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A Comparative Analysis of Levels of FSH, LH, Testosterone, TSH, Oral Glucose Tolerance Test and Ultrasonography in Females with PCO, PCOS and Normal Control Cases from Industrial Town in Western India.

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ABSTRACT

Incidence of anovulation showing PCOS in early age group (22-29 years) leading to problems like infertility, is rising progressively. High BMI and/or hirsutism is disturbing the psychology of early age educated girls. Association of changed lifestyle e.g. sedentary working pattens, lack of physical activities and changed eating habits are altering the HPO axis and Insulin functions. Present study was intended to find out and correlate altered biochemical markers with clinical presentations of the symptoms and polycystic appearance of ovaries on ultrasound, among women with PCOS, PCO and in women with other gyanecological complaints. 43 patients were included in PCOS group according to Rotterdams criteria, 16 in PCO group and 31patients were included as control group who presented with other gyanecological complaints. Clinical features on the basis of PCOS criteria including hirsutism, acne, obesity, infertility and oligomenorrhea were studied along with biochemical markers assessment of FSH, LH, TSH, Testosterone and OGTT. Hormonal milieu in normal weight and overweight/obese women differed in our study consistent with the findings of other studies. Further clinical studies with estimations of hormones associated with PCOS are required in Indian as well as other country women, to understand this complex interplay of different hormones.

Keywords: PCOS, FSH:LH, Obesity, BMI, India.

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INTRODUCTION

Polycystic ovary syndrome (PCOS) is a prevalent and frequently encountered genetically complex endocrine disorder of women of uncertain etiology [1]. It has been studied that this condition occurs in as many as 4-10 percent of women of reproductive age, with manifestation of symptoms as early as puberty [2,3].

Because of the diversity of clinical and metabolic findings in PCOS, there has been great debate as to whether it represents a single disorder or multiple associated pathologic conditions. In recent years, there have been a number of developments in the understanding of the genetics and pathophysiology of PCOS which have provided a fruitful basis for the development of new strategies for its management. It is now better to consider this problem as of persistent an-ovulation with a spectrum of etiologies and clinical manifestations.

Its clinical manifestations include menstrual dysfunction and hyperandrogenic symptoms, and association with metabolic dysfunction like hyperinsulinemia and peripheral insulin resistance. During the reproductive years, PCOS is associated with significant reproductive morbidity, including infertility, abnormal uterine bleeding, miscarriage, and various complications of pregnancy [4].

A mild form of PCOS including women who have mild hyperandrogenism and an isolated ultrasonographic finding of polycystic ovaries (PCO) with normal ovulatory function has also been described. These women may be susceptible to developing the syndrome as well. Thus, they may also be subject to increased morbidity [5].

While ultrasonography provides an excellent technique for the detection of polycystic ovarian morphology, identification of polycystic ovaries by ultrasound does not confer the diagnosis of PCOS. Using a combination of clinical, ultrasonographic and biochemical criteria, the diagnosis of PCOS is usually made for women who exhibit one or more of the clinical symptoms (menstrual cycle disturbances, hirsutism, acne, obesity, hyperandrogenism), and who display an ultrasound picture of polycystic ovaries, and/or one or more of the recognized biochemical disturbances (elevated LH: FSH, testosterone, androstenedione or insulin) [6].

In our study, we have studied the various biochemical markers associated with PCOS including FSH, LH, LH: FSH, Testosterone, OGTT, and TSH along with ultrasonographic appearance of ovaries in three groups of patient- i) with anovulatory cycles (PCOS), ii) ovulatory cycles (PCO) and iii) in normal women.

The polycystic ovary is the result of a “vicious cycle”, which can be initiated at any entry point, thus producing a heterogeneous condition of PCOS. Because of the complex nature of this disease, it is important that women with PCOS be educated about and understands the health implications related to the syndrome.

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MATERIALS AND METHODS

The study was started as a prospective- observational study at a Tertiary care centre and teaching hospital from April 2011 to November 2013.

90 women from the outdoor patient department were categorized clinically as PCO, PCOS and Normal case control group to be included in the study.

Ethical committee permission was taken for the study. Each woman was counselled and informed consent was taken before the biochemical assay was done.

The major criteria for diagnosis of PCOS were oligomenorrhea and/or anovulation, clinical or biochemical signs of hyperandrogenism and ultrasonographic findings of polycystic ovaries, which is in accord with the revised 2003 Rotterdam criteria of PCOS.

Presence of only ultrasonographic findings with any clinical sign was considered as the criteria of inclusion for PCO group.

Overall, puberty to peri menopausal age group women with clinical history suggestive of PCO, PCOS were included in our study.

Women with no specific clinical features of PCOS in the similar age group were taken in normal control group.

Women with clinical presentations similar to the criteria for diagnosing PCOS but with other known disorders like thyroid dysfunction, hyperprolactinemia or androgen secreting neoplasms were excluded from the study.

Chemiluminescence immunosorbant assay (C.L.I.A) was used to perform the endocrinological tests by luminometer (Lumax). Biochemical markers were done on Day 3 of the menstrual cycle so as to receive standardised results.

