ANTHROPOLOGIE • LXII/1 • pp. 29–38 • 2024

RAMINDER KAUR, MANINDER KAUR, VANITA SURI

EXPLORING LONG TERM HEALTH IMPLICATIONS IN FOUR ROTTERDAM PHENOTYPES OF POLYCYSTIC OVARY SYNDROME

ABSTRACT: Polycystic ovary syndrome is one of the escalating, but underdiagnosed hormonal disorder in women of reproductive age. The present study is an attempt to explore long term health implications in four Rotterdam the phenotypes of Polycystic ovary syndrome. For this purpose, a total of 223 PCOS women with age ranged from 18 to 45 years and living in the Chandigarh Capital Region were selected from the OPD, PGIMER, Chandigarh, (North India). Polycystic ovary syndrome among women were diagnosed as per the Rotterdam Criteria (2004). Findings of the study indicated that hirsutism (47.5%), acne (30.9%), seborrhoea (32.2%), menstrual irregularity (55.6%), and ovarian size >10 cm^3 (54.7%) were most frequently encountered symptoms in women having classic PCOS phenotype as compared to women with non-PCO PCOS, non-hyperandrogenic and ovulatory PCOS phenotype. The correspondence analysis depicted that classic PCOS phenotype were more closely and significantly associated with all the symptoms of PCOS with 83.6% variance, while ovulatory PCOS depicted least association with the symptoms of PCOS indicating that oligo-anovulation play a vital role in the manifestation of symptoms related to PCOS. The classic PCOS phenotype showed higher prevalence of metabolic perturbations than other phenotypes, thereby confirming classic PCOS phenotypes are at greater risk of long-term health consequences.

KEY WORDS: Metabolic syndrome – PCOS women – PCOS phenotypes

INTRODUCTION

Polycystic ovary syndrome (PCOS) is a complex condition exhibiting reproductive, metabolic, and cardiovascular consequences among women throughout their life span (Ehrmann 2005). A considerable ethnic variation was recorded in the manifestation of PCOS prevalence and severity of obesity, metabolic disturbance

Received 22 May 2023; Received in revised form 10 July 2023; Accepted 18 August 2023. Available online 21 February 2024.

DOI: https://doi.org.10.26720/anthro.23.11.09.1

as well as their correlates (Goodarzi *et al.* 2005). According to Rotterdam Criteria, PCOS is diagnosed based on the presence of at least two of these three criteria i.e., chronic anovulation, hyperandrogenism, and polycystic ovarian morphology (PCOM) on ultrasonography. Rotterdam (2004) further distinguished four unique clinical phenotypes of women having PCOS: (i) Phenotype A: Classic PCOS (oligomenorrhea, hyperandrogenism, and PCO), (ii) Phenotype B: NIH Criteria- Non-PCO PCOS (oligomenorrhea, hyperandrogenism, and normal ovaries) (iii) Phenotype C: Ovulatory PCOS (hyperandrogenism, PCO, and regular menstrual cycles), and (iv) Phenotype D: Mild or Nonhyperandrogenic PCOS, which is defined by oligomenorrhea, PCO, and normal androgens.

Metabolic Syndrome has gained more attention in the last decade as it is a cluster of endocrinopathy with disturbances of hyperglycemia /insulin resistance, central obesity, dyslipidemia and hypertension (Huang 2009). In earlier research (Moran *et al.* 2010), it was reported that in PCOS women metabolic syndrome was more prevalent owing to the combining factors of higher prevalence of insulin resistance, obesity, and visceral obesity. Enhanced risk of metabolic disorder with 11-fold higher prevalence of metabolic syndrome among PCOS women than healthy women even at younger age was observed (Dokras *et al.* 2005). Previous researches were mostly focused on the prevalence of PCOS subtypes (Mumusoglu, Yildiz 2020), treatment to reduce clinical features (Podfigurna *et al.* 2020), effect of BMI on symptoms of PCOS (Kaur *et al.* 2021), and somatotype profile of PCOS women (Kaur *et al.* 2021), but the studies concerning the risk associated with clinical phenotypes are still lacking.

Therefore, the present study intends to study which clinical phenotype among PCOS women are at greater risk for long term health consequences. To achieve the aim of the study i) frequency distribution of various PCOS symptoms in four phenotypes were compared ii) clinical, hormonal, and metabolic complications of PCOS women among four phenotypic subtypes were compared iii) prevalence and associated features of metabolic syndrome with different phenotypes were evaluated in North Indian women.

MATERIAL AND METHODS

The present cross-sectional study was conducted on 223 PCOS women from April 2017 to January 2020 in various phases from OPD of Department of Gynaecology and Obstetrics of PGIMER, Chandigarh. The age of the participant selected from Chandigarh Capital Region ranged from 18 to 45 years. The subjects were diagnosed as PCOS based on the presence of at least two symptoms out of the following three symptoms i.e., chronic anovulation, hyperandrogenism and polycystic ovaries (Rotterdam 2004).

