Endometrial Hyperplasia in Polycystic Ovarian Syndrome Patients Having Raised Endometrial Thickness

Saima Farooq,[1] Farah Naz Memon,[2] Fiza Ali Khan,[3] Urooj Naz,[4] Aruna Kumari Hira,[5] Asifa Abdul Jabbar [6]

[1]Department of Gynecology & Obstetrics, Hamdrad University Hospital, Karachi-Pakistan, [2]Department of Gynecology & Obstetrics, Liaquat University of Medical & Health Sciences, Jamshoro-Pakistan, [3,4,5]Department of Gynecology & Obstetrics, DOW University of Heath Sciences, Karachi-Pakistan [6]Department of Gynecology & Obstetrics, Gambat Institute of Medical Sciences, District Khairpur Mirus-Pakistan.

ABSTRACT

Objective: To determine the frequency of endometrial hyperplasia in polycystic ovarian syndrome patients having raised endometrial thickness at tertiary care Hospital. **Study Design:** Cross Sectional Study. **Settings:** Study was conducted at obstetrics and gynaecology department of Dow University Hospital Karachi Pakistan. **Duration:** Six months from November 2015 to May 2016. **Methodology:** Both primary and secondary infertile women having polycystic ovarian syndrome (PCOS) with raised endometrial thickness, age between 18-45 years and willing to participate in the study were included. Patients were evaluated during first week in follicular phase. For evaluating endometrial thickness (ET) of patients, endometrial biopsy and transvaginal sonography were done. Endometrial tissues were taken from patients and were sent to diagnostic laboratory for histopathology and endometrial hyperplasia assessment. All the data was recorded in self-made proforma and analysed by SPSS version 20. **Results:** Total 90 patients were studied; their mean age was 28.6±4.56 years, with mean duration of infertility as 5.15±1.4 years. Endometrial hyperplasia among patients of polycystic ovarian syndrome was 31.1%. Age >29 years, infertility >5 years, diabetes and smoking were significantly associated with endometrial hyperplasia, (P=0.001). There was no significant impact of BMI, parity and hypertension on frequency of endometrial hyperplasia; p-values were quite insignificant. **Conclusion:** In the polycystic ovarian experiencing women with raised endometrial thickness, the endometrial hyperplasia was 31.1%. Elevated age, prolonged duration of infertility, diabetes and smoking may be risk factors of endometrial hyperplasia.

Keywords: Endometrial thickness, Hyperplasia, Polycystic ovarian syndrome.

Corresponding Author

Dr. Saima Farooq, Consultant Gynecologist, Hamdrad University Hospital, Karachi-Pakistan.
Email: fdrsaima@gmail.com

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INTRODUCTION

Polycystic ovary syndrome (PCOS) is explained by the altered activity and production of steroid hormone. This disorder results from the heterogeneous hormone-imbalance, which occurs in around four to eighteen percent of women at reproductive-age worldwide.[1,2] PCOS suffering females are at greater risk of acquiring endometrial hyperplasia (EH). Prolonged exposure to estrogen or lack of progesterone and malfunction resulting from ovarian dysfunction may cause carcinoma and endometrial hyperplasia.[1] The commonest presentation of EH is an uncharacteristic uterine bleeding, which involves intermenstrual bleeding, heavy menstrual bleeding, postmenopausal bleeding and irregular bleeding. In PCOS patients, the endometrium has high activity levels of insulin-like growth factor-1 (IGF-1), diminished level of Sex Hormone Binding Globulin (SHBG), hyperinsulinemia, endometrial aromatase up-regulation, and hyperandrogenemia.[3,4] Consequently, such molecular modifications raise the chances for neoplastic variation in endometrium. Anovulation occurs commonly among females with PCOS; thus, the absence or suboptimal rates of progesterone influence the endometrium, and the tissues remain relatively over-responsive to the proliferative consequences of estrogen (E2), in which its levels have been noted to be analogous to the concentrations of follicular phase. Such relatively high rates of E2 prevent endometrium from undergoing concurrent alterations to gene expression including endocrine processes associated with it. Hyperinsulinemia and Insulin resistance may cause the PCOS development in genetically susceptible individuals, particularly in obese people. Hence, persistent hyperinsulinemia, unopposed oestrogen, raised androgens and free IGF-1 in PCOS can potentially increase mitogenic activity in endometrial cells via triggering mitogen-activated protein kinase (MAPK), resulting in high incidence of hyperplasia as well as endometrial cancer's potential transition.[3-5] However, it remains controversial that whether females experiencing PCOS without endometrial thickness evaluated on ultrasonography necessitate the endometrial biopsy for the assessment of endometrial disorders.[6] A body of evidence shows that endometrial thickness can increase during menstrual cycle within infertile subjects with PCOS, in comparison to the infertile females without PCOS.[6,7] On the other hand, a study stated that patients with irregular menstrual pattern and PCOS had endometrial cancer or endometrial hyperplasia. However, endometrial thickness had no difference among those with normal and abnormal endometrium.[8] After taking above controversial findings this study has been conducted to determine the frequency of

