ORIGINAL ARTICLE

MORPHOLOGICAL SPECTRUM OF ENDOMETRIAL BIOPSIES IN INFERTILE WOMAN

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ABSTRACT

Background: Infertility is a global problem and as a last resort in the investigative protocol endometrial biopsy is performed to find a clue to the cause behind it. The objective of the study was to evaluate the morphological spectrum of endometrial biopsies in infertile women**.**

Material & Methods: This cross-sectional study was conducted in Department of Pathology, Peshawar Medical College Peshawar from 21-04-2013 to 10-08-2013. Out of 168 infertile patients 8 were excluded due to insufficient representative material. The sample size was 160 infertile women of reproductive age group selected through consecutive sampling technique. In eight cases endometrial biopsy could not be assessed so these cases were excluded. Demographic variable was; age in years. Type of infertility, duration of infertility, morpholigical dating & presence of endometial carcinoma were the research variables. Descriptive statistics were calculated from data using SPSS version 18.

Results: Out of 160, 102(63.75%) were primary & 58(36.25) were secondary infertile women. Mean age of the sample was 26.70$\pm$4.90 in primary & 30.55$\pm$4.79 in secondary infertile women. Mean duration of infertility was 7.06$\pm$0.5 in primary & 7.27$\pm$0.5 in secondary infertile women. Morphological changes in endometrium of infertile women included; secretory phase in 102(63.75%), disordered proliferative endometrium in 28(17.5%), irregular maturation endometrium in 11(6.8), proliferative endometrium in 8(5%) complex hyperplasia in 6(3.7%), simple hyperplasia in 3(1.8%) & discordance between glands & stroma in 2(1.2%) cases. No malignant lesion was seen in our study population.

Conclusion: On premenstrual endometrial biopsy, secretory phase was the most common finding. No malignancy was reported.

KEYWORDS: Infertility, Endometrial biopsy, Menstrual disturbances.

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INTRODUCTION

The endometrium is prepared for implantation of fertilized ovum in each menstrual cycle. These morphological changes occur under the influence of various hormones. Estrogen is the main hormone in the proliferative phase and progesterone in the secretory phase leading to transformation and stromal decidualization.[1]

This normal sequence of events may not be followed in infertile women leading to a wide spectrum of morphological changes. Whether these changes will be conveyed by the endometrial biopsy in an infertile woman so that a management plan may be devised? This question is in the back of the mind of every gynecologist who opts for endometrial biopsy as a last resort to diagnose the cause of infertility in a female. He/she is apprehensive that again the results might be inconclusive but nevertheless he/she lives with the hope that this time she might get a clue to ailment of the patient which sometimes she gets. The same dilemma is repeated all around the world because 48.5 million couples suffer from infertility so it is a global problem.[2] However, currently the histological examination of the endometrial biopsy is among one of the reliable parameters for evaluating the cause of infertility in a female.[3]

Normally investigations for infertility include hormone levels, hysteroscopy and laparoscopy in females.[4] Endometrial biopsy is finally indicated which helps in ruling out organic causes like endometritis,[5] hyperplasia and malignancy[6] and can provide some information regarding the influence

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of various hormones required for implantation.[7] To exclude hormonal etiology on the basis of endometrial biopsy, a detailed menstrual history with exact last menstrual period (LMP) is required.

Depending on the phase of the cycle and hormonal influences both glands and stroma show morphological alterations. The glands may be tortuous, tubular or cystically dilated and the stroma may be dense, loose, decidualized, infiltrated by leukocytes and may contain thin walled or thick walled arterioles. These morphological changes are the basis of histological diagnosis and place the endometrium in various categories like secretory phase, proliferative phase, irregular maturation, disordered proliferative, discordance between glands and stroma, simple, complex or atypical hyperplasia and endometrial carcinoma. Some of these indicate normal hormonal cyclical changes and others point at excess or deficiency of hormones.[8]

The ovulation is indicated by LH surge producing subnuclear vacuolation in the glands which helps us in dating the endometrium if LMP and menstrual history is provided. These Interphase changes may be affected or delayed due to hormonal deficiency.[9]

The usual abnormal patterns of endometrium are given below:[10]

1. The presence of both proliferative and secretory glands helps us in labeling it as irregular maturation of endometrium and may be due to abnormal hormonal activity.

2. Discordance between stroma and glandular elements signifies hormonal imbalance.

3. Disordered proliferative endometrium contains normal and focally mildly dilated to irregularly shaped glands lined by pseudostratified columnar epithelium. The stroma surrounding the glands is quite cellular and usually mitotically active. These changes point at excess of estrogen.

4. The gland-to-stroma ratio is increased in hyperplasia which may be due to increased estrogen secretion.

5. Atrophic glands in a markedly decidualized stroma points at exogenous hormonal influences especially progesterone.

The objective of the study was to evaluate the morphological spectrum of endometrial biopsies in infertile women.

MATERIAL AND METHODS

This cross-sectional study was conducted in Department of Pathology, Peshawar Medical College Peshawar, Pakistan from 21-04-2013 to 10-08-2013. Out of 168 infertile patients 8 were excluded due to insufficient representative material.