The prevalence of the PCOS women was expected to be 3.7% for North Indian (Gill *et al.* 2012). Thus sample size ascertained using the following formula with 95% of the confidence interval and 5% probability of type 1 error (Charan, Biswas, 2013);

$n = Z\alpha^2 \times p \times q/d^2$

$n = (1.96)^2 \times 3.7 \times 0.96/(0.05)^2$

Where, $Z\alpha = 1.96$ for 95% level of confidence;

α signifies the risk of type 1 error;

p=expected prevalence;

q=1 – p; and d signifies the error of estimate.

From the above-mentioned formula, the calculated sample size would be 50. Based on inclusion and exclusion criteria, a total of 223 PCOS women were recruited in the study.

The oligomenorrhea/ amenorrhea was depicted using FIGO classification (Munro *et al.* 2018) for menstrual cycles. The normal frequency was considered if periods occurred ≥24 to ≤38 days, oligomenorrhea if > 38 days. Hyperandrogenism was characterized on the basis of presence of clinical or/and biochemical presentation. The clinical hyperandrogenism was present if more than two characteristics out of the following were present i.e hirsutism, acne, and seborrhea. Biochemical hyperandrogenism was determined by the presence of one or more androgens concentration and in this study, we took free testosterone ≥ 2.0 as predictor of biochemical hyperandrogenism in PCOS women.

Hirsutism was defined by Ferriman-Gallwey score ≥ 6. The assessment of m-FG score was determined by using density of the terminal hair at nine different body regions, i.e upper lip, chin, chest, upper back, lower back, upper abdomen, lower abdomen, arm, and thigh. The presence of acne was diagnosed by the presence of lesion on face, back and chest. Presence of oily skin was recorded by asking participants through a scheduled interview.

Ethical approval from the Institutional Ethics committee of Panjab University (PUIEC/2018/109/A /09/01) and Post Graduate Institute of Medical Research and Education (INT/IEC/2018/000450) was obtained. Prior to data collection written consent of all the participant were obtained and they were also

appraised about the nature as well as purpose of the study.

Anthropometric measurements i.e height (cm) and weight (kg) have been taken on the subjects following the standards techniques given by Weiner and Lourie (1981). Body mass index (BMI) was calculated as weight (kg) divided by height squared (m^2). The clinical as well as biochemical parameters were noted from patient's history. Follicle stimulating hormone (FSH), Luteinizing hormone (LH), Thyroid stimulating hormone (TSH), Prolactin (PRL), fasting insulin (FI) assay was evaluated using On ABBOTT ARCHITECT (fully automated Chemiluminescent Microparticle Immunoassay) CMIA technique. Free testosterone was measured using direct EIA (Enzyme Immunoassay), Lipid profile (TC, HDL-C, LDL-C, Triglycerides) was assessed by enzymatic method. Ovary with 12 or more follicles measuring 2–9 mm in diameter and/or an increased ovarian volume (>10 cm^3) as detected by pelvic ultrasound considered polycystic ovary (Balen *et al.* 2003).

The NCEP ATP III criteria of evaluating Metabolic Syndrome (MS) is defined as the presence of at least three or more following conditions: waist circumference ≥88cm, fasting serum triglycerides>150mg/dl, serum HDL-C <50mg/dl, blood pressure ≥130/85 mm of Hg and fasting serum glucose <110mg/dl or insulin >25uU/ml. In this study we used fasting insulin >25uU/ml instead of serum glucose.

Statistical analysis: The data thus gathered were subjected to statistical analysis using Statistical Package for Social Sciences (SPSS version 20) Inc. Qualitative data were expressed as number and percentage. Chi-square was used for assessing the statistical significance of the comparison of categorical variables. Quantitative variables test were presented as mean ± S.D. One way analysis of variance (ANOVA) was used to compare the four phenotypes expression of PCOS groups. The correspondence analysis was used to describe the relationship between PCOS symptoms and different phenotypes of Rotterdam criteria in two-dimensional space. The distance between the points in plots reflects the closeness between different symptoms and four phenotypes of PCOS.

RESULTS

The prevalence of various symptoms of polycystic ovary syndrome in four phenotypes of PCOS women is depicted in *Table 1*. In our investigation, North Indian PCOS women exhibited highest proportion of classic phenotype (55.6%) followed by non-hyperandrogenic (25.5%), non-PCO PCOS (11.2%) and least women in ovulatory phenotype (7.6%). The prevalence of clinical hyperandrogenism in terms of hirsutism was significantly high in the women with Classic phenotype/phenotype A (47.5%) followed by women having non-hyperandrogenic PCOS/ phenotype D (13.9%) and non-PCO PCOS/ phenotype B (9.8%), while least prevalence was recorded in women with ovulatory PCOS/ phenotype C (7.6%).

Similarly, the presence of acne (30.9%) and seborrhea (32.2%) were significantly more prevalent among women having classic PCOS. Women with ovulatory PCOS phenotype revealed least presence of acne (3.1%) whereas, non-hyperandrogenic PCOS women have least prevalence of seborrhea (4%). The prevalence of oligomenorrhea/amenorrhea was maximum in the classic phenotype (55.6%, Chi-square=22.30, $p<0.01$) followed by non-hyperandrogenic PCOS (25.5%). Likewise ovarian morphology depicted that ovarian size >10 cm^3 was most commonly occurring in women with classic phenotype (54.7%, Chi-square=19.61, $p<0.01$) followed by non-hyperandrogenic PCOS (25.1%).

