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Original Article

Biochemical profile in patients of hirsutism presenting in outpatient department of Combined Military Hospital, Jhelum and Combined Military Hospital, Kharian

Qamar-ud-Din Khan[1], Ahnab Raja[2], Uzma Naeem[3], Iftikhar Ahmed Satti[4], Afshan Bibi[5]

[1] Department of Dermatology, Pak Emirates Military Hospital Rawalpindi.
[2] Department of Dermatology, Combined Military Hospital, Jhelum.
[3] Consultant Chemical Pathologist, Army Medical College, Rawalpindi.
[4] Pak Emirates Military Hospital Rawalpindi.
[5] Consultant Chemical Pathologist, Combined Military Hospital, Tarbela.

Abstract

Introduction Hirsutism is a common distressing disease and a frequent reason for dermatological consultation. Although hirsutism is prevalent worldwide, not many studies have been done in Pakistan. A cross sectional study was carried out in Dermatology department of combined military hospital (CMH) Jhelum from 15th March 2019 to 14th September 2019 to find out hormonal and radiological changes in patients reporting with complaint of hirsutism.

Methods 140 females presenting with hirsutism, in the age group of 18 till 50 years were recruited in the study. All Pregnant women, lactating mothers and women taking oral contraceptive pills, oral hypoglycemic, anti-androgen drugs were excluded from the study. Assessment of hirsutism was done by means of Ferriman-Gallwey scoring system. Patients were called on second to third day of menstrual cycle and samples were collected after an overnight medical fasting of 10-12hrs. The patients on the 2nd or 3rd day of menstrual cycle all had their blood tests (LH: FSH, Prolactin and Testosterone) along with ultrasound of ovaries and adrenals.

Results Frequency of hormonal and radiological findings in patients presenting with hirsutism were Polycystic ovarian syndrome 71 (50.71%), adrenal mass in none (0.0%) patients, Raised LH: FSH ratio in 13 (9.29%), raised total testosterone in 28 (20.0%), hyperprolactinemia in 09 (6.43%) and those without any cause was 19 (13.57%).

Conclusion The most frequent cause of hirsutism was polycystic ovarian syndrome and subsequently idiopathic hirsutism.

Key words
Hirsutism; Polycystic ovarian syndrome; Testosterone.

Introduction

In hirsutism there is appearance of unrestricted final hair in androgen-reliant regions like beard, moustache, chest and lower abdomen of women.[1] It appears after the onset of puberty and mainly affects up to 5-10% of the women between 18-50 years of age.[2] The meticulous preponderance rate of hirsutism is not established, but may be elevated upto 10% or more. It is commonly associated with bullying, social isolation and poor academic performance.[2]

Among two types of hirsutism hyper androgenic

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Address for correspondence
Dr. Qamar-ud-Din Khan, Consultant Dermatologist, Pak Emirates Military Hospital, Rawalpindi.
Email: qamar_khan7862000@yahoo.com

hirsutism is caused by overproduction of androgens. It includes congenital adrenal hyperplasia, polycystic ovarian syndrome and androgen producing malignancy of adrenals and ovaries. Non-hyper androgenic hirsutism results as a consequence of endocrinopathies, medications and Idiopathic hirsutism. Endocrinopathies include Cushing syndrome, hyperthyroidism, hyperprolactinemia, insulin resistance and acromegaly. Medications producing excessive hairiness include progesterone, androgens, danazol, interferon, clomiphene, tamoxifen, glucocorticosteroids, minoxidil, diazoxide, cyclosporine, phenytoin, D-and penicillamine. The raised concentration of free or active testosterone is usually the result of elevated levels of GnRH, and androgens, and declined levels of SHBG because of grievous hyperinsulinemia. Hirsutism reported even with steady menstrual cycle, no abnormal ovarian morphology and androgen levels is called idiopathic hirsutism. This should be excluded before establishing other causes. Increased susceptibility of receptors of pilosebaceous follicle towards androgens and peripheral transformation which is prompted by the enzyme 5-α reductase of testosterone that converts to dihydrotestosterone becomes ten-times extra strong in the follicle-sebaceous unit.[3]

