ISSN: 2347-1956

Annals of
Pharma Research

Volume 10 Issue 3 (2022) pp.695-704

Open Access

Research Article

BMI, PCOS and Relationship of Androgen Excess in Indian Ethnic Group of Patients

Dr. Roya Rozati MD[1], Dr. Mohd Ashraf Ganie[2], Dr. Imtiyaz Wani[3] Dr. Humaira Minhaj [4] Wajeeda Tabasum M. Sc[4], Taalia Nazeer Ahmed[4], Dr. Mohammed Sarosh Ahmed[5] , Ayapati Mehdi Gautam[4] and Dr. Vikram Aiman Ayapati[4]

[1]MD (A.I.I.M.S, Delhi), F.R.C.O.G. (London), Medical & Research Director, Maternal Health and Research Trust (MHRT), Banjara Hills, Hyderabad-34,India
[2]Professor Department of Endocrinology SKIMS, Srinagar
[3]Scientist B SKIMS, Srinagar
[4]Research Scholar, Maternal Health and Research Trust (MHRT), Banjara Hills, Hyderabad, India
[5]Assistant Professor,Department of Community Medicine,Deccan College of Medical Sciences,Kanchanbagh,Hyderabad, Telangana- 500058

Abstract

Background: Polycystic ovary syndrome (PCOS) is the most common endocrine condition in reproductive-age women. By comprising reproductive, endocrine, metabolic and psychological features—the cause of PCOS is still unknown. As of now, there is no cure, and management which is persistently suboptimal as it depends on the ad hoc management of symptoms only. Various Research Studies have recently revealed that androgens have an important role in regulating female fertility. Biochemical or clinical profile of hyperandrogenism is important elements of polycystic ovary syndrome (PCOS). Androgen excess is a defining feature of polycystic ovary syndrome (PCOS), which affects 10% of women and represents a lifelong metabolic disorder, with increased risk of type 2 diabetes, hypertension, Insulin resistance and cardiovascular events. In women, the increases in androgens are associated with increases in inflammatory cytokines, and reducing androgens reduces inflammation. The aim of this study was to investigate the complex symptoms of Androgen Excess and the correlations in patients with PCOS from an outpatient reproductive medicine clinic in South India. **Methods and Findings:** We conducted a case control study of 140 PCOS patients and 558 controls to evaluate the Anthropometric measurements were recorded, differences in body mass index (BMI), total testosterone (TT), modified Ferriman–Gallwey hirsutism score, sex hormone binding globulin (SHBG), and free androgen index (FAI) between PCOS patients and controls. **Results:** DHEAS was significantly higher in the PCOS ($p < 0.01$) compared to controls. All androgen parameters were significantly lower and sex hormone binding globulin (SHBG) significantly lower in PCOS ($p < 0.01$) compared to controls. A combination of SHBG, clinical and biochemical hyperandrogenism and menstrual irregularities may be considered as diagnostic markers of PCOS in adolescents and for the identification of a 'risk group' for developing PCOS.Androgen excess plays a prominent role in the development of metabolic disturbances associated with PCOS, with a discernible impact.

Key words: Androgen Excess, PCOS, body mass index (BMI), sex hormone binding globulin (SHBG).

INTRODUCTION

Polycystic ovary syndrome (PCOS) is the most common endocrine disorder in women of reproductive age, it is common cause of chronic ovulatory dysfunction and hyperandrogenism in adolescents with potentially significant lifelong consequences (Witchel, S.F. *et al*., 2015; Carmina, E. *et al*., 2006). It affects 6%–21% of women globally.

(Bozdag, G. *et al*., 2016; Lizneva, D. *et al*., 2016).The clinical manifestations of PCOS are characterised by highly heterogeneous, as PCOS affects multiple aspects of women's overall health and is associated with reproductive, metabolic and psychological dysfunctions like hyperandrogenism (clinical or biochemical), ovarian dysfunction (menstrual irregularities), and polycystic ovarian morphology (Teede, H. *et al*., 2010; Dokras, A. *et al*., 2017). Disturbed hormonal and reproductive features include luteinizing hormone (LH) excess, hyperandrogenism, ovulatory perturbations, aberrant follicular de-

Corresponding Author
Dr. Roya Rozati MD;

DOI- https://doi.org/10.21746/apr.2022.10.3.3

velopment, diminished fertility, and an increased risk of miscarriage(Dumesic, D.A. *et al*., 2015).

Sex steroids are crucial regulators of reproductive function. The insulin resistance (IR) and compensatory hyperinsulinemia are central etiological abnormalities in women with PCOS, which are responsible for the overproduction of ovarian and adrenal androgens and decreased sex hormone-binding globulin (SHBG) concentration [Le, T.N. *et al*., 2012; Ding, E.L. *et al*., 2009], which in turn leads to an increase in androgen bioavailability.

