RESEARCH
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HORMONAL PROFILE AND THEIR ASSOCIATION WITH PCOS AND FIBROID INCIDENCE IN YOUNG PAKISTANI WOMEN

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Abstract
This study was carried out to evaluate levels of fertility hormonal profile in women with intramural fibroid and PCOS. A total of seventy-five 150 patients aged 18–50 years were recruited for the study and were divided into two groups: subjects with intramural fibroid group and PCOS group. The serum follicle-stimulating hormone, luteinizing hormone, Estradiol and prolactin were assayed using the ELISA method. The data was analyzed using SPSS Version 21.0. The probability p = 0.005 was statistically significant. The result obtained showed a significant increase (p = 0.005) in follicle stimulating hormone (9.37±0.37 mIU/mL) in patients with intramural fibroid group when compared with follicle stimulating hormone (6.72±0.48 mIU/mL) in PCOS. There was a significant increase (p = 0.005) in luteinizing hormone (6.19±0.27 iu/ml) in the fibroid uterus group when compared with luteinizing hormone (5.36±0.21 iu/ml) in the PCOS group. There was a significant increase (p = 0.005) in estradiol (207.81±218.694 pg/ml) in the uterine fibroid group when compared with oestradiol (88.14±16.79 pg/ml) in the PCOS group. There was a significant increase (p = 0.005) in prolactin (73.34±9.68µg/l) in the uterine fibroid group when compared with prolactin (14.67±10.96µg/l) in PCOS. It was however confirmed that patients with intramural fibroid have increased serum levels of follicle-stimulating hormone, luteinizing hormone, estradiol, and prolactin. Therefore, it was concluded that intramural fibroid affects higher serum concentrations of follicle-stimulating hormone, leitinizing hormone, estradiol, and prolactin as compared to PCOS. Due to this, it can contribute to the reduction of fertility or risk of miscarriage and complicated delivery in women with intramural fibroid.

Introduction

Polycystic ovary syndrome (PCOS) is the most common endocrinologic condition in women, affecting from 8% to 13% of reproductive-aged women [1] It is a condition that is very common and difficult to diagnose and treat accordingly; symptoms and treatment also depend on the age of an individual. Due to its variable forms and limited treatment options, the world is very concerned about this disease. [2] There are various mechanisms involving its pathogenesis, like loss of GnRH pusatility with increased LH secretion by pituitary, HYPERINAULINEMIA, ovarian insulin resistance, theca cell dysfunction, and hyperandrogenism [3]. Clinical presentation of PCOS depends on four clinical types [4]. Phenotype A is described as hyperandrogenism; phenotype B, in which hyperandrogenism presents with ovultry dysfunction; in phenotype C, polycystic ovary morphology is involved; and finally, on phenotype D, there are no signs of hyperandrogenism [5]. Hyoerandrogenism is a key feature of PCOS, Although an adrenal contribution cannot be excluded. Acute administration of GnRHor human chorionic gonadotrophin is followed by greater 17-hydroxyprogesterone (17OHP) production than in normal women. 22,23 This and other observations have led to the hypothesis that 17-hydroxylase and 17,20-lyase activities, constituents of the enzyme P450c17, are altered in PCOS. The consequence of the intrinsic dysregulation of this enzyme is a relative inhibition of 17,20-lyase with respect to 17-hydroxylase, and thus an increase in 17OHP compared with normal women. Clinically, Hyperandrogenaemia may induce acne and hirsutism, which are treated with antiandrogen drugs that bind to androgen receptors. 24 In addition, contraceptives may reduce acne and hirsutism and improve menstrual cycles in PCOS women. Phenotypes A and B are more commonly seen in the clinical setting because of severe metabolic abnormalities, while the milder phenotype D with fewer symptoms of metabolic disturbances is more prevalent in the general population. The variation in observed phenotype is thought to be influenced by DNA methylation in the presence of histones, microRNAs, as well as other gene regulatory proteins. The

underlying pathophysiology is multifactorial with complex polygenic inheritance [6]. Multiple loci have been identified by genome-wide association studies, and epigenetic regulation has been explored. In one study by Chen and colleagues, miR-93, which is responsible for downregulation of GLUT4, appeared to be overexpressed in PCOS patients. GLUT4 is a protein responsible for insulin-mediated glucose translocation into adipocytes and is required for glucose metabolism. Its downregulation results in insulin resistance, as observed in PCOS [7]. Though several candidate genes have been found to be causative, routine genetic testing is currently not recommended.