It is evident from the *Table 1* that presence of LH/FSH ratio was maximum in the classic phenotype (13.4%) followed by non-hyperandrogenic PCOS (3.5%) phenotype. It can be inferred from the *Table 1* that PCOS symptoms were most frequently encountered in classic PCOS (phenotype A) as compared to non-PCO PCOS (phenotype B), non-hyperandrogenic (phenotype D) and ovulatory PCOS phenotype (phenotype C).

The graphical representation of the association of PCOS symptom with different types of phenotypes was further analysed by correspondence analysis (*Figure 1*). The two-dimensional graph portrayed that Classic PCOS were more closely and significantly (Chi-square=76.23, df=15, $p<0.01$) associated with all the symptoms of PCOS with 83.6% variance in model. Ovulatory PCOS showed least association with symptoms of PCOS thereby indicating that oligo-anovulation play a vital role in the manifestation of symptoms related to PCOS.

The descriptive statistics of hormonal, clinical and lipid profile of four phenotypes of PCOS women were compared in *Table 2*. The highest mean FSH concentration (7.98±11.01, $p<0.05$) was observed in Phenotype B (H+O), while lowest in classic phenotype/ Phenotype A (4.82±1.5). The higher concentration of mean LH was witnessed in women with non-PCO

TABLE 1: Frequency distribution of various symptoms of PCOS in four phenotypes of PCOS women. Level of significance, p<0.05*, p<0.01 ** FSH = Follicle stimulating hormone; LH = Luteinizing hormone.

Variables	Classic PCOS P+H+O N (%)	NIH Criteria (non-PCO) H+O N (%)	Ovulatory PCOS P+H N (%)	Non-hyperandrogenic PCOS P+O N (%)	Chi-square
Clinical Hyperandrogenism					
Hirsutism	106 (47.5%)	22 (9.8%)	17 (7.6%)	31 (13.9%)	16.37**
Acne	69 (30.9%)	12 (5.3%)	7 (3.1%)	8 (3.5%)	27.87**
Seborrhea	72 (32.2%)	14 (6.2%)	10 (4.4%)	9 (4%)	30.14**
LH/FSH≥2	30 (13.4%)	4 (1.7%)	0	8 (3.5%)	7.26
Menstrual dysfunction					
Oligomenorrhea/ Amenorrhea	124 (55.6%)	25(11.2%)	0	57 (25.5%)	22.30**
Polycystic ovarian morphology (>10 cm^3)	122 (54.7%)	0	17(7.6)	56 (25.1%)	19.61**

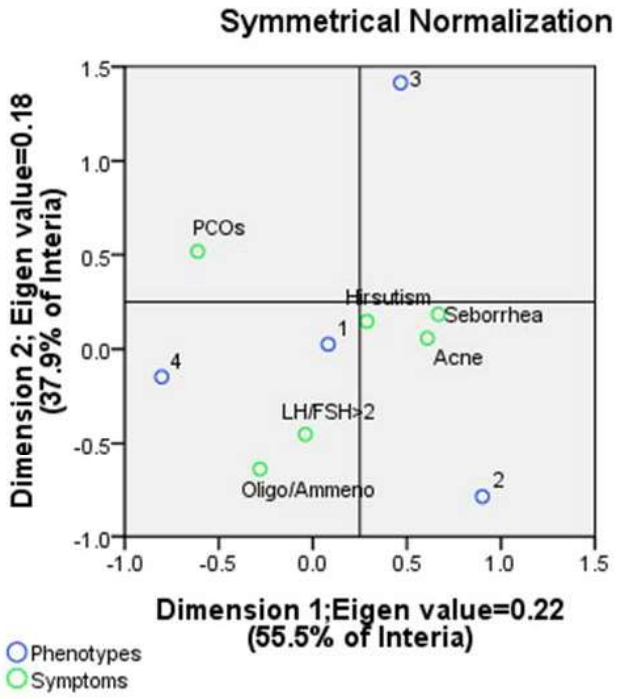

FIGURE 1: Multiple correspondence analysis of PCOS phenotypic expression with symptoms. Chi-square = 76.23, df = 15, p<0.01.

phenotype (H+O), (7.71±5.2, p>0.05) followed by non-hyperandrogenic PCOS/ Phenotype D (7.06±6.1). Ovulatory PCOS/ Phenotype C has non-significantly higher value of mean TSH (2.49±1.6, p>0.05) followed by Classic phenotype (2.11±1.3). The women with non-PCO phenotype (16.05±8.5, p>0.05) depicted highest prolactin concentration level, while least observed in non-hyperandrogenic phenotype (14.62±6.9, p>0.05). The mean free testosterone (FT) concentration was significantly maximum in the classic PCOS (2.09±1.6, p<0.01) whilst, lowest in non-hyperandrogenic phenotype/ Phenotype D (1.47±0.3).

