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Histopathological study of endometrium in cases of infertility in tertiary care hospital

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Abstract
A study of 513 cases of primary and secondary infertility with 211 control cases was carried out in the department of pathology GMERS Medical College, Junagadh, Gujarat, India. Endometrial specimens were evaluated in the light of menstrual history to find out the incidence of various endometrial changes in cases of infertility. All cases underwent endometrial biopsy ware premenstrual. Haematoxylin and eosin staining was done for dating of endometrium and diagnosis of corpus luteal defect and anovalutory cycles. Periodic Acid Schiff (PAS) was also done. Menstrual problems were seen in 41% of patients. Anovulatory infertility was present in 29% cases. Luteal phase defect was seen in 19% cases. Cystoglandular hyperplasia was seen in 5% cases & tuberculous endometritis was present in 2% cases. Glycogen deficiency was seen in 25.34% cases of luteal phase defect.

Keywords: Infertility, endometrium, Anovulatory infertility

Introduction
Infertility is worldwide problem. Approximately one marriage in ten is barren [1]. In India there are an estimated 10.2 million couples of infertility [2]. The purpose of investigating the infertile couple is to assess their chance of achieving a pregnancy and to identify the factors amenable to treatment. In spite of many investigatory tools available endometrial histology is a sensitive indicator of ovarian function. Premenstrual endometrial biopsy plays an important diagnostic role in cases of infertility.

Materials and Methods
Endometrial biopsies of 513 cases of primary and secondary infertility were received in department of pathology, GMERS Medical College, Junagadh, Gujarat, India, during the period of December 2014 to July 2017. Detailed clinical history regarding menstrual cycle, last menstrual period, age at marriage and obstetric history was obtained. Clinical examination was carried out in each case. Premenstrual endometrial biopsy specimens were obtained. The material was processed and paraffin embedded sections of 5 microns were cut. Haematoxylin and eosin stained sections were studied to date the endometrium accurately based on the criteria describe by Dallenbach Hellweg [3]. Periodic acid Schiff staining was done in 513 cases & 211 normal controls to detect the amount of glycogen. PAS positivity was graded as nil, scanty, moderate and abundant [4]. The findings were analysed to find out the proportion of various changes in infertile endometrium.

Observation
Amongst 513 cases of infertility 374 cases (73%) were of primary infertility, 139 (27%) cases were of secondary infertility. The maximum numbers of patient were in the age range of 21-30 years. The youngest patient was 19 years old and the oldest was 38 years. In primary infertility group 40% patient came in 2-3 years duration of infertility. In secondary infertility group 38.46% patients came in 6-7 years duration after last conception. 513 endometrial specimens were analysed for the incidence of changes in endometria (Table 1) (Figures 1-2).

Table 1: Incidence of changes in endometria

Histological diagnosis	Primary infertility no of cases 374	%	Secondary infertility no of cases 139	%
Normal secretory Endometrium	228	61	97	70
Proliferative (anovulatory) endometrium	112	30	32	23
Simple cystic endometrial hyperplasia	19	05	07	05
Tuberculous endometritis	15	04	03	02

Histology and glycogen content in the endometrium of patient with infertility is given in Table 2.

Table 2: Histology and glycogen content in the endometrium of patient with infertility.

Glycogen Content Grade (PAS Staining)	Proliferative Phase 144 Cases		Secretory Phase 325 Cases		Luteal Phase Defect 98 Cases	
	Primary	Secondary	Primary	Secondary	Primary	Secondary
0	112	18	--	--	--	--
+	--	--	--	--	18	6
++	--	--	11	08	20	12
+++	--	--	34	12	--	--
++++	--	--	56	03	--	--
Total	112	18	101	23	38	18
Grand Total	130		124		56	

The glycogen content was graded as follow Arzac & Blanchet [4]: O – Negative reaction, + - Very small granules, ++ - Coarse granules, +++ - Small masses, ++++ - Large masses

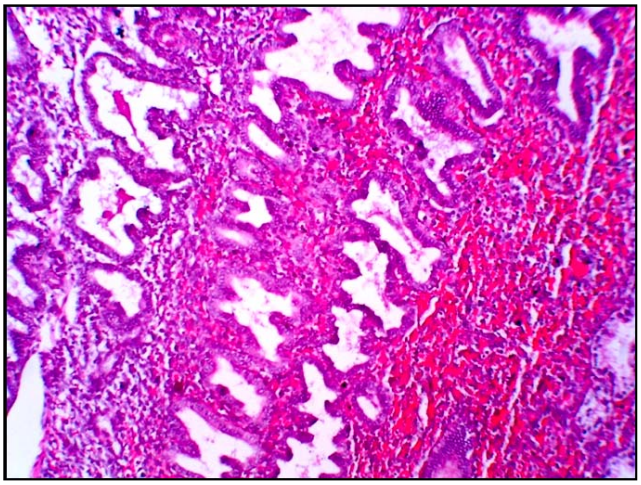

Fig 1: Microphotograph of Secretory endometrium (H&E stain 10x view)

