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BIOCHEMICAL FACTORS INFLUENCING FAMILIAL HIRSUTISM IN THE SOUTHERN REGION OF KPK

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ABSTRACT

Familial hirsutism is a prevalent disorder marked by excessive hair growth in women, often arising from genetic and physiological influences. This research seeks to examine the molecular factors contributing to familial hirsutism in the southern region of Khyber Pakhtunkhwa (KPK), Pakistan. A cross-sectional analysis was conducted involving female participants with a familial history of hirsutism. Biochemical markers such as androgen levels (testosterone, dehydroepiandrosterone sulphate), indicators of insulin resistance, and hormonal profiles were assessed. The results demonstrate increased androgen levels and insulin resistance in the affected individuals relative to the control group. Family pedigree analysis revealed a significant hereditary pattern related to genetic predisposition. The findings indicate that hormonal imbalances and genetic variables are pivotal in the occurrence of familial hirsutism within this community. Comprehending these characteristics might facilitate the formulation of focused treatments and enhance management techniques for impacted persons. Additional investigation is advised to examine the fundamental genetic pathways and possible environmental factors.

Keywords: PCOS, FSH, LH, TSH

INTRODUCTION

Hirsutism is characterized by excessive hair development in females in regions often associated with male hair distribution, indicating a departure from the standard female hair pattern. Hair follicles are found all throughout the body, with the exception of the palms, soles, lips, and mucosal surfaces of the external genitalia. Except for the scalp and brows, which are covered with coarse, pigmented terminal hair, the majority of the body is covered in vellus hair, which is fine and soft before puberty. Hirsutism impacts 5% to 10% of women, with variations according on age,

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menopausal status, and ethnic origin. For an appropriate clinical diagnosis, it is essential to specify the kind of hair growth (Elliott, Liu, & Motan, 2023).

During puberty, androgens facilitate the transformation of vellus hair into terminal hair in sex-specific regions. In males, sexual hair emerges on the face (beard area), chest, lower back, and anterior thighs, while in both sexes, it appears in the genital region and lower belly. Hirsutism results from elevated androgen production and/or bioavailability in women, resulting in the growth of sexual hair in regions often associated with masculine characteristics. The emergence of coarse dark hair on the top lip and chin is notably upsetting and a prevalent reason for women to get medical consultation. Excessive hair growth in places characteristic of males is indicative of androgen-induced growth, regardless of normal blood androgen levels. In contrast, a widespread proliferation of long fine hairs, encompassing regions like the forehead and sides, is not influenced by androgens (Zeng et al., 2022).

Figure. 1 the above pic show Hair follicles in females

The role of ethnic and genetic variables in hirsutism has been the subject of several prior investigations. Family trees and twin studies have shown that hirsutism runs in families. This may be due to a hereditary control mechanism that involves an abnormal response of the sebaceous glands to neurohormonal signals (Lam, Zhang, Guo, Ho, & Li, 2017).

There has been speculation about polygenic inheritance as well as a straightforward mendelian pattern of heredity. It is said that mongoloids are less hirsute than Caucasians, and hypertrichosis is more common in white women than in Japanese women (Rudžianskaitė, Dabužinskienė, Green, & Kriaučiūnienė, 2021).

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Moreover, the prevalence of hirsutism has been documented to be nearly double among Mediterranean populations compared to Nordic individuals (Langan, Philpott, Kloepper, & Paus, 2015). Polycystic ovarian syndrome (PCOS) is characterized by ongoing anovulation, obesity, and elevated androgen levels. These days, everyone knows that insulin resistance and hyperandrogenism go hand in hand. However, there is not enough data showing whether patients with IH also have insulin resistance (Peña et al., 2020).

Figure 2. The image illustrates Polycystic Ovary Syndrome (PCOS) as a cause of face hirsutism.

The interplay between obesity, oligomenorrhea, and hirsutism is frequently associated with increased plasma androgen concentrations and diminished testosterone-binding globulin (TEBG) levels, particularly in the context of polycystic ovary syndrome. Multiple investigations suggest that each of these clinical traits, when evaluated separately, could be associated with irregularities in plasma androgen and/or TEBG profiles. The extent to which oligomenorrhea and obesity might indicate elevated androgen levels, regardless of the presence of hirsutism, remains inadequately explored. This study was carried out with the objective of achieving it (Vermeulen & Vervloet, 2023).

