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Association of Endometrial Status and Estrogen Levels with Varying Menstrual Patterns in PCOS

[1]Meenal Chugh, [2]Bharat Bilwal, [3]Chanchal Arora and [4]Vismandeep Kaur Sandhu

[1-3]Department of Obstetrics and Gynecology, RNT Medical College, Udaipur, India

[4]RNT Medical College, Udaipur, India

ABSTRACT

The Polycystic Ovarian Syndrome (PCOS) is a prevalent endocrine disorder among women of reproductive age, characterized by hyperandrogenism, chronic an ovulation and polycystic ovaries. The syndrome presents with diverse menstrual irregularities, influenced by hormonal imbalances such as hyperestrogenism. To examine the correlation between endometrial thickness and astraddle levels with the clinical presentation of menstrual patterns in women diagnosed with PCOS. A cross-sectional observational study involving 100 patients diagnosed with PCOS per the Rotterdam criteria was conducted from May to October 2024 at RNT Medical College, Udaipur. The study assessed the endometrial status and serum astraddle levels in relation to menstrual patterns among participants. The study revealed that 97% of participants presented with menstrual complaints. Hyper estrogenic states were associated with varied menstrual patterns, notably oligomenorrhoea, which was the most common presentation. Notably, 15% of patients with oligomenorrhoea had menorrhagia with a corresponding increase in endometrial thickness. Despite elevated astraddle levels, a significant proportion of participants had normal endometrial thickness, indicating a disconnect between estrogen levels and endometrial response. The findings suggest that while hyperestrogenism impacts the frequency and volume of menstrual bleeding, it does not uniformly affect endometrial thickness in women with PCOS. This highlights the complexity of hormonal interactions in PCOS and suggests potential areas for further study, including the inclusion of estrogen levels as a diagnostic criterion for PCOS.

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Key Words
PCOS, estrogen levels, menstrual patterns

Corresponding Author
Vismandeep Kaur Sandhu,
RNT Medical College, Udaipur, India
vismansandhu16@gmail.com

Author Designation
[1]Assistant Professor
[2]Professor
[3]Senior Resident
[4]Resident

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INTRODUCTION

Polycystic ovarian syndrome (PCOS), also known as Stein and Leventhal syndrome, was initially described as a condition associating amenorrhea with bilateral polycystic ovaries and obesity. Characterized by a triad of hyperandrogenism, chronic an ovulation and polycystic ovaries, PCOS was defined comprehensively during the Rotterdam consensus workshop in 2003. It represents the predominant cause of hyper androgens, hirsutism and an evaluator infertility, standing as the most prevalent endocrine disorder among women of reproductive age. Globally, the incidence of PCOS ranges from 5-10% among women[1], with prevalence rates varying from 4-22% in the general population and reaching as high as 50% among women attending infertility clinics. The syndrome is typically marked by low follicle-stimulating hormone levels, leading to anovulation, elevated luteinizing hormone levels that promote hyperandrogenism and notable insulin resistance[2].

The Diagnostic Criteria Set by Rotterdam-Requiring Two out of Three Conditions-Include:

- Oligoovulation or an ovulation,
- Clinical and/or biochemical signs of hyperandrogenism,
- Polycystic ovarian morphology, characterized by the presence of 12 or more follicles measuring 2-9mm in diameter in each ovary or increased ovarian volume exceeding 10ml[3,4]. The diagnosis necessitates the exclusion of other etiologies such as congenital adrenal hyperplasia, androgen-secreting tumors and Cushing's syndrome.

Pathophysiology: In PCOS, excess androgen inhibits follicle development and reduces estradiol production while increasing testosterone production and the peripheral conversion of estradiol to estrone through aromatase.

Purpose of Study: Given the hyper estrogenic state typical of polycystic ovarian disease, one might expect patients to present with menorrhagia. However, changes in lifestyle have led to a significant number of patients presenting with hypomenorrhea and/or oligomenorrhoea. This study was conducted to examine the correlation between endometrial thickness and astraddle levels with the clinical presentations of the syndrome, aiming to enhance the understanding of its complex clinical manifestations.

