

HISTOPATHOLOGICAL STUDY OF ENDOMETRIUM IN INFERTILITYGireesh Vishnupant Achalkar¹¹Associate Professor, Department of Pathology, Raichur Institute of Medical Sciences, Raichur, Karnataka, India.**ABSTRACT****BACKGROUND**

Infertility is a medical as well as social problem. This causes severe mental stress in infertile couples, especially in women. The parenthood is the natural way of life. In ordinary course of life, couples usually have children in majority of cases. The incidence of infertility varies from region to region.

Aims and Objectives- To find out the incidence of various endometrial pathologies in cases of infertility.

MATERIALS AND METHODS

A descriptive study was carried out in the Department of Pathology, RIMS, Raichur. 200 cases of primary and secondary infertility were studied. Endometrial biopsies were evaluated with available menstrual history. Premenstrual phase endometrial biopsies were obtained. Haematoxylin and eosin staining was done for dating of endometrium and diagnosis of luteal phase defect and anovulatory cycles. PAS staining was also done. Proportions and percentages of primary and secondary infertility having various pathology were calculated.

RESULTS

Menstrual problems were seen in 38% of patients. Anovulatory infertility was present in 41.73% cases. Luteal phase defect was seen in 20% cases. Simple hyperplasia without atypia was seen in 8.4% cases and tuberculous endometritis was present in 10.7% cases. Glycogen deficiency was seen in 28.13% of cases of luteal phase defect.

CONCLUSION

In the present study of 200 cases, majority were primary infertility cases. Common age group affected was 26 - 30 years. Anovulatory cycles accounted for significant numbers of cases.

KEY WORDS

Infertility; Endometrium, Hyperplastic, Tuberculous.

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BACKGROUND

Infertility is a medical as well as social problem. This causes severe mental stress in infertile couple, especially in women. The parenthood is the natural way of life. In ordinary course of life, couples usually have the child in majority of cases. The incidence of infertility varies from region to region. Approximately, one marriage in ten is barren.¹

In India, there are about 10.2 million couples of infertility.² There is a stigma in India of being infertile and it has negative implications in routine life. Infertility causes include both men and women almost equally.

About one-third of cases are due to male factor, one-third due to female factor and the remaining one-third unexplained where both of them are responsible and advanced medical techniques may help them in achieving pregnancy.

The purpose of investigating the infertile couple is to know their chance of achieving pregnancy and to identify the important causative factors amenable to treatment. In spite of many investigatory tools available,

endometrial histology is a sensitive and gold standard indicator of endometrial and ovarian function.

Premenstrual endometrial biopsy plays an important diagnostic role in cases of infertility. Infertility is defined as no conception after 12 months of unprotected sexual intercourse. It is further classified as primary in which no evidence of conception has occurred and as secondary in which prior conception has occurred, not necessarily a live birth.

Sterility is the extreme case, where there is intrinsic inability in achieving pregnancy. Proper investigation must be started as soon as they seek medical attention. Age is one of the important factor with regard to fecundability, hence investigation must be started at the earliest.² Hence, the importance of detailed pathological study.

Objective

To find out the incidence of various endometrial pathologies in cases of infertility.

MATERIALS AND METHODS

It is a descriptive study. The present study was carried out in Department of Pathology, RIMS, Raichur. Endometrial biopsies of 200 cases of primary and secondary infertility were received in Department of Pathology from Department of OBG, during the period from June 2015 to June 2017.

Detailed clinical history was taken with special emphasis on monthly periods, any chronic illness and married life. Past medical and obstetric history was noted. Any radiological and ultrasonographic findings were noted. Premenstrual

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Corresponding Author:

Dr. Gireesh Vishnupant Achalkar,

Associate Professor,

Department of Pathology,

Raichur Institute of Medical Sciences,

Raichur, Karnataka, India.

E-mail: drgireesha@yahoo.com

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endometrial biopsy specimens were obtained. Tissue was fixed in formalin and processed.

Paraffin blocks were made. 4 - 5 micron thick sections were cut and stained with Haematoxylin and Eosin. The sections were studied with regard to dating of endometrium and other pathologies. Haematoxylin and eosin stained sections were studied to date the endometrium accurately based on the criteria described by Dallenbach Hellweg.³

Periodic acid-Schiff (PAS) staining was done in all 200 cases and 25 normal controls. This stain is used primarily to detect the amount of glycogen in the cytoplasm. The findings were studied and analysed to find out the incidence of various changes with regard to glycogen content in the cytoplasm in the endometrium glands.⁴

The proportions and percentages of primary and secondary infertility of various pathologies were calculated.