Likewise, conditions stemming from adrenal sources of androgens, including adrenogenital syndrome and post-pubertal adrenal hyperplasia, may play a role in the development of hirsutism in females. In cases of reproductive disorders and hirsutism, cortisone therapy can lead to complete or partial resolution in nontumoral situations, effectively restoring the pituitary-adrenal balance that has been disrupted by enzymatic adrenal deficiency. In women experiencing "simple" or


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"idiopathic" hirsutism, there is a documented correlation with menstrual irregularities, accompanying symptoms of endocrine dysfunction, and altered biochemical profiles of sexual hormones (Eldridge, Sridaran, & Brann, 2024). Despite established high production rates and plasma levels of androgens, particularly testosterone (T) and androstenedione, in most women with hirsutism, the sources and frequency of androgen hypersecretion in idiopathic hirsutism remain contentious issues. A clear definition is essential prior to conducting the analysis of the given data. Secretion is generally characterized by a higher concentration of hormones in the efferent blood compared to the afferent blood of a gland. Two criteria are commonly used to assess glandular secretion: a) the concentration ratio of efferent to peripheral vein, and b) the secretory gradient, defined as the concentration of the efferent vein minus that of the peripheral vein. The latter metric seems to serve as a more reliable measure of glandular secretion. The secretory gradients of the adrenal and ovarian glands in women with optimal health. However, further factors need to be considered when analyzing different steroids.

This involves glandular or peripheral tissues converting a specific steroid into a new molecule, as well as the half-life and volume of distribution, which are not dependent on glandular synthesis but can affect peripheral steroid hormone concentration. The difficulty in directly measuring these traits in humans has resulted in the use of indirect assessments of hormone production via steady-state kinetics following the infusion of radioactive steroids; however, this method does not differentiate between adrenal and ovarian secretion (Zhao, Ye, Yan, Li, & Wang, 2022).

The familial prevalence and distribution of hirsutism and associated symptoms have been determined in 90 girls aged 15 to 45, including their first-degree relatives (mothers and sisters) and a control group. Patients were classified into three categories based on clinical criteria: ovarian hirsutism, adrenal hirsutism, and idiopathic hirsutism. A technique was developed for the semiquantitative assessment of the prevalence of atypical body hair in women and symptoms of endocrine malfunction. The distribution pattern of hirsutism resembles a continuous spectrum, indicating a gradient trend from typical female characteristics to excessive hairiness. A notable family clustering of hirsutism was observed, with the propositi and their relatives forming a distinct group compared to the controls for hirsutism. This outcome, together with the intermediary scores

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across relatives, establishes the foundation for a genetic etiology, with a multifactorial inheritance pattern being a feasible explanation. Hormonal imbalances of varied severity were consistently linked to hirsute women. The hirsutism score distribution was similar to the endocrine symptom score distribution (Yildiz, Bolour, Woods, Moore, & Azziz, 2010).

Any female with acne, hirsutism, or androgenetic alopecia should be evaluated for hyperandrogenism. In addition to being unsightly, these skin issues may be indicators of hormone imbalances, which in turn might impact fertility. Hyperandrogenism in adolescent girls is most often caused by a poorly known functioning disease of the adrenal glands. Understanding the origins of hyperandrogenic illnesses has progressed, and this page explains the basics of androgen physiology while also providing advice on how to diagnose and treat hyperandrogenism in women in their teen and young adult years (Wierman, 2021). The primary goals of this study on familial hirsutism were to biochemically categorize the frequency with which female students (as patients) at Gomal University had abnormally high hair density on their bodies, legs, and faces.

Materials and Methods

Scope of the research

The focus of the study was District. Dera Ismail Khan, often known as D.I. Khan, serves as both a city and the administrative center of the Dera Ismail Khan District in Khyber Pakhtunkhwa, Pakistan. The city ranks as the 37th most populous in Pakistan and holds the position of the fifth most populous in the province of Khyber Pakhtunkhwa.