MATERIALS AND METHODS

Source of Data: The study utilized data collected from a total of 100 patients diagnosed with Polycystic Ovary Syndrome (PCOS) who visited the outpatient department (OPD) of RNT Medical College, Udaipur.

Study Design: A cross-sectional observational study was designed to investigate the correlation between endometrial status and estradiol levels, with the variable patterns of menstrual complaints observed in patients diagnosed with PCOS.

Study Location: The research was conducted at RNT Medical College, Udaipur, which served as the primary site for data collection and patient interaction.

Study Duration: The study was carried out over a span of six months, from May 2024-October 2024, encompassing both the recruitment of participants and the subsequent data analysis phases.

Sample Size: A total of 200 patients were initially considered for the study. After applying the inclusion and exclusion criteria, data from 100 eligible patients were included in the final analysis.

Inclusion Criteria:

- Females between the ages of 18 and 45 years, newly diagnosed with PCOS based on Rotterdam's criteria.
- Patients previously diagnosed with PCOS who had not received hormonal treatment in the last 6 months were also included in the study.

Exclusion Criteria:

- Patients with other causes of an ovulation such as hyperprolactinemia.
- Those diagnosed with endocrinological disorders including Type I and II Diabetes Mellitus, thyroid disorders, congenital adrenal hyperplasia and Cushing's Syndrome.

Procedure and Methodology: Patients visiting the OPD with symptoms or ultrasound reports suggestive of PCOS were initially screened using the established inclusion and exclusion criteria. Detailed medical histories were taken, followed by comprehensive general and systemic examinations. Estradiol levels were measured on the second day of the menstrual cycle. An ultrasound (USG) was performed to assess the state of the ovaries (particularly for polycystic ovarian morphology, PCOM) and the thickness of the endometrium.

Sample Processing: Blood samples for estradiol level measurements were collected and processed using standard biochemical techniques. Ultrasound examinations were conducted by qualified radiologists trained in assessing reproductive health anomalies.

Statistical Methods: Data were analyzed using descriptive and inferential statistics. The association between estradiol levels, endometrial thickness and menstrual patterns was examined using correlation coefficients and regression analysis where applicable. Chi-square tests were employed for categorical data to determine the significance of associations.

Data Collection: Data collection involved structured interviews to capture patient demographics, clinical history and specific symptoms of PCOS. Hormonal profiles and ultrasound findings were systematically recorded in a predefined format to ensure consistency and reliability of the data gathered. All collected data were then entered into a secure database for subsequent statistical analysis.

RESULTS AND DISCUSSIONS

(Table 1) in the study displays the distribution of symptoms among 100 patients at presentation, focusing on menstrual-related complaints and their associations with infertility and clinical signs of hyperandrogenism. Specifically, 34% of the patients presented with only menstrual complaints, 29% had menstrual complaints along with clinical signs of hyperandrogenism, 19% combined menstrual complaints with infertility, 15% reported menstrual complaints with infertility and clinical signs of hyperandrogenism and the remaining 3% had infertility coupled with clinical signs of hyperandrogenism.

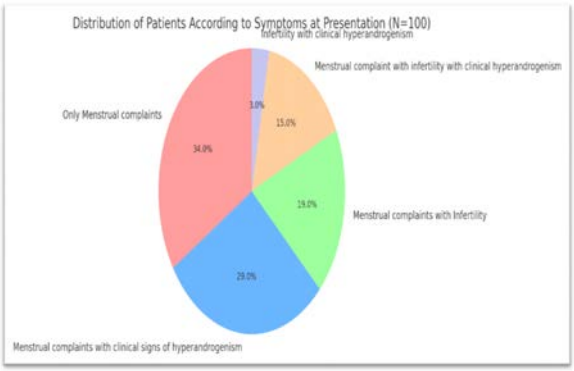

Fig. 1: Pie Diagram

(Table 2) examines the association of endometrial thickness with menstrual patterns and the amount of bleeding. It categorizes endometrial thickness into three groups: <4mm, between 4.1 and 10.9 mm and greater than 11mm and records the frequency of menstrual patterns and bleeding amounts. The data reveals that the majority of observations fall within the 4.1-10.9 mm range across different menstrual patterns and bleeding amounts. The chi-square analysis indicates a highly significant difference (p-value=0.01) when comparing less, normal and more frequent menstrual patterns, but no significant difference in bleeding amount (p>0.05). (Table 3) details the association between types of menstruation and estrogen levels. It demonstrates a statistically significant relationship (p-value=0.002), particularly noting how estrogen levels differ across various menstrual conditions like normal cycles, amenorrhea, and oligomenorrhoea.