Excess androgen is a main clinical hallmark in PCOS patients, which might be caused by other conditions such as obesity and insulin resistance, which commonly manifest with PCOS. Androgens, thought to be male sex steroids, play important roles in female reproduction, both in healthy and pathological states. It helps in regulating dynamic changes in ovarian steroidogenesis that are critical for normal cycling. Androgen effects on follicle development in women with diminished ovarian reserve. Androgen excess leads to disordered follicle development and anovulatory infertility.

Androgen Excess in patients with PCOS, suggests having the pathologic role in the development and progression of PCOS. The incidence rate of Androgen Excess is as high as 60%-80% (Sirmans, S.M. *et al*., 2014) which leads to ovulation disorder, menstrual disorder, hirsutism and acne, suggesting that hyperandrogenism is not only a clinical characteristic of PCOS, but also an important risk factor. Hirsutism affects 5–10% of reproductive-aged female (Liu, K. *et al*., 2017) and acne affects 90% of adolescents (Olutunmbi, Y. *et al*., 2008) Excess androgen appears to be both a cause and a consequence of PCOS in a vicious cycle.

SHBG acts as a transport carrier that binds estrogen and androgens and regulates their biological activity, is usually used as an indicator of Androgen Excess in women with PCOS.

The incidence of obesity in women with PCOS is 50–70% [Diamanti-Kandarakis, E. *et al*., 2009]. Treatment of women who have PCOS and elevated androgen levels with metformin to improve insulin resistance, exhibit a reduction in testosterone levels (Sahin, Y. *et al*., 2007).
The insulin resistance was responsible for the increase in androgens in women with PCOS rather than androgen mediated the insulin resistance.

PCOS also has a significant metabolic component as it is linked with obesity, metabolic syndrome, hyperinsulinemia, insulin resistance, hepatic steatosis and dyslipidemia, which amplify the risk of type-2 diabetes and cardiovascular disease (Joham, A.E. *et al*., 2016; Doherty, D.A. *et al*., 2015).

Around 80% of people with PCOS have BMIs that are above average or high, and they have symptoms like hyperandrogenism, polycystic ovaries, and infertility. These people are frequently undiagnosed until they have reproduction issues as adults. PCOS affects a small but significant percentage of women who have a normal or low BMI and may or may not have symptoms like irregular menstrual periods and acne. Weight maintenance, insulin sensitizers like metformin to restore ovulation, treatment of symptoms like hirsutism, acne, and menstrual dysfunction, and assisted reproductive technologies in refractory instances were all performed, with promising outcomes. (Toosy, S. *et al*., 2018)

It is critical for women with PCOS to consume a diverse range of nutrients, minerals, and vitamins in their diet; as a result, they must ensure that their diet includes lots of vegetables and fruit. Furthermore, PCOS patients do not need to restrict their caloric intake because they do not need to lose weight. (Goyal, M. *et al*., 2017)
The aim of this study was to compare different androgen parameters of testosterone, DHEAS, SHBG, Hirsutism, and Acne in PCOS in comparison to control subjects

MATERIALS AND METHODOLOGY

This is a multi-centric, multi-institutional, and multi-specialty study including ten centres spread across the country's six zones (North, South, East, North-East, West, and Central) with a shared complete predesigned protocol carried out from 2018-2022. It is a National, Task Force, RCT Project, sanctioned by the Government of India, Indian Council of Medical Re-

search. This paper contains the findings of a study conducted by the Medical Health and Research Institute in Hyderabad, Telangana, India, on people from the Telangana region in South India.

Members of the investigator team came from the specialties/departments of endocrinology, obstetrics and gynaecology, community medicine, biochemistry/lab medicine/paediatrics, or any other relevant department based on the investigators' experience and interest in the field of PCOS. The research was carried out in accordance with the 1975 Helsinki Declaration and was approved by the Institute's Ethics Committee (IEC). The coordinating centre (Sher-I-Kashmir Institute of Medical Sciences (SKIMS), Srinagar, India) created a shared predesigned protocol, standardized tools, and standard operating procedures (SOPs) for this prospective and cross-sectional study.

Study Design

On the basis of logistics and convenience, community resident females aged 18-40 years were recruited from both rural and urban areas near the institutions. The electoral roll was obtained, and 8 polling stations in urban areas and 10 in rural areas were chosen to meet the required targeted number of subjects. Women between the ages of 18 and 40 were invited to participate based on their unique voter ID.A pre-designed short screening questionnaire was used for the screening. The screening questionnaire was based on a few symptoms related to the main features of PCOS, such as menstrual history, self-hirsutism scoring, weight gain, acne, and some important risk factors, and it was administered by a trained healthcare professional, and the results were re-confirmed after an interview process to screen for possible cases of PCOS. Medical history of patients and controls was obtained and physical examination was performed .The questionnaire consisted of 21 questions divided into three domains: A. Personal data; B. Anthropometric measurements including weight, height and waist circumference (WC) were recorded; C. PCOS-related inquiries. There were 13 questions in domain C about hyperandrogenism, menstruation, and insulin resistance. Following the completion of the questionnaire, the women were invited to the institution for a comprehensive clinical, biochemical, hormonal evaluation and USG during the follicular phase of their cycle (2nd to 7th Day).

