ORIGINAL ARTICLE

Frequency of Hyperandrogenism in Females with Polycystic Ovary Syndrome

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ABSTRACT

Objective: To find the frequency of Hyperandrogenism and Hirsutism in females with Polycystic Ovary Syndrome.

Study Design: Descriptive Case Series.

Place and Duration of Study: Department of Gynaecology and Obstetrics Nishtar Hospital Multan from 21th October 2016 to 9th April 2017.

Materials and Methods: Eighty polycystic ovary syndrome patients with in reproductive age group (15 – 49 years)[18] were included in the study through non probability consecutive sampling technique. Hirsutism was examined by FG scoring system and the assessment of Hyperandrogenism was by measurement of serum testosterone levels. SPSS 23.2 was used for data analysis. Frequency and percentage was calculated for categorical variables like Hirsutism, Hyperandrogenism mean and standard deviation was calculated for quantitative variables like age, BMI, Height , weight, serum levels of FSH, LH, And testosterone. T test was applied to check the statistical significance. Effect modifiers and confounders like age, height, weight and BMI were controlled by stratification of data. Post stratification CHI square test was used to check effect modification. P value < 0.05 was taken as significant.

Results: Among total 80 patients, the mean age of the patients was 28.93±8.24 years. Only one (0.5%) patient in our study group had normal weight, 21 (27.4%) women were overweight and remaining 58 (72.1%) patients were obese. The mean FSH, LH and testosterone levels were 6.62±5.3 IU/L, 14.01±7.65 IU/L and 65.13±23.75 ng/dl respectively. Total of 34 (43.7%) patients had Hyperandrogenism. A total of 59.5% (n=48) patients had Hirsutism (FG score >8). Among 34 patients with Hyperandrogenism, 57.8% (n=20) had Hirsutism and out of 46 patients without Hyperandrogenism 60.7% (n=28) had Hirsutism; this difference was not statistically significant; p=0.685.

Conclusion: The observations of our study concluded that a significant numbers of patients with PCOS had Hyperandrogenism and there was no difference in the number of patients with Hirsutism between hyper androgenic and non-hyper androgenic PCOS patients.

Key Words: *Ferriman Gallweyscoring, Hirsutism, Hyperandrogenism, Polycystic Ovary Syndrome.*

Introduction

Polycystic ovary syndrome (PCOS) is considered to be the one of the commonest endocrine impairment with unknown etiology in women of different reproductive ages. The condition was also explained by Stein and Leventhal in 1935.[1] The new criteria for defining PCOS is referred as ROTTERDAM criteria, which was given immediately after joint consensus between ESHRE and ASRM (European Society for Human Reproduction and Embryology and American Society for Human Reproduction) in Rotterdam in 2003.[1] Two out of following three criteria must be fulfilled for PCOS definition; Anovulation or Oligo, Hyperandrogenism (clinical or biochemical elevation of testosterone), and Polycystic ovaries assessment especially by using ultrasound (ovarian volume >10ml).[2]

Clinical sign and symptoms of PCOS include irregular menstrual cycle, obesity, Hirsutism and sub fertility or infertility.[3] Out of these clinical manifestations, Hirsutism appearance is observed obviously with Hyperandrogenism and metabolic abnormalities of PCOS. The dominating percentage of Hirsutism in females with polycystic ovary syndrome is 73.9%. But

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another study shows frequency of Hyperandrogenism in PCOS is 38%.[4]

Abnormal growth of terminal hair especially androgen dependent pattern, is seen in females that are suffering from Hirsutism.[5] The involving sites are chest, face, lower abdomen, crural areas and areola.[1] In some of the severe cases lower back, shoulder, upper arm and upper abdomen are also involved in abnormal hair growth. It is very common disorder that has a bad affect on 5-15% females of reproductive life. In 1961 Ferriman-Gallwey (FG) scoring system was given to diagnose this Hirsutism ratio in female population.[6] In conditions like, congenital adrenal hyperplasia, androgen secreting tumors and Cushing syndrome, there is always a direct relationship and association present between serum level of testosterone and Hirsutism.[7] However no sure and definite association has yet been found between serum testosterone level and Hirsutism in PCOS.[8] In such type of cases alpha reductase activity, heritability, socioeconomic, dietary and environmental features are considered to be responsible for Hirsutism.[9]

The frequency ratio of PCOS patients with Hyperandrogenism and Hirsutism have not been studied locally. The aim of this study is to calculate frequency of Hyperandrogenism and association of Hirsutism with Hyperandrogenism in females especially with PCOS. Our study will provide local reference for future research and management guidelines for patients of PCOs and Hyperandrogenism with Hirsutism.