(Table 4) shows the association between endometrial thickness and estrogen levels. It categorizes estrogen levels into less than 100 pmol/L and greater than 100.0 pmol/L and matches these with three categories of endometrial thickness. The majority of the data points again fall into the 4.1-10.9 mm range for both estrogen level categories. (Table 5) presents the correlation between endometrial thickness and estradiol levels across different menstrual patterns. The analysis is split into two estradiol level groups (<100 and >100 pmol/l) and subdivided by endometrial thickness (<4, 4.1-10.9, >11 mm). This table further investigates the frequency and amount of menstrual patterns associated with these divisions, with a significant result (p-value=0.04) indicating an association between estradiol levels and menstrual patterns at higher estradiol levels. Polycystic Ovary Syndrome (PCOS) is a complex endocrine disorder historically diagnosed through exclusion. Recent diagnostic criteria emphasize the importance of clinical and/or biochemical hyperandrogenism alongside other PCOS features. Our study observed that 97% of patients presented with menstrual complaints: 65% with oligomenorrhea, 22% with menorrhagia, 30% with hypomenorrhea, 6% with polymenorrhea, while 5% maintained a normal cycle and 11% experienced amenorrhea. Majumdar A[5-8]. noted a higher prevalence of menstrual irregularities in overweight and obese patients (79.2%) compared to those with lean PCOS (44%). Similarly, Emily Zheng[9] found that oligomenorrhea was the predominant presentation in 71.4% of 178 PCOS patients with irregular menstruation, where 13.1% maintained regular cycles and 6.3% reported polymenorrhea. Common presentations typically include menstrual complaints, primarily oligomenorrhea. In this study, 92% of patients demonstrated polycystic ovarian morphology via ultrasound and 61% exhibited a normoandrogenic PCOS type, characterized by oligomenorrhea with PCO morphology on ultrasound. A community-based study by Beena Joshi[10] in Mumbai identified oligomenorrhea with polycystic ovaries as the most frequent phenotype (52.6%). Regarding endometrial thickness, 85% of our patients had thicknesses between 4.1-10.9 mm, with an average of 6.86mm. Among those, 89.23% of patients with oligomenorrhea showed normal endometrial thickness, while 72.72% of those with amenorrhea and 13.63% with menorrhagia presented with a normal and thickened endometrium, respectively. Cheung[11] conducted a prospective study in 56 PCOS patients with infertility due to anovulation, finding 64.3% had a proliferative endometrium with a thickness <7mm and 35.7% exhibited endometrial hyperplasia. Shah[7] explored uterine and ovarian ultrasonographic features in adolescent females with PCOS, noting that 31.4% had an endometrial thickness greater than 7mm. Additionally, 84% had >10 follicles per ovary, with at least one cyst over 10mm observed in 25% of the cases. Our data shows that 86% of patients had estradiol (E2) levels on day 2 of over 100

Table 1: Distribution of Patients According to Symptoms at Presentation (N=100)

Complaints at Presentation	No. Of Patients	Percentage(%)
Only Menstrual complaints	34	34
Menstrual complaints with clinical signs of hyperandrogenism	29	29
Menstrual complaints with Infertility	19	19
Menstrual complaint with infertility with clinical hyperandrogenism	15	15
Infertility with clinical hyperandrogenism	3	3

Table 2: Association of Endo Material Thickness with Menstrual Pattern and Amount of Bleeding

Endo Material thickness	Frequency			Amount		
in mm/ Menstrual pattern	Less	Normal	More	Scanty	Average	Heavy
<4	4(6.15%)	2(6.89%)	1(16.7%)	3(10%)	4(8.33%)	0
4.1-10.9	58(89.23%)	22(75.86%)	8(83.3%)	26(86.67%)	40(83.34%)	19(86.36%)
>11	3(4.61%)	5(17.24%)	0	1(3.33%)	4(8.33%)	3(13.63%)
Total	65(100%)	29(100%)	6(100%)	30(100%)	48(100%)	22(100%)
Chi-square value	9.36			0.49		
p-value	0.01(Highly Significant)			p>0.05(Not Significant)		

