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ASSOCIATION OF HORMONAL CHANGES AND ULTRASOUND FINDINGS IN POLYCYSTIC OVARY SYNDROME IN THE SUBSET OF ALDOLESCENT POPULATION

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ABSTRACT

Aim: To determine the association of ultrasound findings with follicle-stimulating hormone (FSH), Luteinizing hormone (LH) and free testosterone in adolescents with the polycystic ovarian syndrome (PCOS).

Study Design: Cross-sectional study.

Place and Duration of Study: the study was conducted at Gynecology OPD of Ziauddin hospital kiamari, Karachi, from June 2019 to December 2019.

Methodology: Total 44 adolescents (16-22years) with PCOS diagnosed according to Rotterdam ESHRE/ASRM Consensus criteria 2003 were enrolled in the study. Non-probability consecutive sampling technique was used. After taking informed consent, participants were evaluated through clinical interviews, questionnaire, and anthropometric measurements. The participants underwent the following assessments i.e. transabdominal ultrasonography, hormonal tests (free testosterone, follicle-stimulating hormone, luteinizing hormone), and metabolic tests (including fasting blood sugar).Participants were divided into two groups based on ultrasound findings. Those with normal ultrasound were gathered as Group - I and others who had polycystic ovarian morphology (PCOM) were categorized as Group - II.

Results: In our results, most of the adolescents had polycystic ovarian morphology 77.7 % and 23.3% had normal ultrasound findings. There were significant high LH and free testosterone levels in those having PCOM group.

Conclusion: Significant differences were observed among free testosterone and LH levels between Group-I having normal Ultrasound and Group-II PCOM. In addition to this, there is a significant association of LH and testosterone with ultrasound findings which play a role in the early evaluation of reproductive and metabolic status in adolescents.

Keyword: PCOS, Ultrasound, PCOM, LH, FSH

INTRODUCTION

Polycystic Ovary Syndrome (PCOS) is a heterogeneous disorder that manifests typically with a combination of menstrual irregularities, infertility, hyperandrogenism, acne, and obesity. **[1-4]**. It is a complex disorder caused by multiple factors including genetic as well as environmental **[5, 6]**. Normally during puberty, maturation of the hypothalamic-pituitary-ovarian axis causes a consequent increase in circulating levels of luteinizing hormone (LH). This increase in LH is exaggerated in the females with a predisposition to PCOS and leads to increase in production of androgen by the theca cells. Along with this insufficient conversion of these high androgens to estradiol in the peripheral tissue causes an ovulation due to failure in selection of a dominant follicle **[7, 8]**. It is also reported that there are Gonadotropin-releasing hormone(GnRH) stimulatory and inhibitory neurotransmitters that are responsible for elevated level of GnRH and LH in PCOS (1). Greenwood et al has also concluded that the recent trend of increasing obesity among teenagers is one of the causative factors of the increasing prevalence of PCO in adolescents due to the Insulin resistance and they all culminate in hyperinsulinemia that leads to hyperandrogenism **[9]**.

Despite the high globalprevalence (4% to 21%) of PCOS, **(Lizneva, Suturina, *et al.* 2016)**, its diagnosis remains one of the most challenging issue in reproductive medicine, especially in adolescents **[10]**. Most accepted and used criteria is Rotterdam criteria that require the presence of two out of three hallmark features (hyperandrogenism, oligomenorrhea, and polycystic ovary) for the diagnosis of PCO. It has been seen that it is difficult to interpret the ovarian morphology on ultrasound during the period of puberty,due to the physiological increase in the volume of ovaries and follicle count in teenagers **[11]**. In addition to this, obesity which has also become rampant creates difficulty in interpreting ultrasound imaging and it also needs an expert who can measure follicle

number in the 3D stroma (as some follicles are too small) and ovarian volume accurately **[10]**.

Currently, ultrasonography is not a diagnostic tool for PCOS in adolescents but it provides supportive evidence **[12]**. Although early identification and management of adolescents with PCOS can prevent the long-term reproductive, cardio-metabolic, and emotional consequences associated with syndrome **[13]** and misdiagnosis can also influence an adolescents' quality of life and create an early and unwarranted anxiety about future fertility, so there is a need to find association of the hormonal changes in PCOS with ultrasound findings so that we can properly diagnosis of the PCOs in adolescents with their puberty changes.