The sample size was 160 infertile women of reproductive age group selected through consecutive sampling technique. In this study all those patients were included who went through diagnostic laparoscopy for primary or secondary infertility and their spouse had normal semen analysis reports.

Endometrial biopsy was taken at 22nd or 23rd day of their menstrual cycle by dilatation and curettage (D&C).The specimen was fixed in 10% buffered formalin and sent to Peshawar Medical College, Peshawar laboratory for further processing.[5,6] micron sections were cut and stained with H and E for morphological studies. Noye's criteria was used for dating of endometrium.

Demographic variable was; age in years. Type of infertility, duration of infertility, morpholigical dating & presence of endometial carcinoma were the research variables. Type of infertility had two attributes; primary and secondary. Morpholigical dating of endometrium had seven attributes. presence of endometial carcinoma had two attributes; yes & no.

Age and duration of infertility were numeric variables whereas type of infertility, morpholigical dating & presence of endometial carcinoma were categorical variables. Data was recorded on a predesigned performa. Descriptive statistics were calculated from data using SPSS version 18.

RESULTS

Out of 160, 102 (63.75%) were primary & 58(36.25) were secondary infertile women. Mean age of the sample was 26.70 $\pm$4.90 years in primary

Table 1: Endometrial morphological changes in primary and secondary infertile women

Endometrial Morphology	Number & %age of Primary infertile	Number & %age of Secondary Infertile	Total
Secretory Phase	61 (59.80)	41 (70.69)	102 (63.75)
Disordered Proliferative	19 (18.63)	9 (15.52)	28 (17.50)
Irregular Maturation	8 (7.84)	3 (5.17)	11 (6.88)
Proliferative Phase	6 (5.88)	2 (3.45)	8 (5.00)
Complex Hyperplasia	4 (3.92)	2 (3.45)	6 (3.75
Simple Hyperplasia	3 (2.49)	0 (2.94)	3 (1.88)
Discordance between glands and stroma	1 (0.98)	1 (1.72)	2 (1.25)
Grand Total	102	58	160 (100.0)

& 30.55 ±4.79 years in secondary infertile women. Mean duration of infertility was 7.06 ±0.5 years in primary & 7.27 ±0.5 years in secondary infertile women.

Morphological changes in endometrium of infertile women included; secretory phase in 102 (63.75%), disordered proliferative endometrium in 28(17.5%), irregular maturation endometrium in 11(6.8), proliferative endometrium in 8(5%) complex hyperplasia in 6(3.7%), simple hyperplasia in 3(1.8%) & discordance between glands & stroma in 2(1.2%) cases.(Table 1)

No malignant lesion was seen in our study population.

DISCUSSION

Practical outcome of endometrial biopsies in infertility is debatable but its role as a part of investigative process cannot be denied. There are many steps from taking endometrial biopsy to its interpretation in the light of which further workup is carried out by the gynecologist.The first one is adequacy of the material[10] which in the hands of an experienced gynecologist rarely happens but out of 168 infertile women eight cases (4.76%) were excluded due to insufficient material. Steven Silverberg has discussed in detail about inadequacy in material in endometrial biopsy.[11]

An endometrial biopsy of an infertile female patient cannot be interpreted with justification without the provision of detailed clinical and menstrual history. A large number of biopsies show normal secretory phases of the endometrium which by themselves do not provide useful information but gain significance in the light of LMP with the help of which it can be dated and may point at the cause behind suffering of the patient. Keeping this in view we made sure that endometrial biopsy in our cases had been obtained on 22nd to 23rd day of the menstrual cycle.

In the same line various phases of secretory endometrium (figure 1) were found in 63.75% of endometrial biopsies in our study, which is comparable to studies carried out in Nigeria as 68%[7] and 56%.[12]

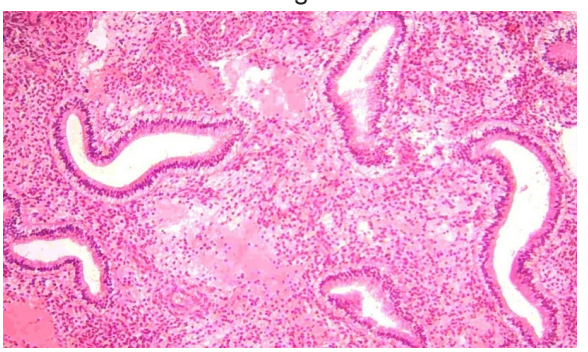

Figure 1: Early secretory phase endometrium compatible to day 16/17 (H&Ex10 magnification)

Many of endometrial biopsies (36.25%) showed abnormalities incompatible to implantation of ovum in place of expected typical secretory pattern. The undesired morphologies on endometrial biopsies reflected hormonal imbalance. These included proliferative phase,disordered proliferative endometrium,irregular maturation of endometrium, discordance between stroma and glands, simple hyperplasia and complex hyperplasia (table 2). A certain percentage of these abnormal morphologies on endometrial biopsy in infertile women has been reported by many authors.[7,13,14]

In this study the proliferative phase endometrium (figure 2) was present in 5% cases which is close to 3.6% in a Nigerian study.[7] In contrast another study showed proliferative phase to be 11% among infertile females.[15] The proliferative phase signifies estrogen effect with unopposed progesterone which if persistent is detrimental to implantation of ovum.