Table 3: Association Between Types of Menstruation and Estrogen Level (N=100)

Types of menstruation/ Estrogen level (in pmol/L)	<100	>100.0	Total	Chi- square value	p-value
Normal cycles	4(28.57%)	1(1.16%)	5(5%)	24.18	0.002
Amenorrhea	3(21.43%)	8(9.3%)	11(11%)		(Highly Significant)
Oligomenorrhoea	4(28.57%)	25(29.6%)	29(29%)		
Hypomenorrhea	1(7.14%)	8(9.3%)	9(9%)		
Polymenorrhoea	0	3(3.48%)	3(3%)		
Menorrhagia	0	4(4.65%|)	4(4%)		
Oligomenorrhoea with hypomenorrhea	2(14.28%)	19(22.09%)	21(21%)		
Oligomenorrhoea with Menorrhagia	0	15(17.44%)	15(15%)		
Polymenorrhoea with Menorrhagia	0	3(3.48%)	3(3%)		
Total	14(100%)	86(100%)	100(100%)		

Table 4: Association Between Endo Material Thickness and Estrogen Levels

ET [In mm]	Estrogen levels (In pmol/L)	
	≤100	>100.0
<4	2(14.28%)	5(5.81%)
4.1-10.9	12(85.72%)	73(84.89%)
>11	0	8(9.3%)
Total	14(100%)	86(100%)

Table 5: Correlation Between Endo Material Thickness (ET) with Estradiol Levels with Menstrual Pattern

Estrogen levels	Menstrual pattern/	Frequency			Amount		
(in pmol/l)	Endo Material thickness	Less	Normal	More	Scanty	Average	Heavy
<100	<4	1 (1.53%)	1 (3.44%)	0	1 (3.33%)	1 (2.08%)	0
	4.1 – 10.9	4 (6.15%|)	8 (27.58%)	0	2 (6.66%)	10 (20.83%)	0
	>11	0	0	0	0	0	0
Total		65 (100%)	29 (100%)	6 (100%)	30 (100%)	48 (100%)	22 (100%)
Chi-square value	1.34				9.54		
p-value	0.72(Not Significant)				0.04(Significant)		

pmol/L, of which 15% presented with oligomenorrhea and menorrhagia. Frederick[12] highlighted that normal E2 levels on day 3 of the menstrual cycle range from 31 to 75 pmol/L, as observed in 45% of patients with anovulatory infertility. This study underscores the need for more research on the correlation between estrogen levels, endometrial thickness and menstrual irregularities in PCOS, highlighting gaps in current knowledge and potential areas for future investigation.

CONCLUSION

In this study, the majority of patients with oligomenorrhea presented with normal endometrial thickness in a hyperestrogenic state. All patients with menorrhagia exhibited hyperestrogenism, suggesting that elevated estrogen levels positively affect menstrual patterns and blood flow, although they do not significantly influence endometrial thickness. Most patients with thickened endometrium experienced a normal frequency of menstrual cycles and average bleeding. Similarly, almost all patients with oligomenorrhea and average blood flow maintained normal endometrial thickness. These findings indicate that endometrial status does not positively correlate with menstrual frequency or blood flow. We conclude that despite rising estrogen levels, endometrial status remains unaffected, yet menstrual patterns are altered. Therefore, menstrual complaints or endometrial thickness-whether associated with polycystic ovarian morphology or not-should not be the sole criteria for diagnosing PCOS, as they do not provide a comprehensive overview of the condition. Incorporating estrogen levels as one of the diagnostic criteria for PCOS could enhance diagnostic accuracy. Despite the presence of hyperestrogenemia, the incidence of endometrial hyperplasia is low, suggesting that excessive estrogen might contribute to infertility. This relationship between estrogen levels and reproductive outcomes warrants further investigation to elucidate the mechanisms underlying PCOS and its management.

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