility and 21 patients (22.83%) comes after 4-5 years of duration of marriage, only 2 (2.17%) moves after 12 years of marriage. Histopathological Finding of Endometrial Biopsy shows, 31 (33.69%) patients had Proliferative phase, 8 (8.69%) patients had irregular proliferative endometrium, 5 (5.43%) patients had simple hyperplasia, 32 (34.78%) patients showed adequate secretory phase and 3 (3.26%) patients had tuberculous endometritis.*
Conclusion: *The purpose of investigating the infertile couple is to assess their chance of achieving pregnancy and to identify the factors amenable to treatment to clarify the causes of infertility, an impressive array of diagnostic tests are available to clinicians. Almost all functional disturbances involved in infertility result in morphological changes in the endometrium since hormone levels fluctuate depending upon various biorhythms, the histological examination of the endometrial biopsy is the most confirmatory tools for the diagnosis of infertility.*
Keywords: *Proliferative phase, Histopathological Finding, Endometrial Biopsy, infertility.*

Introduction

Every married woman nurtures a deep felt desire to become a mother, unfulfillment of which is not only a cause of distress mentally but also socially to the women and their family especially in India. The barren marriage is a problem as old as the history of mankind.

Failure of married couple of reproductive age group to conceive after twelve months or more of unprotected intercourse or six months if the women is over age 35yrs or the inability to carry a pregnancy to live birth is called Infertility.

Infertility affects approximately 10 to 12% of population. Since infertility strikes diverse group affecting people from all socioeconomic levels and cutting across all racial, ethnic and religious lines. Chances are great that a friend, relative, neighbor, or perhaps you are attempting to cope with medical and emotional aspect of infertility. Approximately one third of infertility is attributed to the female partner, another one third to the male partner and one third is caused by combination of problems in both partner or is unexplained.

Infertility can be primary when it occurs in women who has never established a pregnancy or it can be secondary when it occurs in a women who has a history of one or more previous pregnancies. Medically the cause of infertility may be divided as ovulatory dysfunction (40%), tubal and pelvic pathology (40%), unexplained infertility (10%), cervical factors (5-10%) and uterine factors (5%). Though there may be multiple reasons, disturbances in development of endometrium during the postovulatory phase could be an important factor, as the endometrium is the site of implantation infertile patients often has out of phase endometrium under normal physiological conditions the uterine mucosa is a close gauge to the ovarian activity.

The cyclic alterations occurring in the endometrium during reproductive life are a prerequisite for the ultimate function of uterus to house and support the conception, where the morphological and biochemical changes of uterine mucosa are likely to play an important role in the implantationn of fertilized oocyte. Thus the, alteration of the human endometrium during normal menstruation cycle is prime concern. Evidence of ovulation and cause of ovulatory dysfunction can be obtained by study of serial vaginal cytology, endometrial biopsy and hormonal assessment.

As the endometrial biopsy and histology demonstrate secretory endometrial development which results from the action of progesterone thus evidence of ovulation or anovulation luteal phase deficiency besides giving information regarding various endometrial pathology, was long considered the gold standard among methods for evaluating the quality of luteal functions for diagnosis of luteal phase deficiency with certain limitations in accuracy and precision.

Thus in this study we have stressed on histopathological features of endometrium in primary infertility, to date the endometrium and to categorize them in various types based on microscopy of endometrial tissue being sent in our pathology department.

Material and Method

Present study was conducted in the Department of Pathology, Sri Krishna Medical College, Muzaffarpur, Bihar, with the help of Obstetrics and Gynecology, Department, during the period of January 2017 to August 2018. A total of 92 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

88 endometrial biopsy and 4 curettage material. This was grossly grayish white to grayish 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

Table – 1 Shows Age group of patients in years

Age group of patients in years	Total no. of patients	Percentage
18-20	18	19.56
21-25	42	45.65
26-30	28	30.43
31-35	3	3.26
36	1	1.08
Total	92	

Table 2 Shows duration of infertility

Duration of Marriage (Infertility) In years.	Total no. of patients	Percentage
2-3	40	43.48
4-5	21	22.83
6-7	15	16.30
8-9	8	8.69
10-11	6	6.52
12	2	2.17
Total	92	

Table 3 Show Histopathological Finding of Endometrial Biopsy Tissue.

