Histopathological Study of Endometrial Biopsy in Cases of Infertility

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ABSTRACT

BACKGROUND

Reproduction is an essential aspect of marriage. Primary infertility is the inability to conceive after one year of unprotected coitus. Secondary infertility implies inability to conceive for 5 years of unprotected coitus after last conception including ectopic and recurrent abortions. The schedule of evaluation or investigations in infertility range from detailed clinical history, physical examination, basal body temperature, vaginal cytology, cervical mucus changes, endometrial biopsy, laparoscopy, ultrasonography, follicular study, hormone assays to immunoglobulin profile and new genetics. However, the most reliable method for diagnosing the cause of infertility in women remains the histopathological study of endometrial tissue.

METHODS

This is a prospective study carried out at a teaching hospital with the help of Department of Obstetrics and Gynaecology from 01/12/2014 to 01/08/2016. Patients who were reporting for infertility were the subjects of the study. The study included 150 cases of infertility.

RESULTS

Out of a total of 150 cases studied, 111 cases were primary infertility and 39 cases were secondary infertility with maximum incidence in the age group of 19-23 years and 29-33 years in primary and secondary infertility respectively with 2-13 years duration after marriage. Proliferative (anovulatory) endometrium is seen in 31 cases of primary and 15 cases of secondary infertility. Tuberculosis is seen in 2 cases primary infertility.

CONCLUSIONS

Primary infertility is more common than secondary infertility. It was observed that total duration of infertility in study group was 2-13 years. Anovulatory endometrium is the commonest cause of endometrium followed by tuberculous endometrium. Endometrial hyperplasia is the least common cause of infertility.

KEYWORDS

Infertility, Endometrial Biopsy, Anovulatory Cycle

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BACKGROUND

The French word "Fertilite" entered the English language in 1490 to characterize the 'richness in soil'. By 17th century writers adopted fertility to describe "creative imagination". In the course of 19th century the term fertile came to account for the number of children a woman bore. Couples leave no leaf unturned to seek for the joy of being called "parents". Infertility affects 10% of people of the reproductive age and 15% of couples globally. Reproduction is an essential aspect of marriage. Primary infertility "is inability to conceive after one year of unprotected coitus. Secondary infertility implies inability to conceive for 5 years of unprotected coitus after last conception including ectopic and recurrent abortions."

The schedule of evaluation or investigations in infertility range from detailed clinical history, physical examination, basal body temperature, vaginal cytology, cervical mucus changes, endometrial biopsy, laparoscopy, ultrasonography, follicular study, hormone assays to immunoglobulin profile and new genetics. However, the most reliable method for diagnosing the cause of infertility in women remains the histopathological study of endometrial tissue.

According to Jones (1974) the endometrial biopsy serves as a bioassay measuring the hormones at tissue level. Thus premenstrual endometrial biopsy is still considered as the most important investigation in cases of infertility, as it provides an opportunity to examine the largest tissue for oestrogen and progesterone, for evaluation of occurrence of ovulation and the information about the pathological lesions like endometrial tuberculosis, luteal phase defects, anovulatory cycles, cystic glandular hyperplasia, which may cause infertility.

Efforts are being made globally to bring the joy of parenting in couple's life. New methods like assisted reproductive technologies (ARTS) comprising IVF; zygote intrafallopian transfer (ZIFT); gamete intrafallopian transfer (GIFT); intracytoplasmic sperm infestation (ICSI); facilities of sperm banks; surrogate parenting; IUI (Ovarian hyperstimulation with intrauterine insemination); ovum donation are prescribed. Despite all these some are not acceptable socially, rest not economical. About 40% of the cases of female infertility are due to ovulatory failure, about 40% due to endometrial or tubal disease, about 10% are due to rare causes, about 10% remain undefined after full workup.

The histological evaluation of the endometrium has been the gold standard investigating female infertility. Biopsies to determine anovulatory cycles are most informative when performed approximately 2 days before the expected onset of menstruation.[1] This study has been a humble step in studying the endometrium of females navigating the maze of infertility.