Sample Size

A total of 1000 women between the ages of 18 and 40 were screened. According to the questionnaire, 698 participants were eligible for the study based on the inclusion criteria, with 364 from urban regions represented by 8 polling booths and 334 from rural communities represented by 10 polling booths (Figure 1).

Methods

Clinical evaluation (anthropometry-Body mass index (BMI) was calculated by the formula: (weight in kg)/ (height in m2)., Clinical hyperandrogenism was assessed by the presence of acne and/or hirsutism (modified Ferriman–Gallwey score>8) oligomenorrhea, androgenic alopecia, primary infertility), biochemical evaluation (blood biochemistry, OGTT), and hormonal estimations (T4, TSH, PRL, LH, FSH, total testosterone, SHBG, DHEAS, 17-OHP) were performed on all enrolled women using CLIA/ECLIA. ECLIA examined SHBG and serum total testosterone levels, among other things. The qualifying criteria was based on the NIH consensus conference criteria from 1990. The presence of the following two requirements is required for this: oligo-and/or anovulation (intermenstrual interval 35 days and/or presence of 8 cycles per year); clinical signs of and/or biochemical evidence of hyperandrogenism after ruling out disorders with similar clinical presentation such as hyperprolactinemia, Cushing's syndrome, congenital adrenal hyperplasia, and androgen secreting tumours (cortisol, 17OHP and DHEAS). The Rotterdam 2003 criteria were compared to the AE-PCOS 2009 standards. Two of the following three requirements are required under the Rotterdam 2003 criteria: i) Oligo-and/or anovulation; ii) Clinical indications of hyperandrogenism and/or biochemical evidence iii) ultrasonography of a polycystic ovary.

The existence of the following characteristics is required by the AE-PCOS 2009 standards: i) Polycystic ovary and/or oligo-and/or anovulation (intermenstrual interval 35 days and/or existence of 8 cycles per year) in ultrasonography. (ii) Clinical indications of hyperandrogenism

and/or biochemical proof.