This paper will review the diagnostic criteria and hormonal profile association with PCOS. PCOS impacts all aspects of the reproductive hormone physiology; however, the precise pathophysiology and association between the two remain incomplete. The current evidence for leading pathophysiologic disturbance in PCOS will be reviewed, as well as the best evidence of reproductive, psychological, hormonal, and metabolic consequences. Finally, an update on the best evidence-based treatments for PCOS will be reviewed. Uterine fibroid is a tumor of myometrium; is the most common solid pelvic tumour in young females associated with abnormal bleeding and infertility [8]. It is ooestrogen-dependent, and these raised levels of ooestrogen lead to the formation of uterine fibroid [9]. As a result of their strong network of interactions with progesterone, an increasing amount of research now views this hormone as having a greater role in the initiation of myometrial abnormal differentiation and growth than it does in the pathophysiology of uterine fibroid [10]. The fact that uterine fibroid rarely develops prior to menarche and tends to decline following menopause is evidence of the critical role oestrogens play in the pathophysiology of uterine fibroid. Furthermore, in the hyperoestrogenic state, uterine fibroid growth rates were found to significantly increase. Similarly, a higher frequency of uterine fibroid was demonstrated in obese women with a high percentage of adipose tissue (strongly associated with hyperoestrogenism) [11]. According to Jakimiuk et al., women with high levels of both testosterone in midlife are more likely to develop incident uterine fibroids than women with low levels of the hormones [12]. Higher testosterone levels in menopausal women may increase their risk of developing fibroids, especially if they also have higher oestrogen levels, according to research [13]. The objective was to assess the prolactin, luteinizing hormone, and follicle-stimulating hormone levels in women with PCOS and intramural fibroid.

Materials and Methods:

Study Area:

The study was carried out at

Ethics, Advocacy, and Pre-Survey Contact:

A letter of introduction was collected from the Head of Department of Medical Laboratory…….. was collected and submitted to the Head of Clinical Services and also Chairman Ethics Committee... who subsequently granted an ethical approval for the study. A structured questionnaire was given to participants, and those who gave consent to participate in the study were recruited.

Study design: It was a simple comparative study, and all eligible women who filled out the questionnaire and gave written informed consent for the study period were sampled. A total of 150 female subjects participated in the study. The study was grouped into two groups, group A representing (75) suffering from intramural fibroid and 75 with PCOS. The age limit was 20–50 years. After confirmed diagnosis of uterine fibroid and PCOS, their blood samples were collected and used for the laboratory evaluation of oestrogen, FSH, LH, and prolactin.

Study Population:

A total of seventy (150) subjects were recruited for the study, of which 75 were subjects suffering from intramural fibroid while twenty 75 were suffering from PCOS.

SAMPLE SIZE:

Sample size was determined in accordance. With the WHO calculator, two groups were made: one group with PCOS and the other group with fibroid.

n=z2 pq x d

n = desired sample size

z is the standard normal deviation, usually set at 1.96

p= the proportion of female with intramural fibroid and PCOS using a confidence interval set at 95% is 3.5%

q=1-p

d= degree of accuracy set at 0.05

Total sample size was 150.

Selection Criteria.

Inclusion criteria:

i. Female subjects confirmed of intramural fibroid or PCOS and had been attending clinic for not less than 3 months

ii. Patients who were not diagnosed with other gynaecological pathologies like ovarian cancer.

iii. Subjects with intramural fibroid but not on any contraceptive pill.

iv. Patients who were apparently healthy And between the age of 18 and 50

vi. Subjects whose informed consent was obtained.

Exclusion criteria

i. females below the age of 18 years and above 50 years.

ii. Patients diagnosed with known gynaecological disorders.

iii. Patients on contraceptive pills.

v. Patients whose informed consent was not obtained.

SAMPLE COLLECTION:

Blood samples were collected aseptically by vein puncture using 5 ml sterile disposable syringes and were disposed into a labelled plain dry specimen container. The samples were centrifuged at 3,000rpm for 5 minutes to separate and to obtain the serum. The serum was extracted using a pipette and was introduced into another specimen container and stored at -20 oC until required.

All hormones like oestradiol, FSH, LH, and serum prolactin levels were determined by using ELISA methods.

STATISTICAL ANALYSIS:

All values were expressed as mean ± standard deviation. The results were analyzed for statistical significance using the student T-test. P values <0.05 were considered statistically

significant. The statistical analysis was carried out using statistical packages for social sciences (SPSS) version 21.0.

RESULTS:

TABLE 1: Clinical characteristics of the study groups

Characteristics	PCOS	Uterine fibroids
number of women	75	75
Age (years)	28	36
weight (kg)	52	64
hieght (ft)	5.2	5.1

TABLE 2: Reproductive hormones in intramural fibroid and PCOS groups.