The lipid profile of PCOS women exhibited higher mean concentration of the total cholesterol (185.16±43.2, p>0.05), LDL-C (105.84±35.4, p>0.05) and mean TG (135.32±59.7, p<0.01) in non-PCO PCOS/ Phenotype B, whereas, lower mean concentration of HDL-C (46.53±10.4, p>0.05) in non-hyperandrogenic/ Phenotype D. The mean fasting insulin (11.68±6.3) was recorded highest in the ovulatory PCOS and lowest in the non-hyperandrogenic group (11.23±5.1). Therefore, it is comprehended from the *Table 2* that high level of free testosterone hormone and lower level of FSH was noted in the women with classic phenotype as compared to other phenotypes.

The prevalence of metabolic syndrome in four phenotypes of PCOS is depicted in *Figure 2*. Overall,

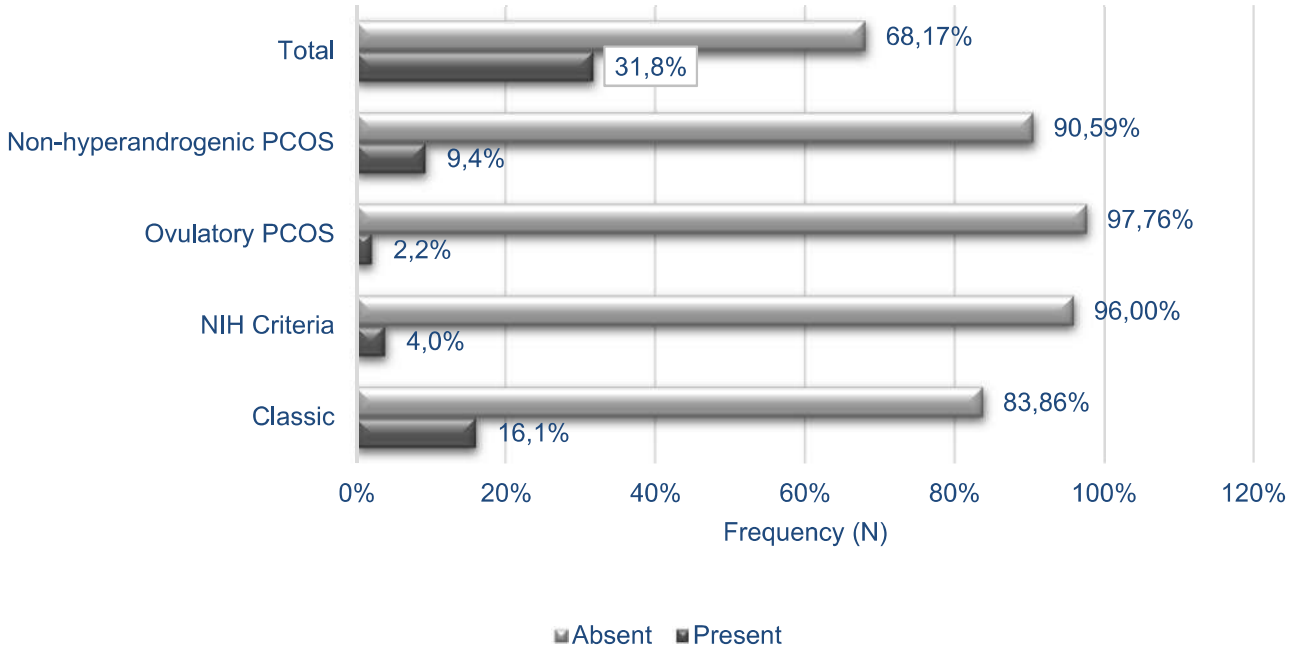

FIGURE 2: Frequency distribution of metabolic syndrome in the four phenotypes of PCOS women.

TABLE 2: Descriptive statistics of biochemical and lipid profile of four phenotypes of PCOS women. FSH = Follicle stimulating hormone; LH = Luteinizing hormone; TSH = Thyroid stimulating hormone; PRL = Prolactin; FT = Free testosterone; TC = Total cholesterol; HDL-C = High density lipoprotein-cholesterol; LDL-C = Low density lipoprotein- cholesterol; TG = Triglycerides; FI = Fasting insulin; level of significance, p<0.05*; p<0.01**.

Parameters	Phenotype A Classic PCOS P+H+O	Phenotype B NIH Criteria (non-PCO) H+O	Phenotype C Ovulatory PCOS P+H	Phenotype D Non-hyperandrogenic PCOS P+O	F-values
FSH (mIU/mL)	4.82±1.5	7.98±11.01	5.18±2.4	4.90±1.3	4.65**
LH (mIU/mL)	6.95±4.7	7.71±5.2	6.09±3.1	7.06±6.1	0.34
TSH (IU/ml)	2.11±1.3	1.81±0.8	2.49±1.6	2.04±1.1	1.00
PRL (ng/ml)	15.70±7.6	16.05±8.5	14.75±7.6	14.62±6.9	0.36
FT (pg/mL)	2.09±1.6	1.82±0.5	1.68±0.4	1.47±0.3	3.39**
TC (mg/dL)	168.39±33.4	185.16±43.2	160.88±38.7	164.43±33.3	2.40
HDL-C (mg/dL)	51.92±13.2	50.76±17.9	49.17±9.5	46.53±10.4	2.29
LDL-C (mg/dL)	92.38±27.1	105.84±35.4	90.76±24.9	91.73±26.4	1.83
TG (mg/dL)	108.40±41.8	135.32±59.7	100.64±36.0	124.66±49.0	3.92**
FI (uU/ml)	11.45±5.1	11.64±6.1	11.68±6.3	11.23±5.1	0.05