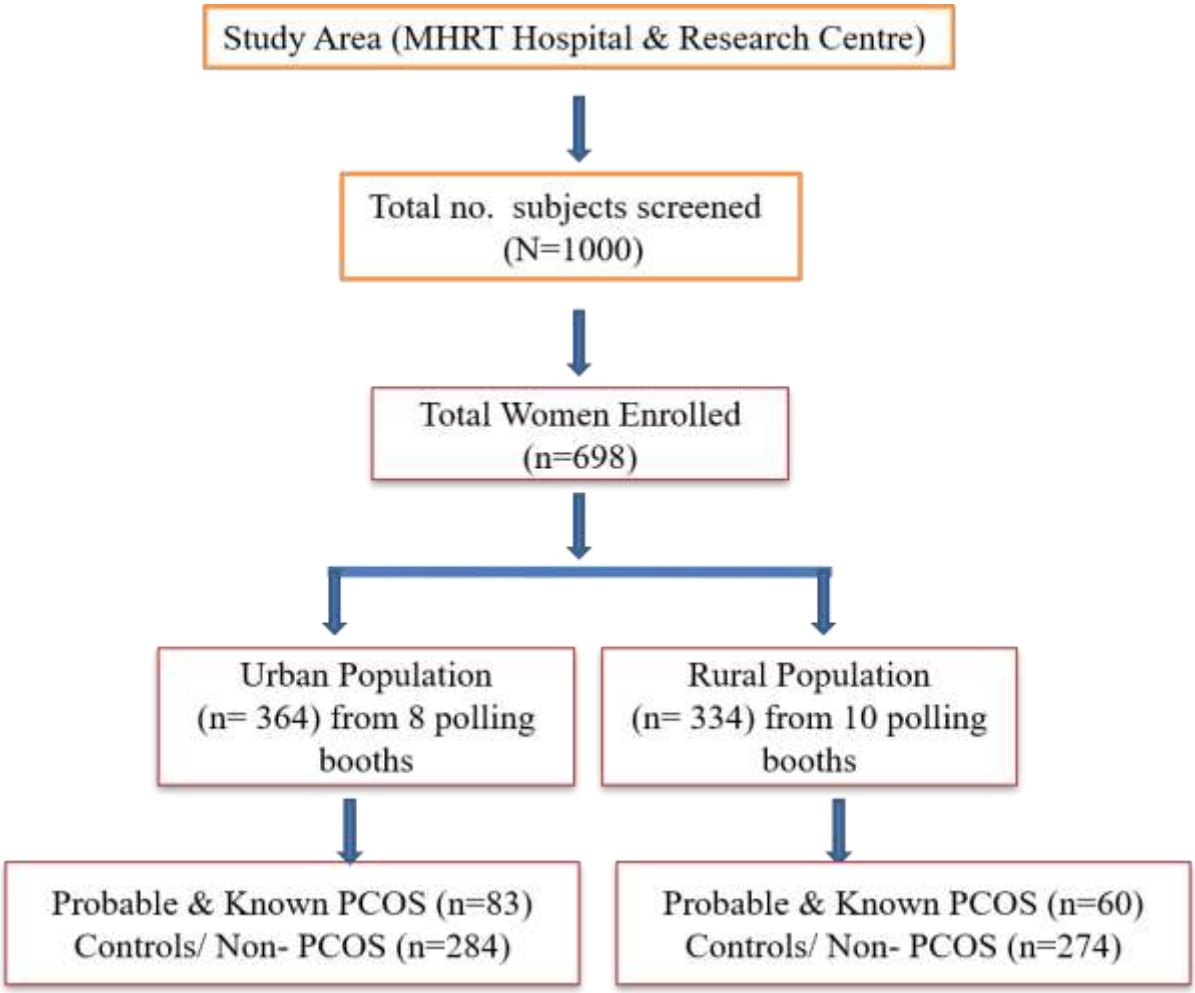

Figure 1: Study Design conducted in Telangana region of Southern India at MHRT Hospital and Research Centre

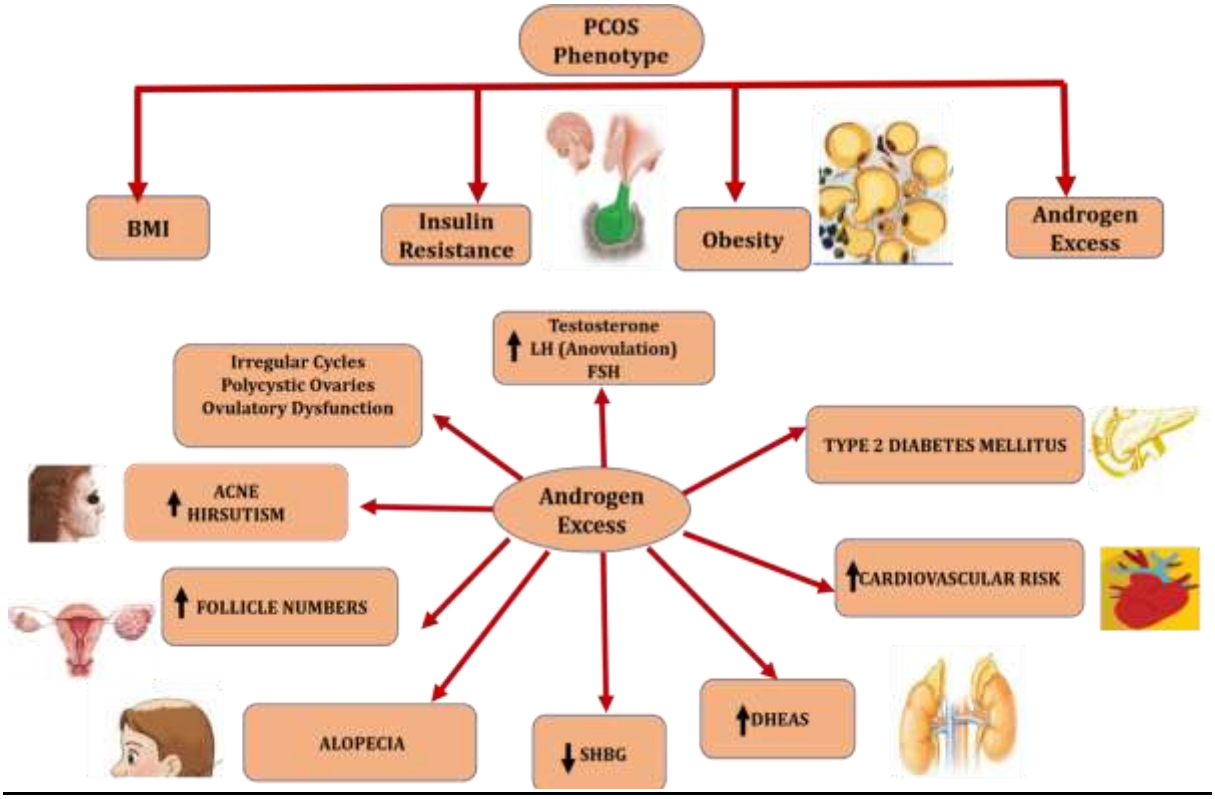

Figure 2: Factors contributing for PCOS phenotype and the impact of androgen excess.

