A STUDY ON ENDOMETRIAL MORPHOLOGY AND GLYCOGEN CONTENT IN INFERTILE WOMEN

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ABSTRACT

BACKGROUND

Infertility is a common problem in day-to-day practice. Therefore, the common uterine pathology should be excluded while investigating infertility. Endometrial biopsy plays an important role in diagnosing infertility and assessing the glycogen content of endometrium, which is essential for implantation of fertilised ovum.

The aim of the study is to find out endometrial pathologies and glycogen content of endometrium as causes of infertility.

MATERIALS AND METHODS

A study of 139 cases of primary and secondary infertility was carried out in the Department of Pathology, M.K.C.G. Medical College, Berhampur. Women with history of infertility were subjected to premenstrual endometrial biopsy. Routine haematoxylin and eosin staining was done for dating endometrium. Endometrial specimens were evaluated in the light of menstrual history to find out various endometrial changes in them. Periodic Acid-Schiff stain was done to detect amount of glycogen in the endometrium.

RESULTS

Primary infertility was detected in 85.6% of cases (n=119) and secondary infertility in 14.4% (n=20) of cases. Maximum incidence of infertility was seen among patients between 23 and 27 years of age. Anovulatory cycles were seen in 29.5% (n=41) of cases. Glycogen deficiency was seen in 28.88% (n=26) of cases. Tubercular endometritis was found in 3.9% (n=4) of cases and cystic glandular hyperplasia seen in 2.5% (n=3) of cases of primary infertility.

CONCLUSION

Endometrial pathologies are important causes of infertility and depletion of glycogen results in inadequate preparation of endometrium, which maybe one of the causes of infertility.

KEYWORDS

Endometrium, Anovulatory Cycle, Endometrial Pathology, Tuberculosis, Infertility.

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BACKGROUND

Infertility is a global public health problem due to its complexity and the difficulty in diagnosing, treating and preventing it. The incidence of infertility ranges from 8-12%.[1] Approximately, one marriage in ten is barren as stated by Sophia.[2]

In India, 10.2 million couples are infertile. Infertility results from physiological and pathological factors. One of the pathological factors of infertility is poor quality endometrium that leads to death of the ovum before and after implantation.[3] Glycogen content of the endometrium is believed to be the direct source of nutrient for the early conceptus. It undergoes cyclical change under the influence of oestrogen and progesterone. The endometrium, which fails to produce adequate amount of glycogen is termed as "glycopenic uteri.[4]" The purpose of investigating infertile couple is to identify the various causes of infertility amenable to treatment. Notwithstanding many other investigating tools available, endometrial biopsies is an important, safe, cheaper diagnostic tool in primary and secondary infertility as it is a sensitive indicator of ovarian function.

The present study has been undertaken to determine histological and histochemical profile of endometrium during different phases of menstrual cycle in infertile women and to study the role of glycogen in infertility.

MATERIALS AND METHODS

The present prospective study was conducted in the Department of Pathology, M.K.C.G. Medical College, Berhampur, after ethical clearance from its ethics committee between June 2014 to July 2016. The study included 139

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cases with complaints of infertility both primary and secondary. Those patients who failed to conceive after one year of unprotected coitus following marriage were investigated as cases of primary infertility and patients who failed to conceive after having prior conception 4-5 years ago were investigated as cases of secondary infertility. The cases with history of chronic diseases such as diabetes mellitus, hypertension and hypothyroidism were excluded from our study. Detailed information of clinical history of menstrual cycle, last menstrual period, age at marriage and obstetric history were obtained. Clinical examination was carried out in each case. The husband's seminal analysis was done routinely to rule out male factors causing infertility in every case. The premenstrual dilatation and curettage was done in Obstetrics and Gynaecology Department of M.K.C.G. Medical College, Berhampur, and the endometrial samples received were subjected for histopathological examination in our pathology department. The endometrial tissues were processed and subjected to routine Haematoxylin and Eosin (H and E) stain and Periodic Acid-Schiff (PAS) stain for histochemical study of glycogen content of endometrium and graded according to Arzac and Blanchet[5] method to show the intensity of staining microscopically in four groups as given below.

0 = Negative reaction (no staining)
+ = Very small granules
++ = Course granules
+++ = Small masses
++++ = Large masses

The findings were analysed to find out the incidence of various changes in infertile endometrium.