Idealized location of working

The investigation was conducted at the Department of Biological Sciences, Gomal University, within the Molecular Biology Research Lab located in Dera Ismail Khan. The volunteer subjects for the study were enrolled after they provided their written consent in a fully informed manner.

Exclusion criteria

The study's exclusion criteria were based on the following features and hirsutism. Exclusion from the research was granted to those who fulfilled the following criteria:

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Infections caused by viruses and bacteria, Anemia in its broadest sense, Diabetes mellitus, Autoimmune disorders, cardiovascular diseases, Disorders related to genes, Conditions affecting the lungs.

Inclusion criteria

People with hirsutism who were not taking any medication were eligible to participate in the planned trial.

Duration of research study

The duration of the current research project was one year.

Size of the blood sample

The overall sample size of the research was 20. All individuals exhibiting hirsutism in the Dera Ismail Khan area, aged 20 to 45.

Collection of the blood samples

Twenty volunteers aged between 20 and 45 provided venous blood samples. Each individual had approximately 2 milliliters of blood extracted into standard tubes. After collection, blood samples were sent to the Molecular Biology Research Laboratory at Gomal University's Biological Science Department and stored at -20°C.

Processing of Samples

The blood sample was collected and thereafter maintained undisturbed at room temperature to promote coagulation. The standard duration for this is one to three hours. A chilled centrifuge was employed to centrifuge the sample at 1,000 to 3,000rpm x g for 15 minutes to eliminate the clot. The liquid that ascends to the surface, referred to as the supernatant, is serum. The subsequent examination occurred in the molecular biology laboratory at the Department of Chemical & Life Sciences, Qurtuba University D. I. Khan, Dera Ismail Khan, after the collection and brief preservation of the serum sample at 15°C

RESULTS

This study examined the biochemical prevalence of aberrant hair thickness on the body, legs, and faces of Qurtuba University female students (patients) in the context of familial hirsutism. Although they were of diverse ethnicities, the patients were nearly all from the same group. In

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order to analyze the hormonal profile, blood samples were taken from each patient. Additionally, 30% of these patients were married. Only 10% of married patients have really had a kid. T3, T4, and TSH levels were biochemically determined in all individuals. Additional testing was conducted to identify any irregularities in the production of testosterone, FSH, and LH.

Table 1: Age and ethnicity-based patient distribution

S. No.	Punjabi	Pashtun	Balochi	Total
18-20 years	1	1	1	4
21-23 years	2	2	2	5
24-27 years	3	2	0	5
>27 years	2	4	0	6
Total	8	9	3	20

Table 1 demonstrated that the predominant percentage of patients was from the Pashtun ethnic group (45%), followed by the Punjabi ethnic group (40%) and the Balochi ethnic group (15%). The predominant cohort of patients was found in the 24–27-year age bracket, consisting of 6 out of 20 people, succeeded by the 21-23 year and above 27-year age categories, each including 5 individuals.

Table 2: Biochemical analysis of thyroid hormones T3, T4, and TSH in females with hirsutism

Patient's name	T3 (ng/ml) 0.69-2.15	T4 (ng/ml) 52-127	TSH IU/ml (0.7-27)	Testosterone (ng/ml) (0.10-0.90)
Aiman Gul	0.44	62.3	4.67	5.6

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Lubna	0.43	65.4	5.32	7.9
Shazia Gul	1.08	67.7	6.34	7.98
Rabia Bibi	1.05	70.51	5.78	9.73
Asia Gul	0.97	68.3	5.25	11.24
Yaseen Bibi	1.00	61.15	5.48	8.36
Farzana Gul	1.83	63.62	5.14	8.56
Haseena Nawaz	1.14	66.6	6.14	7.6
Tanzila Gul	0.14	60.53	6.50	10.5
Rabia Khan	0.89	67.83	5.83	10.52
Sadia Khan	0.65	69.5	6.98	13.5
Saima Gul	0.61	71.3	6.91	17.0
Salma Khan	0.91	70.5	7.12	15.22
Palwasha Rehman	0.89	81.23	7.55	15.6
Barerha	0.72	68.62	6.35	14.87
Samreen	0.66	73.78	7.89	14.45
Sadaf Bibi	0.10	71.77	7.21	13.1
Raheela	0.10	73.41	6.90	14.63
Amna Hayat	1.91	69.08	7.50	13.9