Inclusion Criteria

Women aged 18-40 years, permanent residents of that area, willing to participate in the study and sign informed consent forms and women who are known to have PCOS were included in the study.

Exclusion Criteria

Pregnant or lactating women and those with cognitive and/or physical limitations that prevented them from answering the questionnaire will be excluded from the study, those with history of drug intake such as steroids, androgens, oral contraceptives, anti-epileptics or drugs known to interfere in glucose or lipid metabolism were excluded from the study.

Anthropometric Measurements

Women who provided written informed consent underwent a detaileda thorough medical history, including menstrual history, height, and waist and hip circumference were recorded for each patient and control woman. The BMI was calculated by dividing weight (kg) by squared height (m), menstrual history, Ferrimen-Gallwey scoring for hirsutism, grading of acanthosis nigricans (I-III), grading of androgenic alopecia (I-V), acne vulgaris (I-III), blood pressure measurement, and a brief relevant systemic examination. Biochemical and hormone measurements were taken at the beginning of the menstrual cycle, from the 2nd to the 7th day in PCOS patients and control women

Laboratory Evaluation

Biochemical tests like blood glucose, OGTT, lipid profile, hs-CRP, liver function, kidney function, and hormonal assays like T4, TSH, LH, FSH, PRL, cortisol, testosterone, DHEAS, 17-OHP, SHBG, AMH, progesterone, insulin, SHBG, testosterone were performed. After a 10- to 12-hour fast, women were contacted and blood counts, CRP, lipids, LFT, KFT, glucose, insulin, basal hormones, and SHBG were taken. After a 75-gram oral glucose challenge, blood was drawn to test glucose and insulin levels. Insulin samples were placed in the refrigerator right away, separated in a cold centrifuge, and kept at -20°C until the test. After a 10- to 12-hour overnight fast, the oral glucose tolerance test (OGTT) was done at 0800 hrs. The metabolic parameters were calculated by the auto analysers at the centre using established biochemi-

cal techniques.

Assays

Fully automated chemistry analysers were used to perform LFT, KFT, Lipids, and other biochemistry, and plasma glucose was quantified using the glucose oxidase-peroxidase method. CLIA/ECLIA was used to calculate serum T4, TSH, Cortisol, P4, PRL, LH, FSH, and plasma insulin using commercial kits. Electrochemiluminescence (Cobas e411, Roche Diagnostics Limited) was used to quantify plasma testosterone, SHBG. The 17-OHP, on the other hand, was measured using RIA. Sensitivity, specificity, interassay, and intra-assay coefficients of variation were all kept within the manufacturer's protocol's specified ranges.

Radiological Examination

The ultrasonography of the abdomen was performed to evaluate the polycystic ovary morphology in the follicular phase of the women.

Statistical Analysis

All data collected using the clinical checklist and SF-12 questionnaire were recorded in an SPSS spreadsheet after coding and carefully defining all the studied variables. Analysis was then performed in two steps. The first step included descriptive analysis wherein patients' clinical condition and various variables were analyzed for the respective frequencies, percentages, and measure of central tendency. In the second step, inferential statistics were used to determine the associations among patient- and therapy-related variables, clinical outcomes, and QOL using Pearson's chi-square test, analysis of variance (ANOVA), and post hoc analysis, with a p-value of <0.05 indicating statistical difference.

RESULTS

All the participants were taken from the urban and Rural areas of Telangana. The demographic characteristics of the participants are presented in Table 1. Baseline parameters of subjects are shown. PCOS groups were compared to the control subject.

There is statistical difference observed in the age, and waist circumference in PCOS and non-PCOS subjects (P<0.001) whereas the BMI was almost normal in both groups. Anthropometric parameters like hirsutism and acne severity were observed more among the PCOS women than controls and the results were significant (P <0.001) and needs to be taken into consideration because of their possible association with medical disorders, their substantial effect on self-esteem and quality of life. Ferriman- Gallwey score was higher in PCOS women in comparison with controls and the difference was quite significant (P<0.001). Number of follicles in right and left ovaries were greater in PCOS women and were compared with non PCOS women it had significant difference among the two (P<0.001) as shown in Table 2 .Although prolactin levels in PCOS cases were higher than non- PCOS subjects, the different was not significant (P=0.6).Significant differences was observed in the levels of FSH and LH/FSH ratio (P<0.001).However, testosterone , LH, sex hormone binding globulin and dehydroepiandrosterone sulphate did not appear to have significant difference among the two groups. While levels of LH and FSH were increased in PCOS women, there was not much difference observed in the levels of LH. Table 3.