Materials and Methods

With the ethical approval from the ethical committee of the institution this descriptive case series was conducted. The study was conducted over six months from 21th October 2016 to 9th April 2017. Sample size was calculated with WHO sample size calculator using following data level of significance = 5%, Confidence level = 95%, Sample size n = 80 patients. Patients were included using Non probability consecutive sampling technique. Other causes of Hirsutism, Congenital adrenal hyperplasia, Cushing's syndrome, Hyperprolactinemia, Androgen secreting tumors were excluded from study.

A specially designed Performa that had a complete demography of the patient to record all finding points of this study. Eighty cases of polycystic ovary syndrome who had met the inclusion criteria of our study were selected, who were also going for proper examination to the Department of Obstetrics & Gynecology, Nishtar Hospital Multan.

Informed consent was taken from all the patients one by one. The complete history and thorough clinical examination was conducted for assessment of different features of PCOS and to easily exclude other causes of Hirsutism. Biochemical work was done to record FSH, LH and serum testosterone level on the second day of regular menstrual cycle as well as on any day when the irregular menstrual cycle take place. Normal values of levels of all these hormones were also present on Performa report on which biochemical work was recorded. Assessment of Abdominopelvic ultrasound for polycystic ovary was done by ovarian volume >10ml and was used to rule out any tumor of ovary and adrenal gland. The patients who were fulfilling specific inclusion criteria of Hirsutism and PCOS were examined by FG scoring system. If total core was >8 then it was considered as diagnosis of Hirsutism.

Data was analyzed by SPSS version 23.2. Frequency and percentage was calculated for categorical variables like Hirsutism and hyperandrogenism, mean and standard deviation was calculated for quantitative variables like age, BMI, Height, weight, serum levels of FSH, LH, and testosterone, T test was applied to check the statistical significance. Effect modifiers and confounders like age, height, weight and BMI were controlled by stratification of data and post stratification CHI square test was use to check effect modification. P value < 0.05 was taken as significant.

Results

A total number of 80 female patients were included in this study. Only one (0.5%) patient in our study group had normal weight, 21 (27.4%) women were overweight and remaining 58 (72.1%) patients were obese. The mean age, BMI, height and weight of patients were 28.93±8.24 years, 32.44±4.25 BMI, 157.3 ±6.6 cm and 79.98±8.43 kg (Table I). The mean serum FSH, LH and testosterone level of patients were6.62±5.31 IU/L, 14.01±7.65 IU/L and65.13±23.75 ng/dl respectively (Table II).

The main outcome variables of this study were Hyperandrogenism and Hirsutism. Among all patients of PCOs 44% were found with

Hyperandrogenism and 56% had normal levels (Fig. 1). Total of 59.5% (n=48) patients had Hirsutism. Among 34 patients with Hyperandrogenism, 57.8% (n=20) had Hirsutism and out of 46 patients without Hyperandrogenism 60.7% (n= 28) had Hirsutism; this difference was not statistically significant; p=0.685(Table III). Hence there was no difference in the number of patients with Hirsutism between hyper androgenic and non-hyper androgenic PCOS patients.

When the patients were categorized into different age, BMI, height and weight categories, it was noted that majority of patients i.e. 56.25% (n=45) were falling in the age group 36-49 years and 43.75% (n=35) were aged from 15-35 years. 42.6 %(n=34) patients have BMI ranging from 36-40, 36.28% (n=29) patient have BMI from 25-35 and 21.26% (n=17) having BMI from 41-49. Similarly, 48.76 % (n=39) patients have height range from 140-150c, 31.27% (n= 25) patients have height range from 163-173cm and 2.05% (n=16) patients have height range from 151-162 cm. 68.78% (n=55) have weight ranging from 60-90 kg and 31.27% (n=25) have weight ranging from 91-120 kg (Table I).