OBSERVATION

Amongst 139 cases of infertility, 85.6% (n=119) of cases were of primary infertility and 14.4% (n=20) of cases were of secondary infertility. The age incidence range of infertility cases was 18-47 years. Maximum incidence of primary infertility 46.22% (n=55) was seen in the age range of 23-27 years. In secondary infertility, maximum cases 55.00% (n=11) were between 28-32 years of age (Table 1).

Infertility Cases	18-22 Yrs.		23-27 Yrs.		28-32 Yrs.		33-37 Yrs.		38-42 Yrs.		43-47 Yrs.		Total	
	Number	%	Number	%	Number	%	Number	%	Number	%	Number	%	Number	%
Primary infertility	37	31.09	55	46.22	17	14.28	5	4.20	3	2.52	2	1.68	119	85.60
Secondary infertility	Nil	0.0	2	10.00	11	55.00	4	20.00	2	10.00	1	5.00	20	14.40

Table 1. Age Distribution

Pattern	Primary Infertility		Secondary Infertility	
	Number	%	Number	%
Regular	78	65.55	14	70.00
Irregular	26	21.85	03	15.00
Menorrhagia	10	8.40	01	5.00
Secondary amenorrhoea	03	2.52	01	5.00
Polymenorrhagia	02	1.68	01	5.00
Total	**119**	**100.00**	**20**	**100.00**

Table 2. Menstrual Pattern

Regular cycle was present in majority of patients 65.55% (n=78) cases in primary infertility and 14 (70%) cases of secondary infertility.

Histological Diagnosis	Primary Infertility (n=119)	Secondary Infertility (n=20)	Total Cases
	Number (%)	Number (%)	
Normal Secretory Endometrium (Early-10, Mid-31, Late-49)	77 (64.2)	13 (65.0)	90
Proliferative (anovulatory endometrium)	35 (29.4)	6 (30.0)	41
Cystic glandular hyperplasia	3 (2.5)	1 (5.0)	4
Tubercular endometrium	4 (3.9)	Nil	4

Table 3. Spectrum of Histomorphological Patterns of Endometrium in Infertility

Anovulatory endometrium was seen in 29.4% (n=35) cases of primary infertility and 30.0% (n=6) cases of secondary infertility. 3.9% (n=4) cases of primary infertility showed endometrial tuberculosis. Out of the 90 cases of secretory endometrium of both, primary as well as secondary infertility, 36 cases showed luteal phase defect.

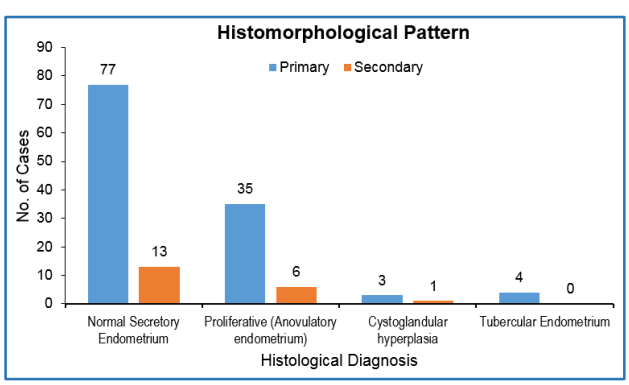

Figure 1. Histomorphological Pattern

PAS Staining	Glands		Stroma	
	Number	%	Number	%
0 (no staining)	3	3.33	8	8.88
+	9	10	18	20
++	24	26.67	25	27.78
+++	30	33.33	27	30
++++	24	26.67	12	13.33

Table 4. PAS Staining in Glands and Stroma in Secretory Endometrium (n=90)

Table 4 shows PAS staining in glands and stroma in secretory endometrium. In 26.67% of cases (n=24) in glands and in 13.33% of cases (n=12) in stroma show intense positivity.

Phase	Total Number of Infertile Cases	Total Number of Glycogen Depletion Cases	% of Glycogen Depletion
Early Secretory	10	02	20
Mid Secretory	31	10	32.25
Late Secretory	49	14	28.57
Total	**90**	**26**	**28.88**

Table 5. Glycogen Depletion in Secretary Endometrium (N=90)

Glycogen depletion was observed in 28.88% (n=26) of cases of secretory endometrium.

DISCUSSION

Human endometrium is the most favoured site for the implantation of fertilised ovum. Present study evaluated the adequacy of endometrial development based on correlation of menstrual history with glandular and stromal morphology.

In our study of 139 cases of infertility, 85.6% (n=119) of cases were of primary infertility and 14.4% (n=20) of cases were of secondary infertility.