Table 1: Socio- demographic details of PCOS and Non- PCOS subjects

S.No	Parameter	PCOS subjects	Non- PCOS subjects	p-value
1	Age	26.62 ± 6.2	29.12 ± 6.06	P <0.001
2	BMI	25.43 ± 3.54	24.11 ± 3.87	P <0.001
3	Waist circumference (cm)	74.26 ± 7.87	72.49 ± 7.63	P = 0.01
4	Hirsutism	0.27 ± 0.45	0	P <0.001
5	Acne Grading	1.43 ± 1.44	0.09 ± 0.34	P <0.001
6	FG Score	7.36 ± 4.07	2.28 ± 1.38	P <0.001

Table 2: Follicle Number in the PCOS and Non- PCOS subjects as per Ultrasound

S.No	Parameter	PCOS subjects	Non- PCOS subjects	p-value
1	Follicle No.(L)	10.81 ± 4.11	5.65 ± 2.13	P <0.001
2	Follicle No.(R)	9.55 ± 3.73	5.47 ± 2.05	P <0.001

Table 3: Hormonal Parameters in the PCOS and Non- PCOS subjects

S.No	Parameter	PCOS subjects	Non- PCOS subjects	p-value
1	Leutinizing Hormone (LH)	13.74 ± 13.64	13.59 ± 13.68	P=0.9
2	Follicle Stimulating Hormone(FSH)	10.02 ± 15.21	6.06 ± 4.41	P <0.001
3	LH/FSH	2.27 ± 3.09	1.36 ± 0.89	P <0.001
4	Total Testosterone	0.28 ± 0.26	0.25 ± 0.19	P=0.3
5	SHBG	64.38 ± 36.76	74.33 ± 42.41	P=0.08
14	DHEAS	145.40 ±84.78	137.33 ± 86.5	P=0.52

Table 3: Hormonal Parameters in the PCOS and Non- PCOS subjects

*SHBG sex hormone binding globulin, DHEAS dehydroepiandrosterone sulphate, LH Luteinizing Hormone, FSH Follicle Stimulating Hormone.

DISCUSSION

Approximately 30% of women with PCOS have hyperandrogenism – a clinical and/or biochemical excess of androgens. Acne and hirsutism are generally considered the primary clinical indicators of androgen excess. Testosterone is the major circulating form of androgen. Obesity significantly affects the circulating concentrations of total testosterone and SHBG. In adult women with hirsutism and PCOS, obesity is associated with increased total testosterone and decreased SHBG, which results in significantly elevated free and bioavailable testosterone. (Kim, M.J. *et al*., 2014)

A combination of SHBG, clinical and biochemical hyperandrogenism and menstrual irregularities may be considered as diagnostic markers of PCOS in adolescents and for identification of an 'increased risk' of PCOS.Androgen Excess represents a chief attribute of PCOS as elevated androgen levels are the most constant feature, with the majority (−60%) of patients (Livadas, S. *et al*., 2014) including testosterone (T) and the pro-androgens androstenedione (A4) and dehydroepiandrosterone sulphate (DHEAS), as well as the enzyme required to convert pro-androgens to bioactive androgens, 3β-hydroxysteroid dehydrogenase (3β-HSD) in serum (Keefe, C.C. *et al*., 2014; Palomba, S. *et al*., 2014).

In this study, we found that PCOS patients with clinical signs of hyperandrogenism tended to have a higher BMI than PCOS patients without signs. However, the differences in serum total testosterone and SHBG were insignificant between PCOS patients with and without the symptom of hyperandrogenism. PCOS patients and normal women seemed to have equal risks of suffering from hyperandrogenism.

SHBG (sex hormone-binding globulin) is a glycoprotein that controls sex steroid hormone bioavailability. Because of its inverse relationship with polycystic ovarian syndrome (PCOS), obesity, insulin resistance, metabolic syndrome, and diabetes type II, interest in SHBG has grown in recent years. Our Study has shown that high serum DHEAS level in women with PCOS was associated with the presence of acne, hirsutism and lower levels of SHBG in patients which is in coordination with the research published.

Low SHBG levels are also common in PCOS co-morbidities such as type 2 diabetes, impaired glucose tolerance, insulin resistance, and obesity. (Rosenfield, R.L. *et al*., 2007). Low serum SHBG levels are considered a biomarker of metabolic abnormalities and are associated with insulin resistance (IR), hyper androgenism, and abnormal glucose and lipid metabolism which is associated with Androgen Excess in PCOS patients(Moran, L.J. *et al*., 2013).Our results have manifested those lower levels of SHBG have been associated in women with PCOS risk.

The production of steroid hormones is shared by the ovaries and adrenal glands. The adrenal glands are the primary producers of dehydroepi-

androsterone (DHEA) and its sulphate ester (DHEA-S) (90 percent of the total circulating amount). Although roughly 40-70 percent of women with PCOS have elevated DHEA-S levels, the specific process that causes the adrenal gland to produce androgens is yet unknown. There hasn't been much research into the relationship between DHEA-S and insulin resistance and glucose metabolism. DHEA-S and ovarian volume have a clear negative relationship, according to observational research. (Christodoulaki, C. *et al*., 2017). Our study has also shown similar results with elevated DHEA-S in PCOS compared to non- PCOS, nevertheless, there was no significant difference observed. Figure 2.