We wanted to evaluate the causes of infertility through histopathological examination of endometrial biopsy in a tertiary care center in Gujarat, India.

METHODS

The present prospective study as carried out at a teaching hospital with the help of Department of Obstetrics and Gynaecology during 01/12/2014 to 01/08/2016. Patients who were reporting for infertility were the subjects for the study. The study included 150 cases of infertility. All the patients were attending gynaecology and Obstetrics outpatient department. Patients who failed to conceive after 1 year of unprotected coitus following marriage were investigated as cases of primary infertility. Patients with history of abortion and those who did not conceive for 5 years of unprotected coitus after last conception were investigated as cases of secondary infertility.

Detailed history was obtained, and thorough clinical examination was carried out in each case as per Performa. In each case, dilation and curettage, premenstrual or with the onset of menstruation was performed under general anaesthesia to obtain endometrial tissue. Then it was subjected to various pathological studies.

The endometrial tissue was collected in 10% neutral buffered formalin for histopathological study and sterile bulb for culture study.

Gross examination of endometrial tissue was done noting the amount of the endometrial tissue and the presence of blood clot or any other abnormality e.g. polypoid structures etc.

Tissue Processing

Tissue processing of material was done by dehydration, clearing, impregnation, paraffin embedding paraffin block making, section cutting by microtome.

Staining

Haematoxylin (Harry's) and Eosin stain were used.

Proforma

Date:	H-NO.:	S-NO.:
Patient's Name:		
Out Door / Indoor no.		
Age of Patient		
Present Complain		
Menstrual History		
a) Menarche		
b) Past and present menstrual cycle		
c) Last menstrual cycle		
d) Complain associated with menstrual cycle		
• Active Marriage Life		
• Primary Infertility		
• Secondary Infertility		
a) Miscarriage		
b) Living child		
c) Dead child		
• Any Associated Symptoms		
• Past History		
• Family History		
• Investigation		
a) Laproscopy		
b) USG		
Endometrial Biopsy	Taken on day	
Gross Examination	Whether it was collectively tissue bit, with haemorrhagic tissue bit.	
Microscopic Examination	Either Proliferative phase (Early, mid, Late phase) or Secretory phase (Early, mid, Late phase) or Menstruation phase or Endometrial Hyperplasia.	

RESULTS

The present study comprised of a total of 150 cases of primary and secondary infertility attending the outpatient department in the hospital. Out of total 150 cases studied 111 (74%) cases were of primary infertility and 39 (26%) cases were of secondary infertility.

In the primary infertility group maximum number of cases belonged to the group 19-23 years i.e. 60 (54.05%), 45 (40.54%) in the age group 24-28 and lowest in 29-33 years i.e. 6 (5.41%). In the secondary infertility group maximum number of cases belongs to the group 29-33 years i.e. 25 (64.10%), 13 (33.33%) in the age group 24-28 and lowest in 19-23 years i.e. 1(2.56%). This difference found statistically significant, there is association between age and type of fertility.

Type of Infertility	No.	%
Primary	111	74
Secondary	39	26
Total	150	100

Table 1. Distribution of Study Participants According to Type of Infertility (n=150)

Age Group (in Completed Years)	Type of Infertility		Total
	Primary	Secondary	
19-23	60 (54.05%)	1 (2.56%)	61 (40.67%)
24-28	45 (40.54%)	13 (33.33%)	58 (38.67%)
29-33	6 (5.41%)	25 (64.10%)	31 (64.10%)
Total	111 (100%)	39 (100%)	150 (100%)

Table 2. Distribution of Study Participants According to Age and Type of Infertility (n=150)

($\chi 2$= 67.31 with yate's correction, p value is < 0.05, d.f.=2)

Duration of Infertility (in Years)	Type of Infertility		Total
	Primary	Secondary	
2-4	99 (89.19%)	7 (17.95%)	106 (70.67%)
5-7	10 (9.01%)	17 (43.59%)	27 (18%)
8-10	2 (1.80%)	13 (33.33%)	15 (10%)
11-13	0	2 (5.13%)	2 (1.33%)
Total	111 (100%)	39 (100%)	150 (100%)