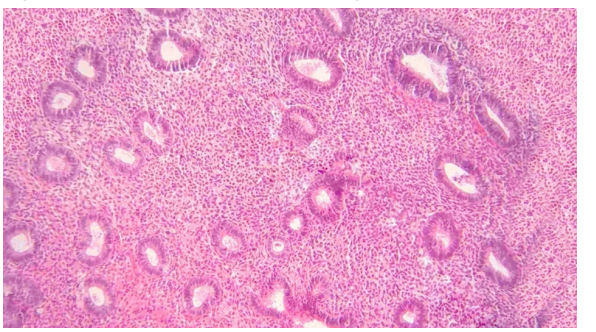

Figure 2: Proliferative phase endometrium (H&Ex10 magnification)

The excess of estrogen is initially reflected as disordered proliferative endometrium.[16] In our study this effect was seen in 17.5% of cases (figure 3) which is second after secretory endometrium and turns out to be the first among the abnormal morphologies found in infertile women. Other researchers have not specifically mentioned about this group in their studies about infertile women.

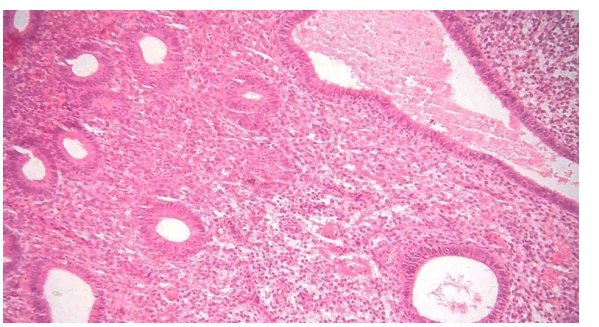

Figure 3: Disordered proliferative endometrium (H&Ex10 magnification)

Irregular maturation of endometrial glands were found be in 6.88% cases in our study. However, these asynchronous glands in the endometrium of women with recurrent reproductive failure by others

have been quoted as 2.1% which is lower than our findings.[17] In another study it was concluded that presence of asynchronous endometrial glands suggest a localized, possibly clonal, defect in epithelial maturation due to aberrant hormone receptor expression which clinically most commonly manifests as menorrhagia.[18]

The discordance between stroma and glands is commonly seen in infertile women which signifies hormonal imbalance. Such findings were seen in 1.25% of our cases (figure 4). Other studies show these to be 0.7%.[6]

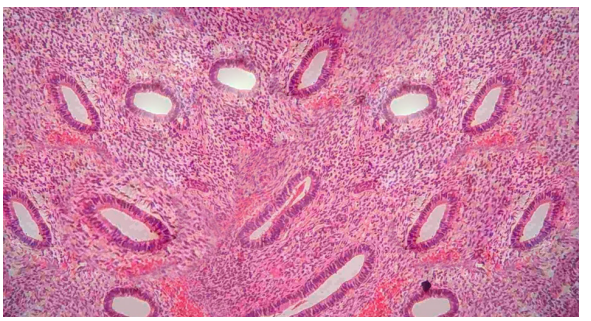

Figure 4: Discordance between glands and stroma signifying hormonal imbalance endometrium (H&Ex10 magnification)

In infertile women various types of endometrial hyperplasia are not commonly found which is also reflected in our study as simple hyperplasia in 1.88% and complex hyperplasia in 3.75%. Endometrial hyperplasia in other studies ranges from 5.1%[7] to 12.5%.[14] In our study no case of atypical hyperplasia was identified in infertile women. However, in a study from 1989 to 2000, endometrial biopsies were performed on 2,573 patients to investigate the cause of infertility. Out of these 24 (0.93%) patients were diagnosed with an endometrial abnormality. Out of them, 3 patients had complex hyperplasia with atypia.[6]

Although nonspecific endometritis and tuberculous endometritis are known causes of infertility[5,19] but we did not come across even a single case in our study population. However, other studies show chronic endometritis as 2.8%[20] and granulomatous inflammation as 2.2%[14] and 1.4%[21] among infertile females which constitute a significant proportion of infertile female population. The reason for this may be due to the special referral pattern which included elite and educated class well aware about hygiene.

Malignancy on endometrial biopsy in infertile women is not usually encountered. Although infertility is risk factor for endometrial carcinoma but no malignant lesion was seen in our study population. In another study endometrial carcinoma has been found in 0.16 % cases as a cause of infertility.[6]

CONCLUSION

On premenstrual endometrial biopsy, secretory phase was the most common finding. No malignancy was reported.

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CONFLICT OF INTEREST
Authors declare no conflict of interest.
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None declared.

AUTHORS' CONTRIBUTION

Conception and Design:	SN, MMK, SA
Data collection, analysis & interpretation:	SN, SA
Manuscript writing:	SN, MMK, SA, SZ, SA