RESULTS

Amongst 200 cases of infertility 173 cases (86.5%) were of primary infertility, 27 (13.5%) cases were of secondary infertility.

The maximum numbers of patients were in the age range of 19 - 36 years. The youngest patient was 18 years old and the oldest was 42 years. In primary infertility group majority came to seek medical help within 2 - 3 years, whereas patients with secondary infertility sought medical help after 6-7 years after last conception.

Menstrual problems were seen in 35 (22.62%) cases of primary infertility and 33 (23.08%) cases of secondary infertility. Irregular menses were seen in 54 (37.84%) cases of primary infertility and 21 (38.46%) cases of secondary infertility.

200 endometrial specimens were analysed for the various changes in endometria (Table 1). The various morphological patterns of endometrium were studied. Of the total of 200 cases were studied. 173 (86.5%) cases belonged to primary infertility and 27 (13.5%) to secondary infertility. Majority were primary infertility cases.

Type of Infertility	Number	Percentages (%)
Primary	173	86.5
Secondary	27	13.5
Total	200	100

Table 1. Incidence of Primary and Secondary Infertility

Age distribution is given in the table below. The youngest patient was 19 years old and the eldest was 42 years old.

Age Group	Primary Infertility	%	Secondary Infertility	%
21-25	28	16.1	-	
26-30	81	46.8	3	11.1
31-35	52	26.1	13	48.1
36-40	12	6.9	10	40.7
41-45	1	0,5	1	0.5

Table 2. Age Distribution in Infertility

The microscopic features of endometrial biopsies were studied, and the results are as follows (Table 3).

Histological Diagnosis	Primary Infertility No. of Cases 173	%	Secondary Infertility No. of Cases 27	%
Normal secretory endometrium	68	39.16	20	74.23
Non-secretory endometrium	72	41.73	2	7.08
Simple hyperplasia	15	8.40	4	14.69
Tuberculous endometritis	18	10.70	1-	3.7

Table 3. Incidence of Changes in Endometria

Anovulatory endometrium was seen in 72 (41.73%) cases of primary infertility and 2 (7.08%) cases of secondary infertility. 18 cases of primary infertility showed endometrial tuberculosis. However, ZN staining for AFB was negative in all cases (Table 4).

Glycogen Content Grade (PAS Staining)	Proliferative Phase Cases		Secretory Phase Cases		Luteal Phase Defect Cases	
	Primary	Secondary	Primary	Secondary	Primary	Secondary
0	40	3	-	-	-	-
+	-	-	-	-	3	1
++	-	-	4	3	4	1
+++	-	-	24	6	-	-
++++	-	-	32	6	-	-
Total	40	3	60	15	7	2

Table 4. Histology and Glycogen Content in the Endometrium of Patient with Infertility

The Glycogen Content was graded as Follow Arzac and Blanchet

- - Negative reaction.
- + - Very small granules.
- ++ - Coarse granules.
- +++ - Small masses.

DISCUSSION

The studies of populations of patients with infertility indicate that approximately 10% - 25% have unexplained infertility, 20% - 30% have ovulatory dysfunction. 20% - 30% have

tubal damage; 12% - 50% sperm dysfunction. 6% to 10% endometriosis; 5% cervical mucus problems and 3% to 5% coital dysfunction.¹ The most important prognostic factors are duration of infertility and the age of the female partner.

The fertility investigation should be instigated as soon as the couples seek help, even if they have been trying for less than a year. General questions should be asked such as irregularities of menstrual cycle, pelvic surgery or orchidopexy.

Determining the cause of anovulatory infertility is the key to treatment, as the correction of the cause will result in cumulative conception rates that mimic those expected for

normal women of the same age. It must be ascertained whether ovulation is occurring.²

The present study of 200 cases of infertility included 173 of primary and 27 of secondary causes. Majority were primary infertility cases. The reason may be the patients with secondary causes do not get investigated for the second child.

Human endometrium is important site for nidation of fertilised ovum.⁵ The present study was done to systematically evaluate the adequacy of endometrial development based on correlating menstrual history, date with glandular and stromal morphological features and pathological findings.

Properly developed follicles and corpus luteum formation is very much essential for the continuation of normal pregnancy. Initially, the hormone progesterone is synthesised and secreted by corpus luteum. Later this work is taken over by the placenta.⁶ The normal physiologically balanced hormonal profile is needed for the uninterrupted progress of pregnancy.