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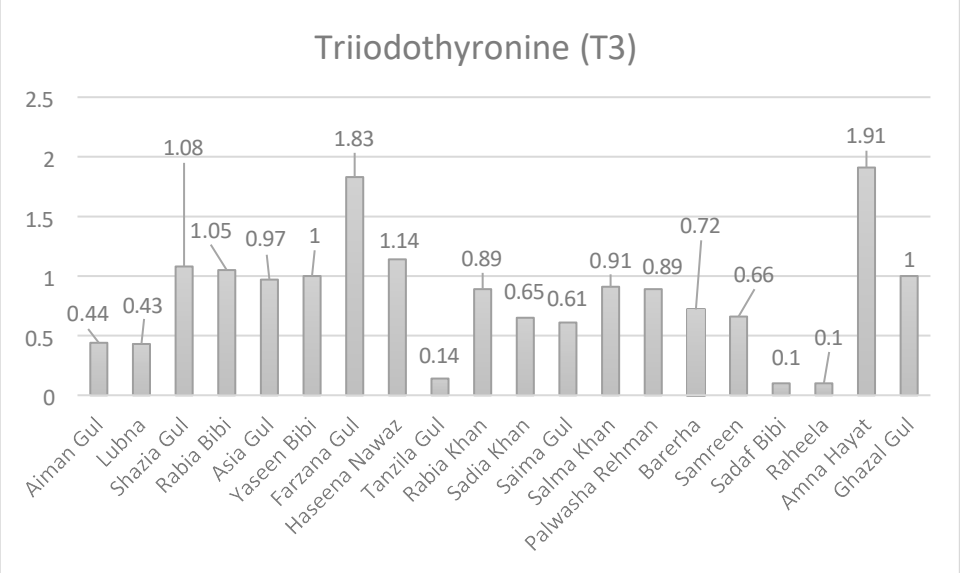
Ghazal Gul	1.00	72.33	6.93	15.55

Regarding T3, just 4 patients (20%) had serum levels beneath the normal limit. No patient had T3 levels beyond the upper limit of the normal range.

Testosterone: The normative level for this hormone in females is under 1 ng/ml. This investigation demonstrated that testosterone levels were markedly elevated. Testosterone is attributed to the development of secondary sexual traits, such as the growth of body hair. The range of values observed in this investigation ranged from 5.6 ng/ml to 17.0 ng/ml.

Figure 1: The histogram displays quantitative measurements of Triiodothyronine (T3) hormone levels in serum samples obtained from females diagnosed with hirsutism.



This figure shows the levels of T3 hormone in hirsutism patients' blood samples. The bottom of the photo shows the reference (normal) value, which is 0.69-2.15 ng/ml. The minimum value