Ovarian volume, diameter of the follicles and endometrial thickness were studied on ultrasonography done on LogiQ 200.

Details regarding the age, weight, body mass index, clinical history, biochemical markers and ultrasonographic findings were systematically obtained and maintained.

ANOVA test and unpaired t- test were applied to the data obtained and P value of <0.05 was considered significant.

DISCUSSION

Of the 90 women eligible for the study, 43 women were diagnosed as PCOS on the basis of the Rotterdam Criteria, 16 women were categorized as PCO based on the ultrasonographic findings and 31 women were randomly selected with any other gynecological complaints and this group was labeled as control group.

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Mean age of the women in PCOS group was 24.42, of PCO was 22.19 and of control group was 24.97 as shown in Table 1.

Table 1: Age distribution of patients diagnosed as PCOS, PCO and Control group.

AGE	N	Minimum	Maximum	Mean	Std. Deviation
PCOS	43	16	32	24.42	4.101
PCO	16	18	26	22.19	2.613
CONTROL	31	18	32	24.97	3.114

75% patients diagnosed with PCOS have been reported to have clinically evident menstrual dysfunction as shown by series of studies conducted on large groups of patients. Balen et al. in 1995 studied patients with PCOS and found that 59.9% had oligimenorrhea, whereas, Haddad et al in 2002 and Chang et al in 2005 showed the incidence of oligomenorrhea to be 82.2% and 83.9% respectively [6,7]. The present study showed similar findings where 37.2% patients diagnosed as PCOS presented with complaints of oligomenorrhea as shown in Table 2.

Table 2: Distribution of duration of menstrual flow in days in PCOS, PCO and control group

DURATION (in days)	N	Minimum	Maximum	Mean	Std. Deviation	*P value*
PCOS	43	1	6	2.98	1.282	0.002
PCO	16	2	6	3.75	1.238	0.002
CONTROL	31	1	6	4.03	1.169	0.002

Body mass index (BMI) contributes significantly to the severity of problems associated with PCOS. Approximately, 50% of PCOS women are overweight or obese, which leads to hyperinsulinemia with insulin resistance and hyperandrogenemia [8].

In our study, mean BMI of women with PCOS was 29.14 graded as overweight as shown in Table 3. These findings were found to be comparable to studies like of Fakhoury et al where mean BMI was 31.9 [9].

Table 3: BMI distribution of patients with PCOS, PCO and control group.

BMI	N	Minimum	Maximum	Mean	Std. Deviation	*P Value*
PCOS	43	24	36	29.14	2.133	0.0001
PCO	16	19	30	24.75	3.376	0.0001
CONTROL	31	19	30	24.87	2.918	0.0001

Weight loss of even upto 10%, has shown to increase the frequency of ovulation, improve conception, and reduces miscarriage, hyperlipidemia, hyperglycemia, and insulin resistance in women with PCOS [10].

A normal reproductive hormonal cycle in women is characterized by fluctuating gonadal hormonal levels, well regulated by hypothalamic-pituitary-gonadal axis which is replaced by a relatively steady state of gonadotropin associated with persistent anovulation in PCOS.

This pulsatile variation of gonadotrophin releasing hormone (GnRH) results in the relative increase in LH as compared to FSH release [11]. Due to this derangement the ratio between FSH and LH levels which normally is around 2 to 1, become reversed and sometimes even more (2 or 3 to 1) in approximately 60% of the patients with PCOS [12].

The present study confirms and extends the previous finding of inappropriately elevated LH release and low FSH secretion, thus leading to abnormal LH:FSH ratio in most patients with PCOS.

According to our study, in PCOS women high LH: FSH ratio is a common occurrence alongwith low level of FSH and a higher LH level. The mean FSH level is low as compared to normal values; also the LH: FSH ratio is raised to 1.4 as shown in Table 4. This is in accordance to Chang et al who had reported that the ratio of LH to FSH in PCO patients was 2.9 compared to a value of 1.1 in the normal group [13].

Table 4: Variation of biochemical markers in PCOS, PCO and Control group

		Serum FSH	SERUM LH	LH:FSH	TOTAL T	FREE T	SERUM TSH	FASTING	PP
PCOS	MEAN	2.981	6.223	1.46035	6.93	1.919	2.356	85.42	135.44
	SD	.6374	1.1974	.347746	5.016	.7159	.8157	7.983	18.560
PCO	MEAN	2.981	3.731	1.43419	6.88	1.756	2.744	78.44	125.00
	SD	.3544	.8122	.371029	4.161	.6271	.7294	3.705	9.798
CONTROL	MEAN	3.155	3.900	1.00639	4.97	1.565	2.610	80.00	124.58
	SD	.4668	1.1192	.376704	1.975	.5930	1.1449	6.583	9.895
P-VALUE		0.001	0.001	0.840	0.102	0.08	0.001	0.04	0.285

Association of obesity with the pathophysiology of PCOS has been proven. But the intriguing fact that not all PCOS women are obese nor they all posses the hormonal and biochemical changes, has inspired many to establish coorelation between disease manifestations. Studies have been conducted to find an answer to the question that whether higher BMI necessarily indicate a higher LH/FSH ratio or greater incidence of hirsutism or menstrual disturbance. The results have been found to be variable.