endometrial hyperplasia in polycystic ovarian syndrome patients having raised endometrial thickness.

METHODOLOGY

Study Design: Cross sectional study.
Settings: Department of obstetrics and gynaecology, Civil Hospital Karachi Pakistan.
Duration: Six month from November 2015 to May 2016.
Sample Technique: Non probability consecutive sampling.
Inclusion Criteria: Women between the age of 18-45 years, infertile women (Both primary and secondary), polycystic ovary syndrome experiencing women having raised endometrial thickness and patients willing to provide consent.
Exclusion Criteria: Patients having acute pelvic inflammatory disease and any fibroid in low vaginal track.
Methods: Informed constant was taken after explanation of procedure to the patients and approval of ethical committee. Patients were recruited from Out Patient Department of civil hospital. An informed consent of the study population with the assurance to keep their information confidential was obtained to include their demographics in the study. The researcher evaluated all the patients with the help of consultant radiologist having post qualification experience of 5 years. Raised endometrial thickness ≥7mm via ultrasound was considered as positive. Endometrial specimens were taken from patients and sent for histopathology. Final outcome was recorded on attached Performa. Data was recorded in self-made proforma. Data was analysed by using SPSS version 19.0. Mean and Standard deviation were calculated for maternal age, weight and duration of Infertility. Frequency and percentage were calculated for outcome variable (endometrial hyperplasia), parity, hypertension, diabetes and smoking status. Effect modifiers through stratification of maternal age, party, weight hypertension, diabetes, smoking status and duration of infertility were done. X^2- test was applied and a p≤ 0.05 was taken as significant.

RESULTS

Total 90 married women were selected their mean age was 28.6±4.56 years, mean BMI was 29.8±3.86 and mean duration of infertility is 5.15±1.4 years. Table.1

Table 1: Descriptive statistics of age n=90

	Mean	SD
Age	28.6	4.56
BMI	29.8	3.86
Duration of infertility	5.15	1.4

Out of all 75.5% women were nullipara and 24.4% were single Para. According to the types of infertility primary infertility was most common 24.4% and 24.4% women presented with secondary infertility. Table 2

Table 2: Parity and type of infertility of patients n=90

Parity	Frequency	Percentage
Nullipara	68	75.5%
Singlepara	22	24.4%
Total	90	100%
Type of infertility		
Primary	68	24.4%
Secondary	22	24.4%
Total	90	100%

In this study 31.1% women had endometrial hyperplasia. Fig. 1.

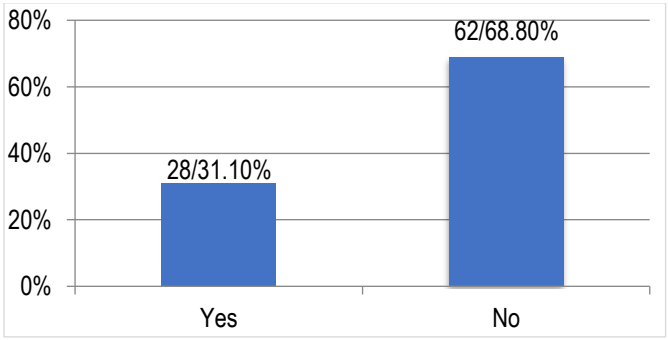

Figure 1: Frequency of endometrial hyperplasia n=90

After stratifying the results with respect to age, 57.1% of the women with endometrial hyperplasia having age less than or equal to 29 year which was statistically significant P=0.001). When results were stratified with respect to BMI, most of the women with endometrial hyperplasia having BMI less than 29 which was not statistically significant P=0.071). With respect to duration of infertility, diabetes, hypertension and smoking, there was statistically significant. With respect to parity and type of infertility, there was statistically insignificant difference, as showed in table 3.