The diagnosis of luteal phase defect was made by using Jones criteria.^{7,8} For this, the histological findings with regard to dating of endometrium were studied. This was compared with date of menstrual cycle as given by the patient. A difference of more than two days defines the luteal phase defect.^{9,10}

The non-secretory endometrium was an important pathological finding in H and E sections and it constituted the most common cause for infertility. The other important cause was luteal phase defects (Table 5). This observation is comparable with that of other authors.

Studies	% of Non-Secretory Endometrium	% of Secretory Endometrium
Shetty (1959) ^[8]	15.2	74.8%
Gupta et al (1980) ^[9]	22.8	68.5%
Sareen (1984) ^[10]	19	79%
Jadhav and Raichur (1987) ^[11]	25	75%
Sabharwal (1987) ^[12]	12	84%
Krishnamohan et al (1993) ^[13]	10%	87.5%
Neil Shastrabudhe (2001) ^[14]	34.2%	62.3%
Present Study (2002)	41.73%	39.16%

Table 5. Histopathological Abnormalities in the Form of Anovulatory Endometrium and Luteal Phase Defect

Anovulatory cycles with non-secretory endometrium are common pathological observations in cases of primary as well as secondary infertility.^{11,12} Our present study showed anovulatory endometrium in 41.73% cases.

Secretory phase endometrium is diagnosed by the histological features of subnuclear vacuolations and intraluminal secretions. The observation and recognition of this feature is one of the most important part of the accurate reporting by the pathologist. This gives information with regard to ovulation.

Luteal phase defect may be the cause of infertility in ovulatory cycles.^{13,14} Twenty-one cases were included in this category. This was compared with the observations made by other authors. The cause for luteal phase defect is hormonal, mostly due to deficiency of progesterone and some are due to

raised TSH. These patients respond to the hormonal treatment accordingly.

Tuberculous endometritis¹⁵ and simple hyperplasia without atypia formed a minor cause of infertility in present study. The present study shows incidence of tuberculous endometritis in more number of cases compared to other studies. The reason may be India having increased number of tuberculosis patients.¹⁶

It takes minimum of 2 weeks for the granuloma to form. It might shed with the endometrium and hence may not be available in the biopsy specimen. Rani PR found that in patients of genital tuberculosis,¹⁷ the most common site of involvement is endometrium in 46.6% cases.

Manjiri¹⁸ and Kumar A,¹⁹ Nagpal M²⁰ found endometrial tuberculosis as compared with present study and that of Andita B and Tripathy²¹ (Table 6).

Author and Year	% of Tuberculous Endometritis
Zawar et al	2.6%
Sathe et al	6%
Schaefer	5.1%
Gupta et al ^[22]	8.7%
Sareen ^[10]	2%
Sabharwal ^[12]	1.34%
P. Chakroborty	6.2%
R. Mishra	4.9%
Shastrabudhe N ^[14]	2.6%
Present Study	10.7%

Table 6. Incidence of Tuberculous Endometritis in Present Series compared with that Observed by Other Author

The endometrial hyperplasia due to excess level of oestrogen can also prevent pregnancy.^{24,25} In present study, simple hyperplasia without atypia was seen in 8.4% of cases (Table 7).

Author and Year	Glycogen Deficiency in %
Zondek and Stein	18.4%
Shetty ^[8]	44.6%
Zawar et al	30%
Anshu et al	24.7%
Rohtangi	22.5%
Sareen ^[10]	39%
S. Sharma ^[23]	28.5%
Present Study	28.13%

Table 7. Glycogen Deficiency as a cause of Infertility observed by Various Authors

In present study, PAS stain was done in 200 cases of infertility to assess the amount of glycogen content. It is necessary for the successful conception and subsequent growth and development of fertilised ovum in the uterus.

It is very much necessary that adequate amount of carbohydrate in general and glycogen in particular must be present in the glandular secretions. The glycogen is a major source of glucose and energy to the developing embryo.^{24,25}

CONCLUSION

In the present study of 200 cases, majority were primary infertility cases. Common age group affected was 26 - 30 years. Anovulatory cycles accounted for significant numbers of cases.

Histopathological study of endometrium is an important, safe and cheaper diagnostic tool in cases of primary and secondary infertility. It gives immense significant information with regard to structure, function and any pathological lesions in endometrium. The secretory endometrium and adequate carbohydrate content in the cytoplasm of endometrial glandular cells is an essential prerequisite for successful implantation and development of embryo.

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