Table I: Demographics Parameters of Patients

Characteristics (n=190)	Frequency	Percentage (%)
Gender		
Female	80	100.0
Total	80	100.0
Stratified Age		
15-35 years	35	43.75
36-49 years	45	56.25
Total	80	100.0
Stratified BMI		
25-35	29	36.28
36-40	34	42.6
41-49	17	21.26
Stratified Height		
140-150 cm	39	48.76
151-162 cm	16	2.05
163-173 cm	25	31.27
Stratified Weight		
60-90kg	55	68.78
91-120kg	25	31.27
Descriptive Statistics		
Age in years	28.93	8.24
BMI	32.44	4.25
Height in cm	157.3	6.6
Weight in kg	79.98	8.43

Table II: Distribution of Serum Level of Different Hormones in study Patients

Serum Hormones	Mean ±S.D	P-value
FSH	6.62±5.3IU/L	0.000
LH	14.01±7.65IU/L	0.000
Testosterone	65.13±23.75IU/L	0.000

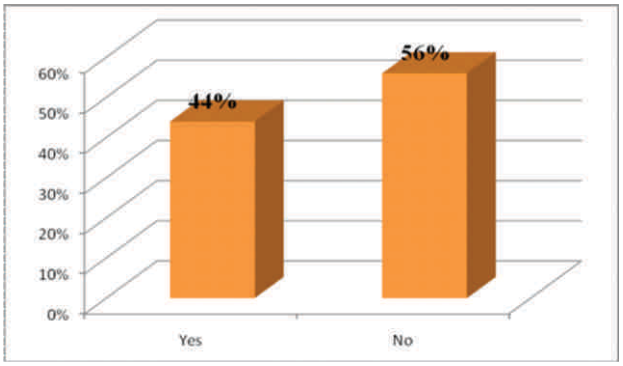

Fig 1: Hyperandrogenism *in Study Group*

Table III: Comparison of Hirsutism and Hyperandrogenism

Characteristics	Hirsutism		Total	P-value
	Yes	No		
Hyperandrogenism	57.8% (n=20)	42.1% (n=14)	43.6% (n=34)	0.685
Non Hyperandrogenism	60.7% (n=28)	39.2% (n=18)	56.3 (n=46)	
Total	60% (n=48)	40% (n=32)	100% (n=80)	

Discussion

Total and free circulating dehydroepiandrosterone sulfate (DHEAS) and testosterone levels are mostly above from normal in 50–75% women who are suffering from PCOS, the free testosterone (FT) circulating in blood is considered as the one of the very important predictive marker of PCOS in 60% PCOS patients[10] who were with increased level.In this study, we have proposed to know the, free testosterone (FT), DHEAS, and prevalence of elevated testosterone in free and combined form as well, in the large cohort of patients suffering from PCOS. By using of this information, we will be able to examine and calculate the utility of nonspecific standards in the evaluation of hyperandrogenemia especially present in PCOS and sensitivity of elevated serum hormone. From this evidence we can conclude that the Hyperandrogenism is remained as very important part of PCOS and Rotterdam criteria

includes this in major symptoms of PCOS.[11] In one of the very common endocrine disorder, nearly 7% women in their reproductive age are affected by the excess amount of androgen.

By the exclusion of specific endocrine disorder of excess androgen .i.e. non-classic adrenal hyperplasia (NCAH). Androgen-secreting neoplasm and hyper androgenic insulin- resistant acanthuses Nigerians syndrome, PCOS is mostly diagnosed in majority of females who were suffering from hyperandrogenism.[3]

By the exclusion, we have got a result that PCOS is one of those problems about which it is very difficult to enlist some standards. Both the biochemical as well as clinical manifestation of Hyperandrogenism had been observed in women suffering from PCOS.[12] One of the important clinical Evidences of Hyperandrogenism is male-pattern hair loss, Hirsutism and acne but in this study we have just explained only one manifestation that is Hirsutism of Hyperandrogenism. The elevated and accurate signs of clinical Hyperandrogenism and Hirsutism might be subjected to individual observer biases[3]. The diagnosis of PCOS could be more difficult within the ethnic variability.[13]

However, contrary to the past trends and methods to make some suitable standards for diagnosing the PCOS, in present time the hyperandrogenemia and elevated hormone levels are considered to be the standards to diagnosis the PCOS the hormonal evaluation of PCOS.[14] Most of the Past studies had normative standards based mostly on small sample size of control patients.[15]

The previous studies show Hirsutism scores and level of androgen, but these studies are unable to demonstrate the relation between severity of Hyperandrogenism and clinical Hirsutism. Coskun et al. reported that elevated hirsutism and level of androgen in the patients and control subjects from the Mediterranean region of Turkey, suggesting these people of this region mostly have much hair on body with high density. But their study is unable to find out the relationship between Hirsutism score and androgen level.