MATERIALS AND METHODS

This was a single centered cross-sectional study, conducted in the gynecological OPD at Ziauddin Hospital Kiamari Karachi from June 2019 to December 2019. It was carried out in adolescent girls between 16 to 22 years **[14]**. By open epi sample calculation (95%CL) sample size was calculated n=44 and the non-probability convenient sampling was used. After taking informed consent all participants were interviewed on an individual basis. Participants were questioned about the pattern of the menstrual cycle, infertility, weight problem, information about past diagnosis or treatment of PCOS or any other illnesses and hirsutism by a preformed proforma. Moreover, weight and height were measured by standard protocol and calibrated instruments. After above mentioned protocol ultra-sonographic findings of participants were recorded.

The Rotterdam criterion, established at Rotterdam ESHRE/ASRM Consensus is used to diagnose PCOS **[16]**. The menstrual irregularity was assessed by the menstrual cycle length of less than 21 days or more than 35 days. Ovaries were considered as polycystic on ultrasound by the presence of more than 12 follicles per ovary with the diameter 2–9 mm and increased ovarian volume >10cm **[17]**.

After ultrasound participants were divided into two groups: Group I normal ultrasound and Group II polycystic ovarian morphology (PCOM).

5-ml blood sample was drawn and serum was separated and stored at -70ºC until the time of assay. Serum LH was measured by Human LH Enzyme Immunoassay (kit Cat NO. CEA441Hu by Cloud Clone). Serum FSH was determined by (Kit Cat. No KAPD1288 by Immune Assays S.A. Belgium) and testosterone levels were measured by ELISA Kit for TestosteroneCEA458Ge by Cloud clone).

Statistical Analysis

Statistical analysis was performed with SPSS, version 20. For categorical variables,

frequencies and percentages were calculated. For numeric variables, mean (SD) andmedian was calculated. For finding association, chi-square test was used.p-value less than 0.05 was considered statistically significant.

RESULT

The mean age of the participants was 19.9±2.3 years. Most of the adolescents were overweight 20 (45.5%)or obese:11 (25%). The mean hip waist ratio was86.02±8.46. The meanhormonal profile was: LH 12.28±5.06, FSH 7.35±3.36 and free testosterone 87.8± 35.092 **(Table 1)**.

Result showed that patients diagnosed with PCOS had the menstrual irregularities: 77.3 % had oligomenorhea, 15.9% had normal flow and 7.4 %had menorrhagia.

On Ultrasonographyn=12 (27.3%) participants were recruited in GroupI (normal ultrasound) and n=32(72.7%) were recruited inGroup II(PCOM). The comparison between the two groups is shown in **Table 2**. There was no significant difference in the age, weight, height, BMI, WHR, FSH and FBS in the two groups. However, there was a significant difference in LH (p-value 0.00) and testosterone (p-value .00) levels between group I and II.

Regarding the association of hormones with ultrasound findings **(Table 3)**. In Group I we found normal LH levels in n = 8(18.2 %) and high LH levels in n=4 (9.2%) with significant p-value = 0.002. In GroupII n= 5(11.4%) were having normal LH levels and high LH levels were seen in n=27 (61.4%) with the significant p-value = 0.002

When the ultrasound findings were associated with the testosterone levels we found in group-I n = 12(27.3%) had high testosterone. While in Group II n =12(27.3%) had normal testosterone level and n=20 (45.5%) had high testosterone levels with significant p-value = 0.011.

We further observed there was no significant association of ultrasound findings with FSH levels in both groups.

Table 1: Demographic and Hormonal Data of Participants

ANTHROPOMETRIC DATA	MEAN±SD
AGE	19.90±2.34
WEIGHT	70.88 ±9.86
HEIGHT	5.40 ±.29
BMI(kg/m^2)	26.77 ±4.36
BP(SYS)	112.52 ±7.89
BP(DYS)	79.02 ±5.47
WHR(cm)	86.02 ±8.46
BIOCHEMICAL DATA	
FBS	91.40±17.20
HORMONAL DATA	
FSH (mIU /ml)	7.35 ±3.36
LH(mIU /ml)	12.28 ±5.06
FREE.TESTOSTERONE (ng/dl	105±35.09

Table 2: The Difference in The Normal Ultrasound and Polycystic Ovarian Morphology of Patient