PCOS is divided into two phenotypes: overweight/obese and lean, with the latter being a considerably less prevalent occurrence (Toosy, S. *et al*., 2018). We have observed more or less similar and normal BMI among the PCOS and non- PCOS subjects. Despite a recent consensus advising against its usage, the luteinizing hormone/follicle-stimulating hormone (LH/FSH) ratio is frequently sought to help identify PCOS. The ratio of LH to FSH in healthy women is normally between 1 and 2, but in PCOS women, the ratio gets reversed, and it can reach as high as 2 or 3 in some cases. (Mitrašinović-Brulić, M. *et al*., 2021) We have observed the ratio of LH/FSH significantly elevated in PCOS subjects in comparison with controls. The strengths of this study include well-defined population of subject

Conclusion

The proper balance of androgen activity is necessary to achieve and maintain normal ovarian function throughout the female reproductive lifespan. Both excess and lack of androgens lead to ovarian dysfunction and are associated with the most common causes of infertility in women, increase the risk of metabolic dysfunction in women with PCOS

In conclusion, this study provided evidence that the presence of androgen excess can manifest in many ways by increase in hirsutism and acne and by increased levels in DHEA-S concentrations, may constitute a factor that prevents further deterioration of metabolic profile in women with PCOS. Apart from that the lower levels of serum SHBG levels with metabolic syndrome have been identified as a risk of PCOS in adolescents. These metabolic markers such as DHEAS, SHBG can used for to screen young women for PCOS, in particular in adolescents.

ACKNOWLEDGMENTS

The Task Force study has been sanctioned by the Government of India, Indian Council of Medical Research.

REFERENCES

1. Witchel, S.F., Oberfield, S., Rosenfield, R.L., Codner, E., Bonny, A., Ibáñez, L., Pena, A., Horikawa, R., Gomez-Lobo, V., Joel, D. and Tfayli, H. "The diagnosis of polycystic ovary syndrome during adolescence." *Hormone research in paediatrics* 83.6 (2015): 376-389.
2. Carmina, E., Rosato, F. and Janni, A. "Extensive clinical experience. Relative prevalence of different androgen excess disorders in 950 women referred because of clinical hyperandrogenism." *The Journal of Clinical Endocrinology & Metabolism* 91.1 (2006): 2-6.
3. Bozdag, G., Mumusoglu, S., Zengin, D., Karabulut, E. and Yildiz, B.O. "The prevalence and phenotypic features of polycystic ovary syndrome: a systematic review and meta-analysis." *Human reproduction* 31.12 (2016): 2841-2855.
4. Lizneva, D., Suturina, L., Walker, W., Brakta, S., Gavrilova-Jordan, L. and Azziz, R. "Criteria, prevalence, and phenotypes of polycystic ovary syndrome." *Fertility and sterility* 106.1 (2016): 6-15.
5. Teede, H., Deeks, A. and Moran, L. "Polycystic ovary syndrome: a complex condition with psychological, reproductive and metabolic manifestations that impacts on health across the lifespan." *BMC medicine* 8.1 (2010): 1-10.
6. Dokras, A., Saini, S., Gibson-Helm, M., Schulkin, J., Cooney, L. and Teede, H. "Gaps in knowledge among physicians regarding diagnostic criteria and management of polycystic ovary syndrome." *Fertility and sterility* 107.6 (2017): 1380-1386.
7. Dumesic, D.A., Oberfield, S.E., Stener-Victorin, E., Marshall, J.C., Laven, J.S. and