Ferriman-Gallwey (F-G) score was applied to track hirsutism. This F-G score was used to record the existence and intensity of hirsuitism at various parts of body to put together a cumulative score. Diagnosis of hirsutism was made when the score was 8 or large. Further classification was made on gravity of hirsutism and graded as mild hirsute with grade of 8-16, moderate hirsutism with grade of 17-25 and with grade of >25 as severe hirsutism out of a maximum score of 36.[11] Almost around second to third day follicle stimulating hormone (FSH) and luteinizing hormone (LH) levels, serum testosterone level and serum prolactin levels were done. Radiological evaluation includes ultrasound pelvis to look for polycystic ovaries with positive radiological findings in patients.[5]

In the past only a few studies have been conducted to determine the cause of hirsutism in our community. The motive behind this survey was to assess their hormonal profile (LH: FSH ratio, serum prolactin, serum testosterone levels) and perform ultrasonography of ovaries and adrenals and document it. Such workups unravel the cause in our community and add to our understanding of excessive hair growth.

Materials and Methods

A descriptive cross-sectional study was carried out in dermatology department of CMH Jhelum from 15th March 2019 till 14th June. Those falling in age group of 18-50 years presenting with hirsutism were recruited. All pregnant, lactating women, or having congenital adrenal hyperplasia and women taking contraceptive pills, oral hypoglycemics, and on anti-androgen drugs (Aldactone, Diane-35 etc.) for past three months were excluded.

The ethical review committee gave the consent for the study on November 23, 2021. Informed written consent was taken, using a proforma from each patient regarding duration of disease, presence of symptoms of virilization, androgenetic alopecia, menstrual irregularity, acne and family history. Examination included calculating BMI, looking for signs of virilization, and spread and arrangement of excessive hair growth. In order to assess the gravity of excessive hair growth Ferriman-Gallwey scoring system was used. Hirsutism was sorted out and graded as mild (8-16) moderate (17-25) and severe (>25).[8]

Patients were called on second to third day of

menstrual cycle and samples were collected after an overnight medical fast of 10-12 hrs. Hormonal profile including serum LH: FSH ratio, serum prolactin, and serum testosterone were sent to laboratory. Ultrasound examination of ovaries and adrenals were conducted on the same day to look for polycystic ovaries and adrenal mass.

Data was analyzed with the help of statistical program SPSS V 21.0. The end result to see the effects was calculated by post stratification chi-square test. A P value that is equal to or lesser than 0.05 was appraised as notable.

Results

The age group ranged from 18 to 50 years in 140 patients recruited. The average age calculated was 29.86±6.91 years. In almost 113 patients (80.71%) the age group ranged from 18 to 35.

The average time since hirsutism was present was 6.38±4.18 years. Mean height was 2.54±0.22 m. Mean weight was 70.07±15.42 kg. Mean BMI was 26.72±2.84 kg/m^2. Majority of patients 86 (61.43) had BMI >27 kg/m^2. The grouping of patients based on disease intensity is exhibited in **Table 1**. Mean Ferriman-Gallwey score was 10.86±3.66. Mean FSH Levels (mIU/l) were 4.07±1.83. Mean LH levels (mIU/l) were 4.81±3.59. Mean total testosterone levels (nm/l) were 2.01±1.27. Mean prolactin levels (mIU/l) were 284.80±141.45 **(Table 2)**. Frequency of hormonal and radiological findings in patients were as follows; Polycystic ovarian syndrome was found in 71 (50.71%), adrenal mass in 00 (0.0%) patient, Raised LH:FSH ratio was found in 13 (9.29%), Raised total testosterone was found in 28 (20.0%) and hyperprolactinemia in 09 (6.43%) patients as shown in **Table 3**. **Table 4-7** are presenting stratification of the hormonal and radiological findings according to age, time span, BMI, along with disease severity respectively.