Parameter	Intramural fibroid N = 75	PCOS group N = 75
Follicle Stimulating Hormone (mIU/mL)	9.37±0.37	6.72±0.48
Luteinizing Hormone(IU/ml)	6.19±0.27	5.36±0.21
Prolactin (µg/l)	73.34±9.68	14.67±10.96
Estrodiol (pg/ml)	07.81±218.694	88.14±16.79

Table 1 shows the mean ± standard deviation of fertility hormonal profile on women with
intramural fibroid and PCOS in the study population. The result showed that the mean value of follicle-stimulating hormone is higher in the intramural fibroid group (9.37±0.37 pg/ml), which was statistically significant (p = 0.001) when compared with the PCOS (6.72±0.48). The mean value of leuitnizing hormone was statistically significantly higher (p = 0.001) in intramural fibroid group (6.19±0.27) when compared with the PCOS group (5.36±0.21) The result showed that the mean value of prolactin is higher in the intramural fibroid group (73.34±9.68), which was statistically significant (p = 0.001) when compared with the PCOS (14.67±10.96). The mean value of Estrodiol was statistically significantly higher (p = 0.003) in the intramural fibroid group (207.81±218.694) when compared with the PCOS group (988.14±16.79).

DISCUSSION:

The result of the present study (table 1) showed a significantly higher increase in the mean values of follicle-stimulating hormone in intramural fibroid when compared with the mean value of the production of follicle-stimulating hormone associated with PCOS that can affect ovulation release that may lead to infertility. This present study also showed a significant increase in the luteinizing hormone when compared with the mean value of luteinizing hormone of the PCOS group, indicating that this hormone can contribute to the growth of intramural fibroid; this is in agreement with the work done by Wallach et al., who showed that luteinizing hormone in premenopausal women stimulates intramural fibroid [14]. Therefore, women with higher LH were more likely to have intramural fibroid. Their work also showed that intramural fibroid regrowth was seen in patients, and luteinizing releasing hormone was used as a medical treatment procedure. The study also showed a significant increase in the mean value of prolactin in the intramural fibroid group. This present study also showed a significant increase in the estradiol when compared with the mean values of estradiol in the PCOS group. Women with chronic fibroid showed significantly higher values in follicle-stimulating hormones compared to non-chronic fibroid and non-fibroid women. Follicle-stimulating hormone release is not suppressed by higher levels of progesterone or estrogen, which could explain the increase in FSH (Dickerson et al. 2008) [15]. According to Mihm M et al. (2011), females also exhibit a slight increase in follicle stimulating at the end of the initial phase, which seems to be crucial for starting the ovulatory cycle that follows. Additionally, luteinizing hormone levels were found to be significantly higher in both chronic fibroid and non-chronic fibroid women. The fact that gonadotropin-releasing hormone (GnRH) pulses from the brain regulate luteinizing hormone release at the pituitary gland may be one factor contributing to the hormone's possible dramatic increase. Because the gonads are responsible for providing extugen response to those pulses, an increase in oestrogen synthesis triggers the release of luteinizing hormone [17]. Unlike the previous published studies [18], we have failed to find a significant increase in LH in patients with PCOS. A major factor that tends to affect the results is the variation of hormonal level with the menstrual cycle. According to a published study [11], elevated LH levels are not very reproducible in the early menstrual cycle, which was the time at which we measured LH in this study. Furthermore, it was previously demonstrated that LH is more elevated in lean PCOS patients compared to obese PCOS patients [16].

Limitations:

The results of this study should be interpreted bearing in mind its limitations.

- A major limitation was the sample size, which is 150. Future studies with a larger number are required to further clarify the hormonal variations in PCOS.
- Another limitation is the unavailability of a measurement for insulin level for the study subjects. Most of the cases were overweight or obese, which is a predisposing factor for diabetes or the metabolic syndrome.
- On the other hand, insulin resistance is significantly related to serum LH. Therefore, the absence of data on insulin levels in both groups has impacted some constraints on the interpretation of the hormonal findings.

In conclusion, our study suggests that regardless of the age and weight factor, PCOS patients have higher levels of LH/FSH and total testosterone but lower levels of FSH and progesterone.

CONCLUSION:

The higher increase in this fertility hormonal profile observed in both uterine fibroids and PCOS can contribute to infertility, the risk of miscarriage, and complicated delivery. But these hormones are highly increased in uterine fibroid and PCOS. The findings have made significant contributions to the understanding of fertility hormone changes in women with intramural fibroid.

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