31.8% PCOS women exhibited metabolic syndrome, out of which highest proportion of metabolic syndrome was recorded in the classic phenotype (16.1%) followed by non-hyperandrogenic phenotype (9.4%) and NIH criteria (4%). Whereas, a little percentage of metabolic disorder (2.2%) was observed in the ovulatory PCOS phenotype.

The prevalence of metabolic characteristics in four different phenotypes of PCOS is presented in *Table 3*. All the metabolic characteristics i.e waist circumference ≥88 cm (43.3%), SBP ≥130 (15.2%), DBP ≥ 85 (11.6%), HDL-C<50 (27.8%) and TG ≥150 (8.5%) were maximum in the phenotype A as compared to other phenotypes of PCOS.

The prevalence of FI was meagre among the three phenotypes of PCOS cohort group (*Table 3*), and in the fourth phenotype i.e ovulatory phenotype no participant was observed. Therefore, classic phenotype has worse metabolic features followed by non-hyperandrogenic PCOS, while ovulatory PCOS represented mild metabolic features. Oligo-anovulation may be considered as a risk factor to disrupt clinical and metabolic profile in the PCOS women.

Karl Pearson's correlation coefficient (r) of the characteristics of metabolic syndrome with four phenotypes of PCOS women revealed that the classic PCOS / Phenotype A had a positive and significant correlation with all the features of metabolic syndrome. Similarly, Phenotype B recorded a positive and significant correlation with WC (r=0.55**), SBP (r=0.55**), and DBP (r=0.55**). On the contrary, ovulatory phenotype exhibited significant correlation of metabolic syndrome with HDL-C <50 (r=0.54**), SBP (r=0.60**) and DBP (r=0.87**). Whereas, Triglycerides (r=0.65**), HDL-C<50 (r=0.40**), SBP (r=0.41**), and DBP (r=0.57**) had a positive and significant correlation with non-hyperandrogenic phenotype.

DISCUSSION

Polycystic ovary syndrome is one the most common endocrine and metabolic dysfunction with three diagnostic criteria and four different clinical phenotypes (Mumusoglu, Yildiz 2020). In present research, maximum symptoms of PCOS were recorded in the women with classic phenotype (Phenotype A) followed by non-hyperandrogenic phenotypes/ phenotype D. The prevalence of clinical symptom of hyperandrogenism i.e hirsutism (47.5%), acne (30.9%) and seborrhea (32.2%) were highest in the classic phenotype. The menstrual dysfunction (55.6%) was also highly noticed in the women with classic phenotype as compared to other phenotypes of PCOS women. Similarly, a study carried out by Sachdeva *et al.* (2019) revealed that the Phenotype A has significantly more clinical and biochemical hyperandrogenism than Phenotype C as well as phenotype D and menstrual irregularities were also maximum among women with phenotype A.

Despite of non-hyperandrogenic PCOS subtype, the prevalence of hirsutism, menstrual dysfunction, and polycystic ovary morphology (>10cm^2) was higher in the phenotype D as compared to phenotype B and

TABLE 3: Prevalence of metabolic characteristics in four different phenotypes of PCOS women. WC = Waist circumference; SBP = Systolic blood pressure, DBP = Diastolic blood pressure; HDL-C = High density lipoprotein cholesterol; TG = triglycerides; FI = Fasting insulin; level of significance, p<0.05*; p<0.01**.

Variables	**Classic PCOS P+H+O**	**NIH Criteria (non-PCO) H+O**	**Ovulatory PCOS P+H**	**Non-hyperandrogenic PCOS P+O**	**Chi-square p-value**
WC≥88 (cm)	97 (43.4%)	13 (5.8%)	12 (5.3%)	35 (15.6%)	9.92**
SBP≥130 (mm Hg)	34(15.2%)	6 (2.6%)	6 (2.6%)	14 (6.2%)	0.89
DBP≥85 (mm Hg)	26 (11.6%)	5 (2.2%)	6 (2.6%)	16 (7.1%)	2.56
HDL-C<50 (mg/dl)	62(27.8%)	16 (7.1%)	10 (4.4%)	37 (16.5%)	4.35
TG≥150(mg/dl)	19 (8.5%)	11 (4.9%)	2 (0.8%)	18 (8.1%)	14.14**
FI>25(mg/dl)	2 (0.8%)	2 (0.8%)	1 (0.4%)	0	06.34

phenotype C. A previous study performed by Sachdeva *et al.* (2019) found that phenotype D as least severe phenotype, which is contradicted in the present study, exhibiting that after classic PCOS phenotype, non-hyperandrogenic PCOS women demonstrated adverse clinical symptom as well as metabolic profile.