	GROUP I (n=12)	GROUP II (n=32)	p-value
AGE	20.58±1.92	19.65 ± 2.45	.206
WEIGHT	69.83 ±9.76	71.28±10.03	.607
HEIGHT	5.38 ±.32	5.41 ± .28	.884
BMI(kg/m^2)	27.44 ± 5.07	27.08 ± 3.81	.802
BP(SYS)	113.33 ±7.78	112.21 ± 8.039	.622
BP(DYS)	79.58 ±5.41	78.81 ± 5.56	.711
WHR(cm)	86.20± 11.48	85.96 ± 7.25	.905
FBS	94.83 ±11.61	90.12 ± 18.87	.301
LH	10.05±3.14	14.98 ± 4.20	.000*
FSH	7.02 ±3.14	7.72 ± 3.47	.544
FREE TESTOSTERONE	119.81± 10.73	99.97±94.21	.000*

BMI:body mass index, WHR: waist hip ratio
***significant p-value**

Table 3: The Association of Hormones With Ultrasound Findings

	ULTRASOUND		p-value
	GROUP - I (n=12) 27.3%	GROUP - II (n=32) 72.7%	
NORMAL LH (02-12 mIU/ml)	(n=8) 18.2%	(n=5) 11.4%	0.002*
HIGH LH	(n=4) 9.1%	(n=27) 61.4	
NORMAL FSH (3-8 mIU/ml)	(n=10) 22.7%	(n=20) 45.5%	0.107
HIGHFSH	(n=10) 22.7%	(n=12) 27.3%	
TESTOSTERONE Upto 81ng/dl	(n=0) 0%	(n=12) 27.3%	0.011*
HIGH TESTOSTERONE	(n=12) 27.3%	(n=20) 45.5%	

***significant p-value**

DISCUSSION

The main objective of this study was to test the hypothesis of finding the association of ultrasound findings of the polycystic ovarian syndrome in an adolescent with hormonal levels as PCOS has common heterogeneous phenotype which overlaps with some features of puberty **[18]**.

Our study found that most of the adolescents had polycystic ovarian morphology on Ultrasound this is following the observation of Ibrahim *et al.,* **[19]**. It may be due to high levels of free testosterone and androgens ovaries fail to ovulate and cysts are formed along with an increase in the stroma of ovaries **[12]**. Our result found a highly significant association of ultrasound findings with free testosterone levels in both the groups that may inference that if a female is having normal ultrasound finding but raised levels of free testosterone along with menstrual irregularities may have PCOS. While LH levels were also significantly high in group-II.The aspects of ovarian morphology relay on androgen production and gonadotropin secretion even though there are strong influences of metabolic factors on ovarian

morphology during adolescence which may result in increase of these hormones **[20]**. This is parallel with the findings of Rackow *et al.,* **[20]**.

60% of participants had high levels of free testosterone, the high prevalence of hyperandrogenemia among adolescents, suggests that such females are indeed at the risk of developing PCOS **[21]**. Hyperandrogenism, is commonly demonstrated by an elevated free testosterone in circulation, a major contributor to the pathophysiology of PCOS **[22]**. The LH level was found high in PCOS as reported in Akram *et al.,* **[23]**. The FSH level in our study was normal in adolescents in both groups which is in contrary to Merino PM et al who observed lower serum FSH level in adolescents with PCOM **[24]**.

We observed most of the adolescent girls were overweight in our study as observed by Christensen *et al* **[25]**. Zore *et al.,* showed a high prevalence of obesity and its consequences were significantly higher in the Young Adult group as compared with adolescent girls which is opposing our results **[26]**. During puberty, adolescents have a temporary decline in insulin sensitivity which play an important role in the hyperinsulinemia and insulin resistance which contribute to obesity during this period **[22]**.

Fasting blood sugar had seen normal in PCOS in adolescents as the same finding were observed by Majid *et al.,* **[27]**.

CONCLUSION

Patients with normal ultrasound may have raised levels of testosterone that may be a useful diagnostic tool for PCOS in adolescents. Furthermore, LH levels were also having same association with ultra-sonographic findings as testosterone had.

STRENGTH OF OUR STUDY

Our study has highlighted the role of testosterone, LH with ultrasound findings that may be a diagnostic tool to early detect the PCOS in Adolescents. Same kind of studies are proposed on larger sample size to generalize the findings.

LIMITATIONS

It was a single centered study.

The sampling technique was non-probability convenient sampling so chances of selectionbias cannot be omitted.

ETHICAL APPROVAL

Ethical clearance was obtained from the Ethics Review Committee of Ziauddin University.

Conflict of interest:

There was no conflict of interest.

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