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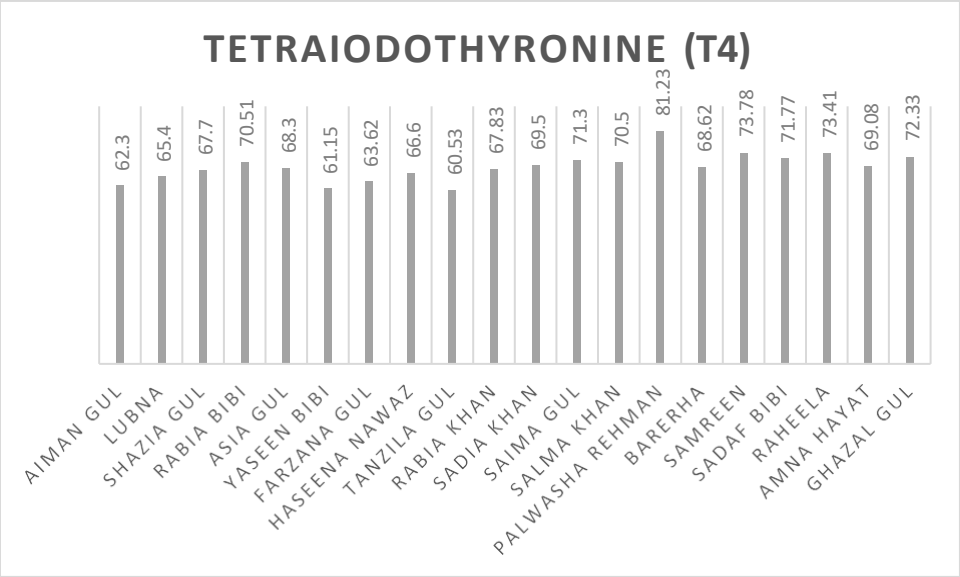
illustrated in the image was 0.43 ng/ml, whereas the maximum value documented was 1.83 ng/ml. Five individuals (25%) exhibited T3 levels at the lower boundary of the normal range. No subjects exhibited T3 levels above the standard threshold.

Figure 2: The histogram depicting quantitative readings of Thyroxin (T4) hormone in females with hirsutism.



This graphic illustrates the concentration of T4 hormone in serum samples from women with hirsutism. The reference value is located at the bottom of the image. The histogram indicates that all measurements were within the specified range. No samples were found to be outside the normal T4 range. All patients had readings much below the peak. From 60.53 ng/ml to 81.23 ng/ml, the range of values was rather wide. In this investigation, no abnormalities in T4 levels were found.

Figure 3: Histogram illustrating the quantitative levels of Thyroid Stimulating Hormone in serum samples collected from females with hirsutism

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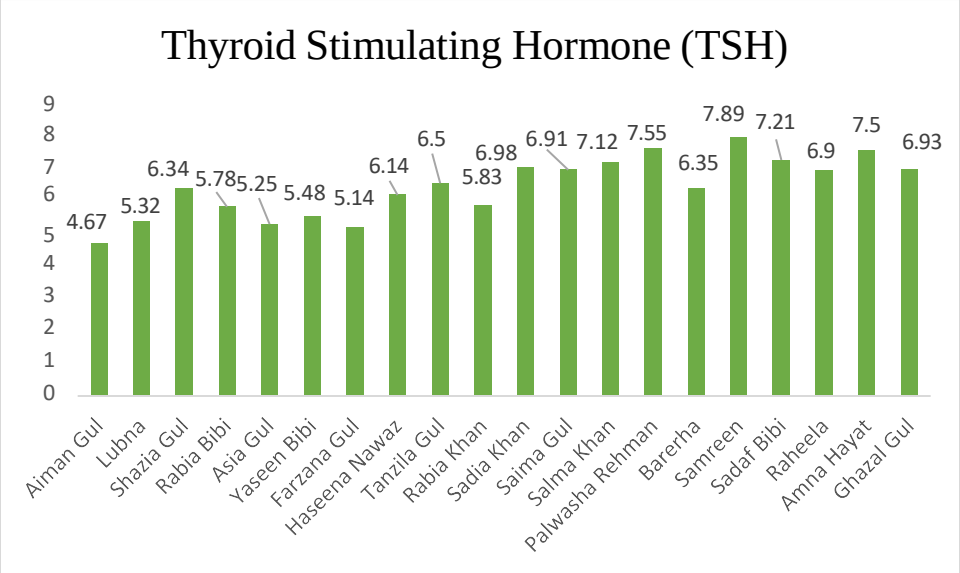
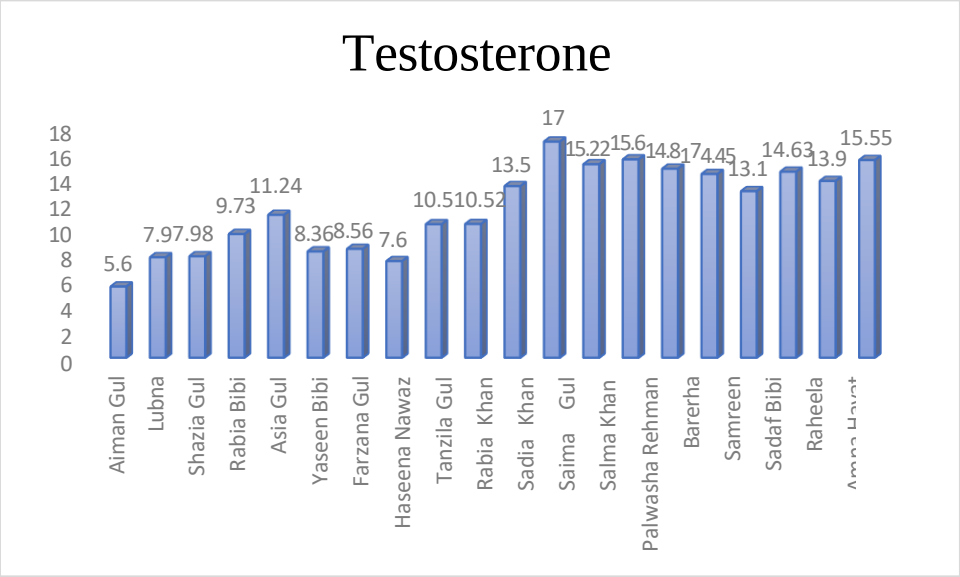