Table 1 Severity of disease indifferent group of patients (n=140).

Severity	*No. of Patients*	*%age*
Mild	124	88.57
Moderate	16	11.43
Severe	0	0.0

Table 2 Mean hormone levels in patient presenting with hirsutism.

	Mean±SD
Ferriman-Gallwey score	10.86±3.66
FSH Levels (mIU/l)	4.07±1.83
LH levels (mIU/l)	4.81±3.59
Testosterone levels (nm/l)	2.01±1.27
Prolactin levels (mIU/l)	284.80±141.45

Table 3 Frequency of hormonal and radiological findings in patient presenting with Hirsutism

Findings	*Frequency (%)*	
	Yes	*No*
Polycystic ovarian syndrome	71 (50.71%)	60 (49.29%)
Adrenal mass	00 (0.0%)	140 (100.0%)
Raised LH/FSH ratio	13 (9.29%)	127 (90.71%)
Raised total testosterone	28 (20.0%)	112 (80.0%)
Hyperprolactinemia	09 (6.43%)	131 (93.57%)

Discussion

About 5-10% of women have hirsutism[9,10] and usually, it has been thought to be a sign of higher levels of androgen in females as a result of the adrenal glands' increased production of androgens (such as testosterone) or as a result of an ovarian disorder.[12,13] Ovarian tumours and polycystic ovarian syndrome (PCOS) are the two ovarian causes of hyperandrogenism. Congenital adrenal hyperplasia (CAH), which is most frequently brought on by a lack of 21-hydroxylase, and androgen-producing tumours are among the causes of the adrenal glands. Acanthosis nigricans syndrome with hyperandrogenic insulin resistance is one of the less frequent causes (HAIRAN). Hirsutism may result from hyperprolactinemia but when compared to this, constitutional hirsutism can be found in 20% of population. In these patients

Table 4 Stratification of the hormonal and radiological findings with respect to age.

	18-35 (n=113)	*36-50 (n=27)*	*P-value*
Polycystic ovarian syndrome			
Yes	47	22	0.0001
No	66	05	
Adrenal mass			
Yes	00	00	-
No	113	27	
Raised LH/FSH ratio			
Yes	09	04	0.257
No	106	23	
Raised total testosterone			
Yes	25	03	0.199
No	88	24	
Hyperprolactinemia			
Yes	07	02	0.817
No	106	25	

Table 5 Stratification of the hormonal and radiological findings with respect to duration.

	≤6 years (n=94)	*>6 years (n=46)*	*P-value*
Polycystic ovarian syndrome			
Yes	52	19	0.119
No	42	27	
Adrenal mass			
Yes	00	00	-
No	94	46	
Raised LH/FSH ratio			
Yes	01	12	0.0001
No	93	34	
Raised total testosterone			
Yes	22	06	0.150
No	72	40	
Hyperprolactinemia			
Yes	08	01	0.151
No	86	45	

serum testosterone assays and ovarian activity are regular. Enhanced peripheral androgen activity in these ladies is regarded to be the root of their increased hair growth.[15] IH develops slowly after puberty, with a gradual onset. 90% of female hirsutism is caused by PCOS and IH. Some premenopausal women may experience hirsutism, which might last for a few years following menopause. As long as androgens are produced continuously, ovarian oestrogen secretion declines.[16]