Demir et al conducted a study to find the severity of Hirsutism in the patients suffering from PCOS and its relationship with total testosterone (TT) serum levels in 87 patients suffering from polycystic ovary syndrome (PCOS) and 85 healthy were in control group belonging from the south-eastern region of Turkey. This shows that Hirsutism incidence was lower in hyper androgenic PCOS patients comparative to nonhyperandrogenic PCOS patients. Opposite to it another study designed in Europe indicates the direct correlation between Hirsutism and Hyperandrogenism in the females suffering from PCOS. However the present day study does not show any significant relationship between Hyperandrogenism and Hirsutism in females suffering from PCOS.

In our study the mean age of group was 28.93±8.24 years but in the study by Demir et al the mean age was younger i.e. 25.0 ±4.4 years. It indicates that in our study the late presentation of females suffering with PCOS may be due to difference in socioeconomic and environmental factors of both areas...72.1% women were obese with BMI > 30and 27.4 % women were overweight in our study, however in the study by Demir et al 19.5 % women were obese and 16.1% women were overweight. Similar to our study however opposite to Demir et al, in 2004 in united states another study was launched, in which 60% women suffering from PCOS were obese, at that time in common adult population about double the rate was observed.

According to the study by Demir et al the mean testosterone level was 69.5±23ng/dl but in our study the mean testosterone level was 65.13±23.75 ng/dl. A meta-analysis has been done on 3464 patients suffering from PCOS and 37% of patients have been found with elevation of serum TT level, comparing it with a previous study by Turkey in which 62% of patients had elevated serum TT level. In recent study 43.7% patients show Hyperandrogenism. It is different from Turkey study but similar to a meta-analysis. It might be possible that the socioeconomic factors as well as the ethnic heterogeneity of people suffering from Hirsutism have different levels of serum total testosterone. The very important key to find PCOS is Hyperandrogenism and it also help to determine the severity of PCOS as well as.

Among women suffering from PCOS the incidence of Hirsutism is different in different woman and it shows to depend upon two factors that is the degree of distribution of hairs on body and each woman's sensitivity to the pattern of body hair.[17] The

evaluation of Hirsutism scores and androgen level has been done by many previous studies; however a relationship between the severity of Hyperandrogenism and clinical Hirsutism has not been explained clearly. DeUgarte et al. concluded that most of the time the diagnosis of Hirsutism depends on the perception as well as mentality of patient instead of total mFG score of patients. Different studies provide different incidence of Hirsutism in patients suffering from PCOS.Some population groups have been evaluated in which rates ranging from nearly 17% and 100%. An incidence of Hirsutism of 87% has been observed by the Turkish study using the FG scoring system, forcing the authors to report that large amount of body hair is the hallmark of women living in the Mediterranean region. The present study indicates that FG scores of ≥ 8 were present in the 60% of 190 PCOS Patients. This is lesser than Coskun et al., who studied a same ethnic population with comparing social and geographical characters and might be correlated to the ethnic. Hirsutism was present almost in 15% of control group in the study from Demir et al, which is very contrasting and different to past reported rates of 4.6 – 10% in the general population. The increased rate of Hirsutism in the common population of the Demir study is according to past studies explaining much higher body density of body hair in the Mediterranean region and Asia as well.[18]

All the local studies based on local population are deficient of suitable knowledge and data. Therefore due to lack of proper statistical data regarding this in all local studies, we are unable to find the exact magnitude of PCOS present in our country. There are some barriers in our study like a single hospital is not enough for the representation of whole population and limited subjects are available. We need large multicentre case control trials to estimate Hyperandrogenism and its relationship with Hirsutism in females suffering from PCOS. To understand this important thing of association between severity of Hirsutism and serum level of testosterone must be studied.

Conclusion

The observations of our study conclude that a significant numbers of patients with PCOS had Hyperandrogenism and there was no difference in the number of patients with Hirsutism between hyper androgenic and non-hyper androgenic PCOS patients.