Table 3. Distribution of Study Participants According to Duration and Type of Infertility (n=150)

($\chi 2$= 74.12 with yate's correction, p value is < 0.05, d.f.=2)

Endometrial Histology	Type of Infertility		Total
	Primary	Secondary	
Endometrial hyperplasia	6 (5.41%)	2 (5.13%)	8 (5.33%)
Proliferative	31 (27.93%)	15 (38.46%)	46 (30.67%)
Secretory	72 (64.86%)	22 (56.41%)	94 (62.67%)
Tuberculosis	2 (1.80%)	0	2 (1.33%)
Total	111 (100%)	39 (100%)	150 (100%)

Table 4. Distribution of Study Participants According to Endometrial Histology and Type of Infertility. (n=150)

($\chi 2$= 2.08, with yate's correction, p value is > 0.05, d.f.=3)

In the primary infertility, duration of infertility was calculated from the date of marriage. In the secondary infertility, duration of infertility was calculated from the date of last delivery and from the date of abortion in cases with history of abortion. It was observed that total duration of infertility in study group was 2-13 years. In the primary infertility maximum number of cases belonged to the duration after marriage was 2-4 years i.e. 99 (89.19%). In the secondary infertility maximum number of cases belonged to the duration after last conception was 5-7 years i.e. 17 (43.59). This difference found statistically significant, there is association between duration and type of fertility.

Proliferative (Anovulatory) endometrium was seen in 31 (27.93%) cases of primary infertility and 15 (38.46%) cases of secondary infertility. Majority of cases revealed histology of endometrium in secretory phase i.e. 72 (64.86%) cases of primary infertility and 22 (56.41%) cases of secondary infertility. Tuberculosis of endometrium was seen in 2 (1.80%) case of primary infertility. Endometrial hyperplasia was seen in 6 (5.41%) cases of primary infertility and 2 (5.13%) cases in secondary infertility. This difference found statistically insignificant, there is no any association between endometrial histology and type of infertility.

DISCUSSION

The purpose of investigating the infertile couple is to assess their chance of achieving a pregnancy and to identify factor amenable to treatment, Driessen F (1980).[2] Walleh EE (1979);[3] Rameshkumer K and Thomas JA (1991);[4] Paterss AJ, Lioyd RP and Coulam CP (1992);[5] Sohmay S et al (1995);[6] Velasco VR et al (1997)[7] concluded that endometrial study is safe, reproducible and adequate means of providing histologic evidence of normal endometrial development. In infertility cases endometrial biopsy performed shortly before or at the beginning of menstrual bleeding plays an important role Driessen F (1980).[2]

The endometrial curettage is an essential step in the examination of infertile women as it is the most sensitive indicator of ovarian function. It provides an opportunity to examine the target tissue for effect of estrogen and progesterone. Chang K and Soules S (1995).

Incidence of Primary and Secondary Infertility

In this study there are 74% cases of are primary infertility and 26% cases are of secondary infertility. The study was done by Bhattacharya et al[8] (1994) there were 74.7% cases were of primary infertility and 25.3% of cases were of Secondary infertility.

Age Groups

Almost all investigations have found that maximum patients seek advice within the maximum fertility period. In the present study the patient's age range was 18-40 years and maximum cases of primary infertility belonged to 19-23 years and those of secondary infertility belonged to age group 29-33 years.

Duration of Infertility

In my study it is observed that maximum patients of infertility came within 2-7 years after marriage. The study was done by Zawar MP[9] (2003), also observed that maximum patients of infertility came within 2-6 years after marriage.

Histopathology of Endometrium

Secretory Phase

When the premenstrual endometrial biopsy shows normal secretory phase corresponding to the day of the cycle then it indicates that cause of infertility is not in the endometrium. According to the day of menstruation period it shows changes in histopathology of endometrium. In below histopathological picture shows Subnuclear vacuolation of epithelium indicative of ovulation and thus it rules out anovulation as a causative factor of infertility.