A significantly higher mean value of testosterone was also noted in the classic phenotype followed by non-PCO, and ovulatory PCOS, while least in the non-hyperandrogenic phenotype. Earlier studies demonstrated that the women with the classic phenotype strongly expressed hyperandrogensim in comparison to the other phenotypes of PCOS (Hosseinpanah *et al.* 2014). This reflects that solely hyperandrogenism is not responsible in the pathophysiology of the PCOS, rather other genetic and non -genetic factor are also accountable.

In the current cross-sectional study, Phenotype B depicted significantly higher concentration of FSH followed by phenotypes D and A, whereas least values of FSH were observed in phenotype C. Similarly luteinizing hormone has higher mean concentration in phenotype B followed by phenotype D. A study carried out by Katsikis *et al.* (2011) reported that LH level was higher among the women having phenotype A in comparison to new phenotypes of the Rotterdam criteria which desensitize the negative feedback regulation mechanism of progesterone resulted in the higher androgen levels. On the contrary, lower level of luteinizing hormone in the obese women contributed to increased aromatization of androgens, which leads to suppression of LH.

Our study displayed that the phenotype C has less prevalent symptom presentation as compared to the classic PCOS. Although, mean TSH (2.49±1.6, $p>0.05$) level was higher in non PCO phenotype/ phenotype C as compared to other phenotypes of the present study. Similarly higher level of TSH was reported by an existing study (Kamrul-Hasan *et al.* 2020) among PCOS women of Bangladesh than their control group. According to the previous findings, TSH level ≥2.5mU/L showed an association with hyperandrogenic PCOS phenotype which plays a significant role in the pathogenesis of PCOS.

Even though, the mean concentration of TC (185.16±43.2, $p>0.05$), LDL-C (105.84±35.4, $p>0.05$) and triglycerides (135.32±59.7, $p>0.05$) were higher among phenotype B. The lipid profile of the classic PCOS/phenotype exhibited higher prevalence of metabolic features than other phenotypes. Likewise, a negative impact of testosterone has been reported on the lipid profile of the PCOS women. Although, in our study triglycerides, total cholesterol, LDL-C and HDL-C presented a significant correlation with Phenotype A, yet main reason is still unclear and might be linked with hyperandrogenism or genetic factors (Kim, Choi 2013). A study conducted on a representative sample of an Iranian PCOS population by Hosseinpanah *et al.* (2014) noted no significant difference among different PCOS phenotypes or between PCOS cohort group and normal subjects in terms of their metabolic characteristics.

Least symptoms of PCOS, metabolic syndrome, and cardiovascular risk were witnessed in non-PCO phenotypes/ phenotype C. These findings of the present study were in convergence with the existing literature (Mehrabian *et al.* 2011) that the non-PCO PCOS phenotype were highly related to the presence of metabolic characteristics. Thus, presentation of different phenotypes of PCOS women exhibited difference in the clinical, metabolic, and hormonal profile, which suggest each subtype of PCOS is a variation of common syndrome (Sachdeva *et al.* 2019). A study conducted by Welt *et al.* (2006) on the women of a large heterogeneous group of New England and Iceland revealed that the ovulatory and non-hyperandrogenic phenotype had mild lipid abnormalities in comparison to women diagnosed with NIH criteria.

The present study reflected that the classic phenotype of PCOS women had worse metabolic profile. Past studies (Sachdeva *et al.* 2019) also highlighted that the hyperandrogenism, obesity, deranged lipid profile and metabolic syndrome were more common in the classic PCOS. Our study reported that the classic PCOS has highest frequency of all the metabolic characteristics exhibiting waist circumference (WC≥88 cm) (43.4%) as the most prevalent feature followed by decreased HDL-C level (27.8%). A report of Azizz (2016) summarized that in the classic phenotype the prevalence of metabolic dysfunction among PCOS women ranged from 75%–85%. Our study depicted a lower prevalence of fasting insulin, thereby exhibiting presence of insignificant fraction in all the phenotypic groups. In divergence to the findings of earlier studies (Kar 2013, Yilmaz *et al.* 2011; Zhang *et al.* 2009) reporting mildest metabolic profile of the phenotype D, present study portrayed Phenotype C as a milder form of metabolic disorder among PCOS women.

In convergence to the findings of present study, various researchers displayed (Diamanti Kandarakis *et al.* 2007, Goverde *et al.* 2009, Wild *et al.* 2010) that the classic PCOS phenotype has worse profile showing higher metabolic and cardiovascular risk factor as

compared to the non-classic PCOS phenotypes. Hyperandrogenism considered as a major determinant of PCOS pathogenesis (Diamanti Kandarakis *et al.* 2012) however, not a sole contributing factor responsible for the progression of polycystic ovary syndrome. Past studies (Escobar-Morreale *et al.* 2007, Christakou *et al.* 2008) reported that androgen excess may worsen the metabolic risk in the PCOS women specifically visceral adiposity and insulin resistance.The phenotypes of PCOS women exhibited heterogeneity in the prevalence of symptoms as well as risks associated with the syndrome, thereby reflecting variation among the presentation of the clinical, hormonal, and metabolic profile in polycystic ovary syndrome.