The most important hormones involved in controlling hair growth are androgens.[24] They contribute to keratinization, there is prolonged anagen stage of the hair rotation, enhanced villous hair conversion to terminal hair in particular regions, and the diminution of hair follicle size on the scalp.[25] The hair follicles sensitivity stimulated by androgen differ to a great extent among women, the severity of disease does not correspond with androgen quantity.[26] Mean FSH levels (mIU/l) in our study were 4.07 1.83. LH levels were 4.81 3.59 mIU/l on average. The mean values of total testosterone (nm/l) were 2.01±1.27. The average prolactin con centration (mIU/l) was 284.80± 141.45. In this study, patients presenting with hirsutism frequently had the following hormonal and radiological results; 71 (50.71%) patients had polycystic ovarian syndrome, 0 (0.0%) had adrenal mass, 13 (9.29%) had elevated LH:FSH ratio, 28 (20.0%) had elevated total testosterone, and 9 (6.43%) had hyperprolactinemia. LH: In 14 (46.7%) and 10 (33.3%) instances, the levels of FSH and prolactin were elevated.[1]

The source of androgens are ovaries and the adrenals. Polycystic ovarian disease, which Stein and Leventhal first identified as the triangle of clinical symptoms including amenorrhea, excessive body hair growth, and overweight some 60 years ago, as a typical cause of hirsutism.[17] However, many female complainers with excessive hair are neither obese nor experiencing monthly irregularities. These ladies are frequently diagnosed with idiopathic hirsutism. However, contrary to this a notable increased incidence (92%) of polycystic ovaries was reported by Adams *et al*. in a set of female patients with excessive hair and regular menstrual cycles.[18]

In polycystic ovarian syndrome, variations in basal levels of luteinizing hormone (LH) are not rare. Franks stated that a high basal level of

Table 6 Stratification of the hormonal and radiological findings with respect to BMI.

	≤27kg/m^2 (n=54)	*>27kg/m^2 (n=86)*	*P-value*
Polycystic ovarian syndrome			
Yes	13	58	0.0001
No	41	28	
Adrenal mass			
Yes	00	00	-
No	54	86	
Raised LH/FSH ratio			
Yes	05	08	0.993
No	49	78	
Raised total testosterone			
Yes	08	18	0.365
No	46	68	
Hyperprolactinemia			
Yes	01	08	0.080
No	53	78	

luteinizing hormone is seen in 50-70% of women with polycystic ovarian syndrome.[19] Adams[18] saw the same result at rates of 66% and 62%, respectively, as did Grule.[20] In comparison to Adams and others[18] (66%) in great Britain along with Yilmaz *et al*. in a sequence of 31 Turkish female patients (55%), our group had fewer patients with an increased luteinizing hormone/ follicle-stimulating hormone ratio.[21] It has been widely advised that the mainstay of diagnosis for polycystic ovarian syndrome should be luteinizing hormone exaggerated response towards stimulation test with gonadotropin-releasing hormone, which emphasizes the importance of dynamic endocrine studies.[20-22]

2016 saw the completion of another study by Anjum, Muhammad Usman, *et al*. to identify the etiological factors in the population of Abbottabad. Around 50 patients with a mean age of 28.30±5.83 years were recruited. 44% of patients had higher levels of free testosterone, 42.1% had higher levels of LH/FSH, and 10% had higher levels of prolactin. Polycystic ovarias (58%) and constitutional hirsutism (38%) were solely the most recurring explanation.[6]

Conclusion

This study concluded that Polycystic ovaries are the most common radiological finding and raised total testosterone is the most common abnormal biochemical finding in patients presenting with hirsutism, followed by idiopathic hirsutism. So, we recommend that all women with hirsutism should be evaluated carefully with radiological and biochemical hormonal profiles for proper evaluation of the cause of hirsutism. Timely treatment can improve the social life and emotional well-being of suffering women.

Declaration of patient consent The authors certify that they have obtained all appropriate patient consent.

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Author's contribution

QDK: Substantial contribution to study design, manuscript writing, has given final approval of the version to be published.

AR: Substantial contribution to study design, acquisition of data, has given final approval of the version to be published.

UN: Substantial contribution to acquisition of data, drafting the manuscript, has given final approval of the version to be published.

IAS: Substantial contribution to acquisition of data, revised the data critically, has given final approval of the version to be published.

AB: Substantial contribution to data interpretation, revised the manuscript critically, has given final approval of the version to be published.

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