Figure 1

In late secretory phase microscopic examination shows Tissue oedema along with Intraluminal secretion (Below).

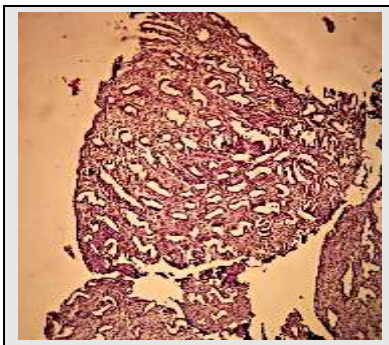

Figure 2

In present study secretory phase was seen in 62.67% of cases which correlates with Neil SS (2001) in which 62.3% of cases were noted.

Proliferative Phase (Anovulatory Cycle)

Anovulatory cycle is quite common in cases of infertility. Anovulatory cycle is due to functional disturbances in hypothalamus, pituitary, ovarian or endometrium. The endometrium may fail to respond because of lack of progesterone receptors. The incidence of anovulatory cycle varies from 10%-34.2%. In present study the incidence of anovulatory cycle is 30.67% which is comparable with Zawar MP[9] et al (2003) in which 28.2% cases were noted.

Tuberculous Endometritis

Tuberculous endometritis is one of the most important causes of infertility and dysfunctional uterine bleeding in tropical countries. In my study the incidence of tuberculous endometritis is 1.33% which is comparable with Sabharawal BD et al[10] (1987). In which 1.34% cases were noted. In below histopathological picture shows Endometrial glands and stroma along with there are present of inflammatory cells mainly lymphocytes, few epitheloid type of histiocytes forming ill-formed granuloma along with Langhans type of giant cell.

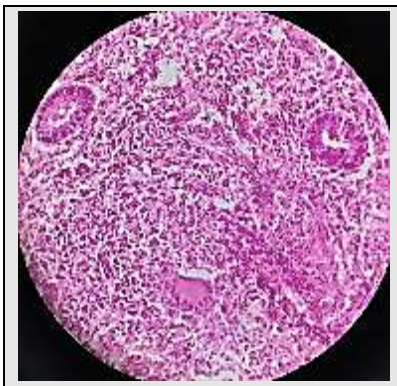

Figure 3

Excess Oestrogen Level

An excess oestrogen level leads to endometrial hyperplasia which can also be a causative factor preventing pregnancy. The present study shows endometrial hyperplasia which is 8% comparable with Gupta AN et al[11] (1980) in which 5.9% cases were noted.

In below Histopathological picture shows Simple typical endometrial hyperplasia Shows mild glandular crowding with at some places cystic changes also seen.

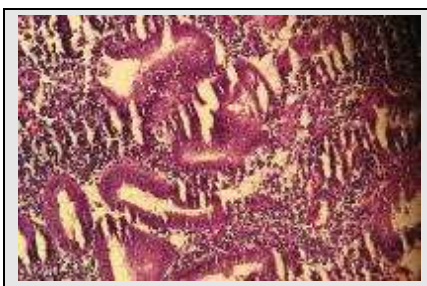

Figure 4

CONCLUSIONS

Primary infertility is more common than the secondary infertility. In the primary infertility group, maximum number of cases belonged to the age group of 19-23 years. It was observed that the total duration of infertility in the study group was 2-13 years. In the primary infertility group, maximum number of cases belonged to the duration post marriage 2-4 years group. Majority of cases had regular cycles. Proliferative (anovulatory) endometrium was one of the most common causes of primary infertility than of secondary infertility. Anovulatory cycle is the commonest cause of infertility which can be detected by microscopic examination of endometrium or serum hormonal study which revels low amount of serum progesterone associated with luteal phase defect also. Though the gold standard method for detection anovulation is serum hormonal assay,

due to cost effectiveness of patients I had done endometrial biopsy for detection. Majority of cases revealed histology of endometrium in secretory phase. Tuberculosis is one of the most common causes of primary infertility. It can be detected by microscopic examination of endometrium.

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