STRENGTH AND LIMITATIONS OF THE STUDY

The greatest strength of our study is sample size and Rotterdam criteria to diagnose the patients as all different phenotypes were investigated. Very few studies have been conducted to assess the long-term health implications among PCOS women. Therefore, this study will add on existing the data base of the Indian PCOS women for future research perspective.

Fasting insulin is not of much practical importance and could be limitation of our study as glucose ≥100 mgl/dl is most informative to assess insulin impairment. Biochemical hyperandrogenism was determined by free testosterone ≥ 2.0 as other androgens were not assessed during study which might show interaction with clinical symptoms. The control group was not considered in the study due to financial constraint.

CONCLUSION

In conclusion, the different phenotypes are subsets of polycystic ovary syndrome exhibiting variability in the clinical, endocrine, and metabolic manifestation. However, classic phenotype presented more severe clinical hyperandrogenism and metabolic features as compared to other three phenotype. Thus, the present study addresses to predict the adverse metabolic and cardiovascular outcome of PCOS among classic phenotype. Such studies will be helpful to explain the likelihood of the risk of different phenotypes of PCOS and may widen the future treatment options as well as understanding the morbidities associated with PCOS.

ACKNOWLEDGEMENTS

Authors (R. K. and M. K.) are supported by CAS-II awarded to the Department of Anthropology, Panjab University, Chandigarh, India.

REFERENCES

AZZIZ R., 2016: New insights into the genetics of polycystic ovary syndrome. *Nature Reviews Endocrinology* 12, 2: 74-75. DOI: doi.org/10.1038/nrendo.2015.23

BALEN A. H., LAVEN J. S., TAN S. L., DEWAILLY D., 2003: Ultrasound assessment of the polycystic ovary: international consensus definitions. *Human reproduction update* 9, 6: 505-514. DOI:10.1093/humupd/dmg044

CHARAN J., BISWAAS T., 2013: How to calculate sample size for different study designs in medical research? *Indian Journal of Psychological Medicine* 35, 2: 121-6. DOI: 10.4103/0253-7176.116232

CHRISTAKOU C. D., DIAMANTI-KANDARAKIS E., 2008: Role of androgen excess on metabolic aberrations and cardiovascular risk in women with polycystic ovary syndrome. *Women's Health* 4, 6: 583-594. DOI: 10.2217/17455057.4.6.583

DIAMANTI-KANDARAKIS E., CHRISTAKOU C., MARINAKIS E., 2012: Phenotypes and environmental factors: their influence in PCOS. *Current pharmaceutical design* 18, 3: 270-282. DOI: 10.2174/138161212799040457

DIAMANTI KANDARAKIS E., PANIDIS D., 2007: Unravelling the phenotypic map of polycystic ovary syndrome (PCOS): a prospective study of 634 women with PCOS. *Clinical endocrinology* 67, 5: 735-742. DOI: 10.1111/j.1365-2265.2007.02954.x

DOKRAS A., BOCHNER M., HOLLINRAKE E., MARKHAM S., VANVOORHIS B., JAGASIA D. H., 2005: Screening women with polycystic ovary syndrome for metabolic syndrome. *Obstetrics & Gynecology* 106, 1: 131-137. DOI:10.1097/01.AOG.0000167408.30893.6b

EHRMANN D. A., 2005: Polycystic ovary syndrome. *New England Journal of Medicine* 352, 12: 1223-1236. DOI: 10.1056/NEJMra041536

ESCOBAR-MORREALE H. F., SAN MILLÁN J. L., 2007: Abdominal adiposity and the polycystic ovary syndrome. *Trends in Endocrinology & Metabolism* 18, 7: 266-272. DOI: 10.1016/j.tem.2007.07.003

GILL H., TIWARI P., DABADGHAO P., 2012: Prevalence of polycystic ovary syndrome in young women from North India: A Community-based study. *Indian J Endocrinol Metab* 16, 2: S389-S392. DOI:10.4103/2230-8210.104104

GOODARZI M. O., QUIÑONES M. J., AZZIZ R., ROTTER J. I., HSUEH W. A., YANG H., 2005: Polycystic ovary syndrome in Mexican-Americans: prevalence and association with the severity of insulin resistance. *Fertility and sterility* 84, 3: 766-769. DOI: doi.org/10.1016/j.fertnstert.2005.03.051

GOVERDE A. J., VAN KOERT A. J. B., EIJKEMANS M. J., KNAUFF E. A. H., WESTERVELD H. E., FAUSER B. C. J. M., BROEKMANS F. J., 2009: Indicators for metabolic disturbances in anovulatory women with polycystic ovary syndrome diagnosed according to the Rotterdam consensus criteria. *Human Reproduction* 24, 3: 710–717. OI: 10.1093/humrep/den433