REFERENCES

1. Goodman NF, Cobin RH, Futterweit W, Glueck JS, Legro RS, Carmina E. American Association of Clinical Endocrinologists, American College of Endocrinology, and Androgen Excess and PCOS Society disease state clinical review: guide to the best practices in the evaluation and treatment of polycystic ovary syndrome-part 1. Endo Pract. 2015;21(11):1291- 300.
2. Pasquali R, Zanotti L, Fanelli F, Mezzullo M, Fazzini A, Morselli Labate AM et al. Defining hyperandrogenism in women with polycystic ovary syndrome: a challenging perspective. J Clin Endo & Metabol. 20161;101(5):2013-22.
3. Goodman NF, Cobin RH, Futterweit W, Glueck JS, Legro RS, Carmina E. American Association of Clinical Endocrinologists, American College of Endocrinology, and Androgen Excess and PCOS Society disease state clinical review: guide to the best practices in the evaluation and treatment of polycystic ovary syndrome-part 2. Endo Pract. 2015;21(12):1415-26.
4. Legro RS, Arslanian SA, Ehrmann DA, Hoeger KM, Murad MH, Pasquali R et al. Diagnosis and treatment of polycystic ovary syndrome: an Endocrine Society clinical practice guideline.J Clin Endo & Metabol. 20131;98(12):4565-92.
5. Menon M, Ramachandran V. Antithyroid peroxidase antibodies in women with polycystic ovary syndrome. J Obstet and Gynecol India. 20171;67(1):61-5.
6. Palomba S, De Wilde MA, Falbo A, Koster MP, La Sala GB, Fauser BC. Pregnancy complications in women with polycystic ovary syndrome. Hum repro update. 201527;21(5):575-92.
7. Foroozanfard F, Talebi M, Samimi M, Mehrabi S, Badehnoosh B, Jamilian M et al. Effect of two different doses of vitamin D supplementation on metabolic profiles of insulin-resistant patients with polycystic ovary syndrome: a randomized, double-blind, placebo-controlled trial. Horm and Metabol Rese 2017;49(08):612-7.
8. Caldwell AS, Middleton LJ, Jimenez M, Desai R, McMahon AC, Allan CM et al. Characterization of reproductive, metabolic, and endocrine features of polycystic ovary syndrome in female hyperandrogenic mouse models. Endocrinol. 20141;155(8):3146-59.
9. Sadrzadeh S, Painter RC, Lambalk CB. Developmental origins of polycystic ovary syndrome (PCOS), a case control study comparing birth weight in women with PCOS and control group. Gynecol Endocrinol.20162;32(10):856-9.
10. Livadas S, Pappas C, Karachalios A, Marinakis E, Tolia N, Drakou M et al. Prevalence and impact of hyperandrogenemia in 1,218 women with polycystic ovary syndrome. Endo.2014;47(2):631-8.
11. Conway G, Dewailly D, Diamanti-Kandarakis E. The polycystic ovary syndrome. A position statement from the European Society of Endocrinology. Repro Endocrinol. 2015;25:32-52..
12. Pinola P, Puukka K, Piltonen TT, Puurunen J, Vanky E, Sundström-Poromaa I et al. Normo-and hyperandrogenic

women with polycystic ovary syndrome exhibit an adverse metabolic profile through life. Fertil and steril. 2017; 107(3): 788-95.

13. Moran C, Arriaga M, Arechavaleta-Velasco F, Moran S. Adrenal androgen excess and body mass index in polycystic ovary syndrome. J Clin Endocrinol & Metabol. 2015; 100(3): 942-50.
14. Ezeh U, Yildiz BO, Azziz R. Referral bias in defining the phenotype and prevalence of obesity in polycystic ovary syndrome.J Clin Endocrinol & Metabol.2013;98(6):1088-96.
15. Joham AE, Teede HJ, Ranasinha S, Zoungas S, Boyle J. Prevalence of infertility and use of fertility treatment in women with polycystic ovary syndrome: data from a large community-based cohort study. J women's health. 2015;24(4):299-307.
16. Porcaro G, Bizzarri M, Monastra G, Filati P, Unfer V. Strategies for the treatment of polycystic ovary syndrome (PCOS) women: the role of myoinositol (MI) and d-chiro-inositol (DCI) between diet and therapy. Polycystic ovary syndrome (PCOS): clinical aspects, potential complications and dietary management. Hauppauge, NY: Nova science publishers. 2016.
17. Clark NM, Podolski AJ, Brooks ED, Chizen DR, Pierson RA, Lehotay DC et al. Prevalence of polycystic ovary syndrome phenotypes using updated criteria for polycystic ovarian morphology: an assessment of over 100 consecutive women self-reporting features of polycystic ovary syndrome. Repro Sci.2014;21(8):1034-43.
18. Kelley CE, Brown AJ, Diehl AM, Setji TL. Review of nonalcoholic fatty liver disease in women with polycystic ovary syndrome. World J Gastroenterol. 2014; 20(39): 14172.