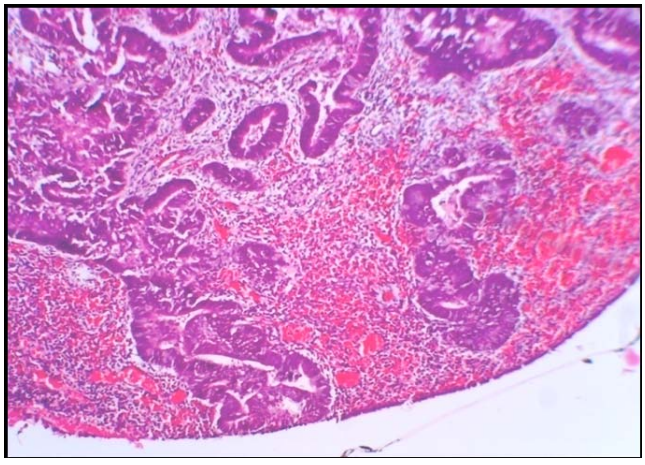

Fig 2: Microphotograph of Proliferative endometrium (H&E stain 10x view)

Discussion

Human endometrium is important site in nidation in young fertilized ovum [5]. In this study evaluated the adequacy of endometrial development based on correlating menstrual history with glandular and stromal morphology and glycogen contain.

Adequate follicular development & functionally efficient corpus luteum formation are the essential prerequisites for the preparation of good endometrial bed which is essential for successful implantation of blastocyst & continuation of pregnancy [6].

The diagnosis of luteal phase defect was made by using Jone's criteria [6]. According to him luteal phase defect is defined as lag more than two days in histological development of endometrium compared to the day of cycle.

Histopathological abnormalities in the form of anovulatory endometrium and luteal phase defect of present study and other study. (Table 3)

Table 3: Histopathological abnormalities in the form of anovulatory endometrium and luteal phase defect.

	% of anovulatory endometrium	% of ovulatory endometrium
Shetty [8]	15.2	74.8
Gupta *et al*. [7]	22.8	68.5
Sareen [9]	19	79
Jadhav and raichur [10]	25	75
Sabharwal BD [11]	12	84
Krishnamohan *et al*. [12]	10	87.5
Shastrabudhe [13]	34.2	62.3
Present study (2017)	26.5	65.5

Anovulatory cycles are quite common in cases of infertility. In present study anovulatory endometrium was present in 26.5% cases. The secretory phase of endometrium in the premenstrual period is indicative of ovulation and thus it rules out anovulation as a cause of infertility. Luteal phase defect may be the cause of infertility in ovulatory cycles. In present study luteal phase defect was, seen in 19% cases. Wentz ac [14, 16], Soules M [15] and Kumar A [17] found luteal phase defect in 19%, 16% and 5% of infertility patients respectively.

Tuberculous endometritis and cystoglandular hyperplasia formed a minor cause of infertility in present studies. Incidence of tuberculous endometritis in present study and compere observed by other author. (Table 4)

Table 4: Incidence of tuberculous endometritis in present series observed by other author.

Author & year	% of tuberculous endometritis
Schaefer [19]	5.1
Gupta *et al*. [18]	8.7
Sareen [9]	2
Sabharwal [11]	1.34
Shastrabudhe N [13]	2.6
Present study	3.5

Glycogen deficiency as a cause of infertility observed by various authors and present study. (Table 5)

Table 5: Glycogen deficiency as a cause of infertility observed by various authors.

Authors	Glycogen deficiency in %
Shetty [8]	44.6
Sareen [9]	39
Sharma [20]	28.5
Present study (O – Negative reaction, + - Very small granules, ++ - Coarse granules)	32.08

The endometrial hyperplasia due to excess level of estrogen can also prevent pregnancy. In present study Simple cystic endometrial hyperplasia was seen in 5.0% of cases. (Table 1) Gupta *et al*. [7], sabharwal [11], Krishnamohan [12] and shastrabudhe [13] found hyperplasia in 5.9%, 2.66%, and 4.4% respectively.

In present study, PAS stain was done in 513 cases of infertility to assess the amount of glycogen content. For the proper implantation and subsequent growth and development of fertilized ovum in the uterus it is necessary that adequate amount of carbohydrate in general and glycogen in particular should be present in the glandular secretions. In the endometrium the high glycogen content (+++ - Small masses, ++++ - Large masses) of these glands serve as a major source of energy for maintain an embryo.

Conclusion

Histopathological study of endometrium forms an important safe and cheaper diagnostic tool in cases of primary and secondary infertility.

In present study anovulatory endometrium and luteal phase defect formed etiological basis of many cases in infertility. In the present studies of glycogen deficiency (O – Negative reaction, + - Very small granules, ++ - Coarse granules) seen mainly in the luteal phase defect indicating histopathological immaturity of endometrium.

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