The maximum number of patients were in the age range of 23-27 years irrespective of type of infertility. The youngest patient was 18 years old and oldest was of 35 years. Majority of the patients of primary infertility, i.e. 46.22% (n=55) of cases belonged to the age group of 23-27 years. In secondary infertility, 55% (n=11) of cases belonged to the age group of 28-32 years. Our findings correlated to Zawar MP,[6] Sharma V[7] and Girish C J.[8]

The abnormal menstrual pattern observed in the present study were irregular periods, menorrhagia, secondary amenorrhoea and polymenorrhagia. Regular cycles were seen in 65.55% (n=78) of cases of primary infertility and 70% (n=14) of cases of secondary infertility.

Anovulatory cycles are common in cases of infertility. In our study, anovulatory endometrium were seen in 29.4% (n=35) of cases of primary infertility and 30% (n=6) of cases of secondary infertility.

The secretory phase of endometrium in the premenstrual period is indicative of ovulation and thus it rules out anovulation as a cause of infertility.[9] But, luteal phase defect maybe the cause of infertility in ovulatory cycles. The diagnosis of luteal phase defect was made by Jones criteria.[10] According to him, luteal phase defect is defined as lag of more than two days in histological development of endometrium compared to the day of the cycle. In this present study, the luteal phase defect was detected in 25.89% (n=36) of cases on histological basis. Wentz AC,[11] Soules M,[12] Sareen PM[13] and Sharma V[7] detected luteal phase defect in 19%, 16%, 39% and 20% of cases, respectively. Jones GS in a review of clinical experience reported luteal phase deficiency diagnosed by out of phase (≥3 days) endometrial biopsy specimen in 3.5% of infertile patients and 35% of cases of recurrent miscarriage.[10] Luteal phase defect is one of the common cause of infertility in ovulatory cycles as found in our study as well.

Periodic Acid-Schiff (PAS) staining was done in all cases of secretory endometrium in the present study revealed variable glycogen content in the gland and the stroma, also observed by Sabharwal BD.[14] Hughes reported that normally the glycogen was present in highest concentration around 17th to 20th day of the cycle.[15]

Hong Yul Choi[16] reported that the secretory substance in the epithelial cells of the endometrial glands during the secretory phase and menstrual phase was mainly glycogen and concluded that PAS staining is superior to routine haematoxylin and eosin staining for the detection of this epithelial secretory substance.

Dockery P[17] studied the fine structure of the human endometrial glandular epithelium in cases of unexplained infertility and observed that abnormalities associated with intracellular deposit of glycogen rich material in infertile women. Maeyama M[18] found the glycogen content of the endometrium of normal and infertile patient and found that glycogen content is significantly lower in infertile patients.

A synchronised development of embryo and endometrium is a prerequisite for a successful implantation. Pinopods, which appear on the endometrial surface during implantation, play a role in implantation process. Considerable quantity of glycogen was found in the pinopods. It suggests that the formation of pinopods was an energy consuming process.[19] So, several studies in the literature were done to validate that glycogen depletion in secretory endometrium is usually associated with infertility.

In our study, glycogen depletion was noticed in 28.88% of cases (n=26) of secretory endometrium of both primary and secondary infertility cases. These findings are consistent with results obtained by K Rohtagi[4] (22.5%), but differ from those of Hughes EC[20] (30%) and Zawer MP (30%). Decreased glycogen deposition in secretory phase of the endometrium leads to improper nidation of the fertilised ovum, which leads to infertility.

In our study, tuberculous endometritis was found in 3.9% of cases (n=4) of primary infertility on histological basis. In tubercular lesions, discrete granulomas consisting of epithelioid cells, Langhans giant cells, lymphocytes and few plasma cells without central caseation were observed in histosections. The corresponding results of tubercular endometritis found by Tripathy SN,[21] Zawar MP[6] and Sharma V[7] were 8.7%, 2.6% and 2.0%, respectively, which correlated with our study.

Endometrial hyperplasia, which is due to excess level of oestrogen can also prevent pregnancy. In present study, cystic glandular hyperplasia was seen in 2.5% cases (n=3) of primary infertility and 5% cases (n=1) of secondary infertility. The corresponding observations of Sabharwal BD,[14] Shastrabudhe NS[22] and Sharma VC[7] were 2.66%, 4.4% and 18%, respectively. So, tubercular endometritis

and cystic glandular hyperplasia are also the causes of infertility.