Histopathological Finding of Endometrial Biopsy	Total no. of sample	Percentage
Proliferative phase	31	33.69
Irregular proliferative endometrium	8	8.69
Simple hyperplasia	5	5.43
Adeqate secretory phase	32	34.78
Luteal phase deficiency (Deficient secretory)	12	13.04
Tuberculous endometritis	3	3.26
Arias stella reaction	1	1.08

Out of 92 patients, 92 endometrial sample sections were taken, out of which 31 samples (33.69%) 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 21 section, while in 2 sections, endometrial glands were more elongated and lined by tall coloumnar cells, with stromal edema. Remaining 8 sections showed tortuous endometrial glands lined by pseudostratified epithelium with compact stroma and slightly enlarged stromal cells.

Irregular proliferative endometrium was seen in 8 sections (8.69%) where irregularly shaped enlarged glands interspersed among normal proliferative glands resulting in dyssynchronous development of endometrium. The gland were lined by pseudostratified epithelium at places, ciliated epithelium was seen in all these cases. The stroma was mitotically active proliferative type. Simple hyperplasia was seen in 5 (5.43%) 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 32 cases (34.78%) showing subnuclear vacuolation in more than 50% gland (16days), in 2 cases uniform subnuclear vacuolation pushing nuclei towards apex (17days), in 1 cases nuclei return to base with secretion at tip of epithelial cells give frayed appearance (18days), in 3 cases secretion at free margin seen as a globular cap (19days) ,in 1 case dilatation of glands filled with secretion (20days), in 4 cases beginning of stromal edema, stromal cells appear as naked nuclei (21 days), in 2 cases maximal stromal edema (22days), in 2 cases prominent spiral arterioles (23days), in 10 cases predecidualization of periarterial stromal cells (24days), in 4 cases predecidualization of upper compact layer with appearance of endometrial granulocytes (25days), in 1 cases predecidua-lization of entire compacta layer, predominant endometrial granulocytes (26days), in 1 cases saw toothed shaped glands, very dense predecidual stroma (27 days).

Deficient secretory phase or luteal phase deficiency was seen in 12 (13.04%) cases. There were 8 cases (66.67%) of deficient secretory phase with apparent delay and 6 cases (33.33%) of deficient secretory phase with dissociated delay.

Deficient secretory phase with dissociated delay was seen in 6 cases showing widely spaced poorly convoluted glands with variation in development of glands and stroma, with glandular epithelial lining having dense hyperchromatic nucleus, decreased luminal secretion, subnuclear vacuolation, spindle shaped stromal cells with decreased stromal differentiation.

Arias stella reaction was seen in 1 case (1.08%) 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 (3.26%) showing proliferating endometrial glands comprising granulomas with central caseation surrounded by radiating epitheloid cells and lymphocytes.

Discussion

Primary infertility is one of the common condition for 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 this study we have observed that the commonest age group belonging to 18-36 years with a peak at age 24yrs. This study is in accordance with the findings of Ramesh Kumar and Thomas (1991), while the duration of infertility ranged from 2 -12 yrs with a mean of 7 years which are in accordance with findings of Usha ks(1989) having a mean of 6.5 yrs. Majority of cases 65 (70.65%) had regular menstrual pattern, irregular history was noted in 27 cases (29.35%) of which 24 cases (88.88%) were found to have uterine and or ovarian pathology similar to studies done by Gupta a Anatal (1989), MP Zawar (2003), Girish C1 (2006) and Kajal (2008).

In a developing country like India where complex expensive immunological and hormonal assay procedure are not easily available in small city and in rural areas, endometrial biopsy is a valuable investigation for Primary infertility. Proper correlation, clinical data and dating of endometrium helps to diagnose functional abnormalities of the endometriun, 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 its accuracy, endometrial biopsy still remains the most accepted and widely studied parameter providing sufficient information about the hormonal status of the endometrium. However in 35.4% of cases no cause can be found for infertility. The entire reproductive process is controlled by brain, so in today fast paced world factors like chronic stress, high pressure work, emotional distress and even life style take a toll on the reproductive process.

Conclusion

Endometrial biopsy is a simple and safe procedure to rule out presence of any uterine pathology in cases of female infertility, especially tuberculous infection. For that proper timing of biopsy and processing of samples are important determinants.

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