Studies like Insler et al, reported that, the non obese PCOS women had higher level of serum LH than obese women in the study [14]. Kiddy et al reported an inverse correlation of FSH with BMI in obese PCOS with increased frequency of hirsutism in obese as compared with lean PCOS women [15].

In our study, features of hyperandrogenism like hirsutism, acne were found to vary with BMI, thus showing associations consistent with previous studies. With patients studied in range of 26-30 kg/m^2 BMI, 63% had hirsutism and in range of 30-35 kg/m^2 BMI, 75% patients had features of hirsutism as shown in Table 5. This indicates significantly, higher the BMI higher are the chances of hyperandrogenism.

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Table 5: Association of BMI with clinical parameters

		BMI (kg/m^2)				Total
		18 -25	26-30	31-35	More than 35	
Hirsutism	ABSENT	22	19	2	0	43
	PRSENT	7	33	6	1	47
ACNE	ABSENT	8	27	2	1	38
	PRSENT	21	25	6	0	52
Obesity	ABSENT	27	6	0	0	33
	PRSENT	2	46	8	1	57
Infertility	ABSENT	7	20	1	0	28
	PRSENT	6	7	2	0	15

The above results of present study should be considered given the fact that, the cycles in PCOS are anovulatory and irregular. However we attempted to show the possible hormonal imbalance in the form of abnormal LH and FSH secretion underlying the complex endocrinological cascade of PCOS.

The overall prevalence of PCO was found to be about 17%, which was found to be comparable to the study done by Koivunen R et al (14.2%) done in 1999 and slightly lower than that reported (16-23%) in previous studies by Polson et al, Abdel Gadir et al, Clayton et al and Farquhar et al [16-18]. The selection criteria for the patients however varied in each study, making it difficult for comparison.

Women with an isolated ultrasonic finding of PCO have subtle biochemical disturbances similar to PCOS and are susceptible to develop the syndrome. Out of 16 patients with PCO, 3 had altered LH:FSH in our study group as shown in Table 4 . These patients with only PCO changes are planned to be followed up along with treatment options for further evaluation, as these women may also have an increased morbidity such as that associated with PCOS.

In women with PCOS, ovarian volume was found to be significantly increased, with mean volume being 12.23 as shown in Table 6. This was found to be in accordance with current studies which suggest that presence of polycystic ovaries on transvaginal ultrasound may be found in 75% women with clinical features of PCOS [19].

Table 6: Ultrasonographic parameters in PCOS, PCO and Control group

	Mean Ovarian Volume (ml)	Std. Deviation	Mean Diameter of follicles (mm)	Std. Deviation	Mean Endometrial thickness (mm)	Std. Deviation
PCOS (43)	12.23	1.962	5.40	1.545	4.65	.870
PCO (16)	9.81	3.391	3.75	1.949	4.56	.814
CONTROL (31)	8.52	2.219	3.06	1.389	4.03	.795
P - VALUE	0.0001		0.00001		0.00001	

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CONCLUSION

PCOS, an ill-defined symptom complex needs its due attention. Incidence of anovulation showing PCOS in early age group (22-29 years) leading to problems like infertility, is rising progressively. High BMI and/or hirsutism are disturbing the psychology of early age educated girls. Association of changed lifestyle e.g. sedentary working patterns, lack of physical activities and changed eating habits are altering the HPO axis and Insulin functions.

Present study was intended to find out and correlate altered biochemical markers with clinical presentations of the symptoms and polycystic appearance of ovaries on ultrasound, among women with PCOS, PCO and in women with other gyanecological complaints.

In our study, 43 patients were from PCOS group according to Rotterdams criteria, 16 in PCO group and 31patients were included as control group who presented with other gyanecological complaints. Clinical features on the basis of PCOS criteria including hirsutism, acne, obesity, infertility and oligomenorrhea were studied along with biochemical markers assessment of FSH, LH, TSH, Testosterone and OGTT.

Hormonal milieu in normal weight and overweight/obese women differed in our study consistent with the findings of other studies. Insulin resistance is common in PCOS women and can vary with BMI. Out of 16 PCO group patients, only two showed biochemical changes. These patients will be followed up to find out whether they will be developing full PCOS picture in spite of advising lifestyle, physical activity and dietary changes so that timely therapeutic intervention can be made.

Further clinical studies with estimations of hormones associated with PCOS are required in Indian as well as other country women, to understand this complex interplay of different hormones. It is important to break the vicious circle of PCOS, which is largely maintained by high levels of androgens and insulin. Although the results obtained in this study increase our understanding of PCOS, they inevitably lead to further questions and debate.

Further studies are necessary to find out whether nutritional deficiencies are responsible for such type of hyperinsulinism and hyperandrogenism, leading to rising ovarian dysfunction in young age women causing PCO and PCOS.

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