Figure 4: Histogram illustrating the quantitative levels of testosterone hormone in serum samples collected from females with hirsutism



In females, testosterone, which is commonly synthesized by the uterus, kidneys, and various other organs, typically registers below 1.0 ng/ml. This examination disclosed that this particular hormone was produced in remarkably elevated quantities. All the patients exhibited this hormone at levels markedly exceeding the typical range. The minimum quantity detected was 5.6 ng/ml,

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whereas the maximum recorded value reached 17.0 ng/ml. The results observed were notably unconventional within the female demographic.

Discussion

Hirsutism is a medical disease commonly seen in women. Nonetheless, it is essential to differentiate it from hypertrichosis. Hypertrichosis is characterized by an abnormal proliferation of hair growth that is extensive and not associated with high testosterone levels (Xu, Liu, & Senna, 2017). Participants in our research had an average age of 18.30±5.83 years, ranging from 18 to 30 years. This observation is consistent with earlier research regarding hirsutism. Malik et al. established a mean age of 23±5 years (range: 16-35 years) in their study done in Lahore, Pakistan. The average age of patients was 25.84 years, with a standard deviation of 8.30 years, and the age range extended from 13 to 47 years, in line with studies carried out in India by Sharma *et al.* study conducted in India by Chabbra *et al* indicated that the average age of the participants was 24.18±5.61 years. Moran et al. reported in their Mexico-based study that the average age of the participants was 25.5 years, with a range of 13 to 38 years. In contrast, the average age of hirsute women in Saudi Arabia was found to be 24.5±6.6 years (Carmina *et al.*, 2017). The study's common clinical findings indicated that a majority of patients experienced irregular menstrual cycles, with dyslipidaemia observed in more than half of the women. The majority of patients experienced weight gain, with half classified as either class-I or class-II obesity, and a significant correlation between hirsutism and BMI was observed. Hirsutism was observed more frequently in patients with elevated BMI. A study conducted in Saudi Arabia reported similar findings of 51% (Ansari, Syed, Riaz, Askari, & Anjum, 2024).

Conclusion

Hirsutism is prevalent in Pakistan. The primary contributors to hirsutism are PCOS and idiopathic hirsutism. Various factors, including ethnic, cultural, societal, and personal considerations, deter some people with hirsutism from pursuing diagnosis and therapy. Additional extensive research are required to determine the actual frequency and etiological characteristics of individuals with hirsutism.The causes of hirsutism include polycystic ovaries, idiopathic factors, thyroid


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dysfunction, congenital adrenal hyperplasia, and hyperprolactinemia, with polycystic ovaries identified as the most prevalent cause in the studied population.

Recommendation

Patients with hirsutism should undergo a comprehensive evaluation for underlying potentially curable etiologies prior to the commencement of treatment.

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