Legro, R.S. "Scientific statement on the diagnostic criteria, epidemiology, pathophysiology, and molecular genetics of polycystic ovary syndrome." *Endocrine reviews* 36.5 (2015): 487-525.
8. Le, T.N., Nestler, J.E., Strauss III, J.F. and Wickham III, E.P. "Sex hormone-binding globulin and type 2 diabetes mellitus." *Trends in Endocrinology & Metabolism* 23.1 (2012): 32-40.
9. Ding, E.L., Song, Y., Manson, J.E., Hunter, D.J., Lee, C.C., Rifai, N., Buring, J.E., Gaziano, J.M. and Liu, S. "Sex hormone–binding globulin and risk of type 2 diabetes in women and men." *New England Journal of Medicine* 361.12 (2009): 1152-1163.
10. Sirmans, S.M. and Pate, K.A. "Epidemiology, diagnosis, and management of polycystic ovary syndrome." *Clinical epidemiology* 6 (2014): 1.
11. Liu, K., Motan, T. and Claman, P. "No. 350-hirsutism: evaluation and treatment." *Journal of Obstetrics and Gynaecology Canada* 39.11 (2017): 1054-1068.
12. Olutunmbi, Y., Paley, K. and English III, J.C. "Adolescent female acne: etiology and management." *Journal of pediatric and adolescent gynecology* 21.4 (2008): 171-176.
13. Diamanti-Kandarakis, E. and Christakou, C.D. "Insulin resistance in PCOS. *Diagnosis and management of polycystic ovary syndrome* (2009): 35-61.~~(Vol+NO)~~
14. Sahin, Y., Unluhizarci, K., Yilmazsoy, A., Yikilmaz, A., Aygen, E. and Kelestimur, F. "The effects of metformin on metabolic and cardiovascular risk factors in nonobese women with polycystic ovary syndrome." *Clinical endocrinology* 67.6 (2007): 904-908.
15. Joham, A.E., Palomba, S. and Hart, R. "Polycystic ovary syndrome, obesity, and pregnancy." *Seminars in reproductive medicine. Thieme Medical Publishers* 34.2(2016):093-101.
16. Doherty, D.A., Newnham, J.P., Bower, C. and Hart, R. "Implications of polycystic ovary syndrome for pregnancy and for the health of offspring." *Obstetrics & Gynecology* 125.6 (2015): 1397-1406.
17. Toosy, S., Sodi, R. and Pappachan, J.M. "Lean polycystic ovary syndrome (PCOS): an evidence-based practical approach." *Journal of Diabetes & Metabolic Disorders* 17.2 (2018): 277-285.
18. Goyal, M. and Dawood, A.S. "Debates regarding lean patients with polycystic ovary syndrome: a narrative review." *Journal of human reproductive sciences* 10.3 (2017): 154.
19. Kim, M.J., Lim, N.K., Choi, Y.M., Kim, J.J., Hwang, K.R., Chae, S.J., Park, C.W., Choi, D.S., Kang, B.M., Lee, B.S. and Kim, T. "Prevalence of metabolic syndrome is higher among non-obese PCOS women with hyperandrogenism and menstrual irregularity in Korea. PloS one." *PloS one* 9.6 (2014): e99252.
20. Livadas, S., Pappas, C., Karachalios, A., Marinakis, E., Tolia, N., Drakou, M., Kaldrymides, P., Panidis, D. and Diamanti-Kandarakis, E. "Prevalence and impact of hyperandrogenemia in 1,218 women with polycystic ovary syndrome." *Endocrine* 47.2 (2014): 631-638.
21. Keefe, C.C., Goldman, M.M., Zhang, K., Clarke, N., Reitz, R.E. and Welt, C.K. "Simultaneous measurement of thirteen steroid hormones in women with polycystic ovary syndrome and control women using liquid chromatography-tandem mass spectrometry." *PloS one* 9.4 (2014): e93805.
22. Palomba, S., Falbo, A., Chiossi, G., Orio, F., Tolino, A., Colao, A., La Sala, G.B. and Zullo, F. "Low-grade chronic inflammation in pregnant women with polycystic ovary syndrome: a prospective controlled clinical study." *The Journal of Clinical Endocrinology & Metabolism* 99.8 (2014): 2942-2951.
23. Rosenfield, R.L. "Identifying children at risk for polycystic ovary syndrome." *The Journal of Clinical Endocrinology & Metabolism* 92.3 (2007):787-96.
24. Moran, L.J., Teede, H.J., Noakes, M., Clifton, P.M., Norman, R.J. and Wittert, G.A. "Sex hormone binding globulin, but not testosterone, is associated with the metabolic syndrome in overweight and obese women with polycystic ovary syndrome." *Journal of endocrinological investigation* 36.11 (2013): 1004-1010.
25. Christodoulaki, C., Trakakis, E., Pergialiotis, V., Panagopoulos, P., Chrelias, C.,

Kassanos, D., Sioutis, D., Papantoniou, N. and Xirofotos, D. "Dehydroepiandrosterone-sulfate, insulin resistance and ovarian volume estimation in patients with polycystic ovarian syndrome." *Journal of Family & Reproductive Health* 11.1 (2017): 24.

26. Mitrašinović-Brulić, M., Buljan, M. and Suljević, D. "Association of LH/FSH ratio with menstrual cycle regularity and clinical features of patients with polycystic ovary syndrome." *Middle East Fertility Society Journal* 26.1 (2021): 1-9.

Source of interest- Nil
Conflict of Interest- Nil

Cite this article
Rozati, R., Ganie, M.A., Wani, I., Minhaj, H., Tabasum, W., Ahmed, T.N., Ahmed, M.S., Gautam, A.M. and Ayapati, V.A. "Bmi, Pcos and Relationship of Androgen Excess in Indian Ethnic Group of Patients." *Annals of pharma research* 10.03 (2022). Pp 695-704