Table 3: Stratification with respect to age, BMI, infertility, parity, diabetes, hypertension and smoking n=90

Effect modifiers		Endometrial Hyperplasia		p-value
		Yes	No	
Age groups	18-30 years	16	55	0.001
	31-40 years	12	07	
BMI	Less than 29	22	57	0.073
	Greater than 29	06	05	
Duration infertility	Greater than 5 years	15	07	0.001
	Less than 5 years	13	55	
Parity	Nully para	18	49	0.138
	Single para	10	13	
Type of infertility	Primary infertility	18	49	0.138
	Secondary infertility	10	13	
Diabetes Mellitus		22	16	0.001
Hypertension		20	26	0.010
Smoking		07	02	0.001

DISCUSSION

Females with PCOS, mainly the chronic anovulation experiencing females, can possibly have higher risk for endometrial cancer and endometrial hyperplasia (EH). Obesity, hyperinsulinemia, hyperandrogenism, and Hyperestrogenemia are the possible causative risk factors for endometrial cancer and hyperplasia. In this study frequency of endometrial hyperplasia was 31.1%. In comparison to our results, study conducted by Al jefout M et al[3] reported an overall EH incidence at 23.3 %, while it was reported 18.3 % among females with PCOS. The mean ET (14.8 mm) was statistically considerably greater among EH cases (p=0.009). This EH-associated prevalence is comparable to global figures (1% to 48.8%.). [9-11] The high incidence of EH within our populace can have a possible explanation that infertility cases have been reported with chronic PCOS in our populace. Among females with PCOS, endometrial thickness on sonogram is indicative of endometrial hyperplasia.

In this study endometrial hyperplasia with respect to BMI, was statistically insignificant. In comparison to our results, study conducted by Ramezanali F et al[12] reported that Thickness of endometrial stripe on sonogram is indicative of EH among females with PCOS. We could find no association between BMI and serum LH concentration in PCOS subjects with thickness of endometrium. Our analysis however demonstrated a diverse correlation between serum BMI and LH level in PCOS cases. Another study conducted by Holm NS et al[13] reported that 10 females (1.0%) were diagnosed with hyperplasia of endometrium and one female (0.1%) with endometrial cancer. These women's mean BMI was 30.6 kg / m^2 in comparison to overall 26.8 kg / m^2 in the study. As per particular Rotterdam Criteria no differences were seen between the patients and the overall cohort. However, McCormick et al[10] stated that hyperplastic females had significantly greater BMI than those who had no hyperplasia. Heller et al[14] recounted that greater BMI was correlated with hyperplastic endometrium contrasted to lower BMI. Similarly, Zeng et al[15] compared thickness and blood flow of endometrium in three groups of BMI among patients without PCOS; and no associated was found between BMI and thickness of endometrium among these patients.

CONCLUSION

In the polycystic ovarian experiencing women with raised endometrial thickness, the endometrial hyperplasia was 31.1%. Increased endometrium thickness can be considered as a predictor of endometrium hyperplasia. Age, prolonged duration of duration of infertility, diabetes and smoking may risk factor of endometrial hyperplasia.

LIMITATIONS

This was a small sample size and single center study, effect modifiers are also showing significance, which should be studies at large level.

SUGGESTIONS / RECOMMENDATIONS

Further large sample size multicenter studies should be done including association with risk factors like smoking diabetes.

CONFLICT OF INTEREST / DISCLOSURE

There is no conflict of interest.

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AUTHORSHIP CONTRIBUTION

Saima Farooq	Draft formatting and data collection
Farah Naz Memon	Supervision and guidelines
Fiza Ali Khan	Contribution in manuscript writing and data collection
Urooj Naz	Contribution in manuscript writing and literature review
Aruna Kumari Hira	Contribution in data analysis
Asifa Abdul Jabbar	Contribution in data analysis and manuscript formatting