CONCLUSION

This comparative histopathological and histochemical study of endometrium of infertile women showed the major causes of infertility are the anovulatory cycles, luteal phase defect and glycogen depletion in secretory endometrium. Depletion of glycogen results in inadequate preparation of endometrium for implantation of fertilised ovum. So, deficiency of glycogen in endometrium may lead to infertility.

Hence, we conclude, PAS staining should be regularly done in endometrial biopsies of infertility cases to know the glycogen deficiency.

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REFERENCES

[1] Berek JS, Novak E. Novak's gynaecology. 13th edn. Philadelphia: Lippincott Williams & Wilkins 2002.
[2] Kleegman SJ, Kaufmann SA. Infertility in women. 1st edn. Philadelphia, USA: FA Davis Company Publisher 1966:p. 178.
[3] Padubidri V, Daftary SN. The pathology of conception. In: Padubidri V, ed. Shaw's textbook of gynaecology. Edinburgh: Churchill Livingston 1991:205-227.
[4] Rohatgi K, Singh VK, Rajvanshi VS, et al. Study of endometrial glycogen in cases of dysfunctional uterine haemorrhage & subfertility. J Obstet Gynaecol India 1977;27(6):905-910.
[5] Arzac JP, Blanchet E. Alkaline phosphatase and glycogen in human endometrium. J Clin Endocrinol Metab 1948;8(4):315-324.
[6] Zawar MP, Deshpande NM, Gadgil P, et al. Histopathological study of endometrium in infertility. Indian Journal of Pathology & Microbiology 2003;46(4):630-633.
[7] Sharma V, Saxena V, Khatri SL. Histopathological study of endometrium in cases of infertility. J Clin Exp Pathol 2016;6:272.
[8] Girish CJ, Kotur NS, Nagarajappa AH. A correlative study of endometrial glycogen content and other contributory factors on female infertility. International Journal of Biomedical and Advance Research 2012;3(1):30-35.
[9] Driessen F, Holwerda PJ, Kremer J. The significance of dating an endometrial biopsy for the prognosis of the infertile couple. Int J Fertil 1980;25(2):112-116.
[10] Jones GS. The luteal phase defect. Fertility and Sterility 1976;27(4):351-356.
[11] Wentz AC, Kossoy LR, Parker RA. The impact of luteal phase inadequacy in an infertile population. American Journal of Obstetrics and Gynecology 1990;162(4):937-945.
[12] Soules MR. Luteal phase deficiency. An underdiagnosed and overtreated reproductive endocrine disorder. Obstetrics and Gynecology Clin North Am 1987;14(4):865-886.
[13] Sareen PM, Kalra P, Lodha SK. Significance of endometrial glycogen in primary sterility. J Obstet Gynaecol India 1984;34:877-881.
[14] Sabharwal BD, Sofat R, Chander K. Endometrial pattern and its glycogen content in case of infertility. J Obstet Gynaecol India 1987;37:718-721.
[15] Hughes EC. Nutritional physiology of the endometrium. In: Marcus SL, Marcus CC, eds. Advances in obstetrics and gynecology. Baltimore: Williams & Wilkins Co 1967:p. 3.
[16] Choi HY, Lee YB, Kim DS. Histochemical studies of human endometrium with special emphasis on secretory activity and ovulation. Yonsei Med J 1966;7(1):7-12.
[17] Dockery P, Pritchard K, Taylor A, et al. The fine structure of the human endometrial glandular epithelium in cases of unexplained infertility: a morphometric study. Hum Reprod 1993;8(5):667-673.
[18] Maeyama M, Sudo I, Saito K, et al. Glycogen estimation by a rapid enzymic method in very small samples of human endometrium: glycogen content in the endometrium of infertile patients during the menstrual cycle. Fertil Steril 1977;28(2):159-162.
[19] Anneli C, Staverns E. Characteristics and possible function of pinopods seen on the surface of the receptive human endometrium. Middle East Fertility Society 2005;10(1):22-28.
[20] Hughes EC. Relationship of glycogen to problems of sterility and ovular life. American Journal of Obstetrics and Gynecology 1945;49(1):10-14.
[21] Tripathy SN, Tripathy SN. Infertility and pregnancy outcome in female genital tuberculosis. International Journal of Gynecology & Obstetrics 2002;76(2):159-163.
[22] Shastrabudhe NS, Shinde S, Jadhav MV. Endometrium in infertility. J Obstet Gynecol India 2001;51:100-102.