HOSSEINPANAH F., BARZIN M., KEIHANI S., RAMEZANI TEHRANI F., AZIZI F., 2014: Metabolic aspects of different phenotypes of polycystic ovary syndrome: Iranian PCOS Prevalence Study. *Clinical endocrinology* 81, 1: 93–99. DOI:10.1111/cen.12406

HUANG P. L., 2009: A Comprehensive definition for metabolic syndrome. *Disease models & mechanisms* 2, 5–6: 231–237. DOI: 10.1242/dmm.001180

KAMRUL-HASAN A. B. M., AALPONA F. T. Z., MUSTARI M., AKTER F., RAHMAN M. M., SELIM S., 2020: Divergences in Clinical, Anthropometric, Metabolic, and Hormonal Parameters among Different Phenotypes of Polycystic Ovary Syndrome Presenting at Endocrinology Outpatient Departments: A Multicenter Study from Bangladesh. *Journal of Human Reproductive Sciences* 13, 4: 277. DOI: doi.org/10.4103/jhrs.JHRS_34_20

KAR S., 2013: Anthropometric, clinical, and metabolic comparisons of the four Rotterdam PCOS phenotypes: A prospective study of PCOS women. *Journal of human reproductive sciences* 6, 3: 194. DOI: 10.4103/0974-1208.121422

KATSIKIS I., KARKANAKI A., MISICHRONIS G., DELKOS D., KANDARAKI E. A., PANIDIS D., 2011: Phenotypic expression, body mass index and insulin resistance in relation to LH levels in women with polycystic ovary syndrome. *European Journal of Obstetrics & Gynecology and Reproductive Biology* 156, 2: 181–185. DOI: 10.1016/j.ejogrb.2011.01.023

KAUR R., KAUR M., SURI V., 2020: Somatotype profile of obese and lean women with polycystic ovary syndrome. *Anthropologie* 58, 1: 93–102. DOI: 10.26720/anthro.20.02.07.1

KAUR R., KAUR M., SURI V., 2021: Does body mass index have an effect on the prevalence of various symptoms of polycystic ovary syndrome and their associated risk factors? *Anthropological Review* 84, 2:101–116. DOI: doi.org/10.2478/anre-2021-0013

KIM J. J., CHOI Y. M., 2013: Dyslipidemia in women with polycystic ovary syndrome. *Obstetrics & gynecology science* 56, 3:137–142. DOI: doi.org/10.5468/ogs.2013.56.3.137

MEHRABIAN F., KHANI B., KELISHADI R., KERMANI R., 2011: The prevalence of metabolic syndrome and insulin resistance according to the phenotypic subgroups of polycystic ovary syndrome in a representative sample of Iranian females. *Journal of research in medical sciences: the official journal of Isfahan University of Medical Sciences* 16, 6: 763.

MORAN L. J., MISSO M. L., WILD R. A., NORMAN R. J., 2010: Impaired glucose tolerance, type 2 diabetes and metabolic syndrome in polycystic ovary syndrome: a systematic review and meta-analysis. *Human reproduction update* 16, 4: 347–363. DOI: doi.org/10.1093/humupd/dmq001

MUMUSOGLU S., YILDIZ B. O., 2020: Polycystic ovary syndrome phenotypes and prevalence: differential impact of diagnostic criteria and clinical versus unselected population. *Current Opinion in Endocrine and Metabolic Research* 12: 66–71. DOI: doi.org/10.1016/j.coemr.2020.03.004

MUNRO M. G., CRITCHLEY H. O., FRASER I. S., FIGO MENSTRUAL DISORDERS COMMITTEE, HATHTHOTUWA R., KRIPLANI A., WARNER P., 2018: The two FIGO systems for normal and abnormal uterine bleeding symptoms and classification of causes of abnormal uterine bleeding in the reproductive years: 2018 revisions. *International Journal of Gynecology & Obstetrics* 143, 3: 393–408. DOI: 10.1002/ijgo.12666

PAGES E. S. H. R. E., TARLATZIS B. C., REBAR R. W., 2012: Consensus on women's health aspects of polycystic ovary syndrome (PCOS). *Hum Reprod* 27,1: 14–24. DOI: 10.1016/j.fertnstert.2011.09.024

PODFIGURNA A., MECZEKALSKI B., PETRAGLIA F., LUISI S., 2020: Clinical, hormonal and metabolic parameters in women with PCOS with different combined oral contraceptives (containing chlormadinone acetate versus drospirenone). *Journal of endocrinological investigation* 43, 4: 483–492. DOI: doi.org/10.1007/s40618-019-01133-3

SACHDEVA G., GAINDER S., SURI V., SACHDEVA N., CHOPRA S., 2019: Comparison of the different PCOS phenotypes based on clinical metabolic, and hormonal profile, and their response to clomiphene. *Indian Journal of Endocrinology and Metabolism* 23, 3: 326. DOI: 10.4103/ijem.IJEM_30_19

The Rotterdam ESHRE/ASRM sponsored PCOS consensus workshop group, Revised 2003 consensus on diagnostic criteria and long term health risks related to polycystic ovary syndrome (PCOS), 2004: *Human Reproduction* 19, 1: 41–47. DOI: doi.org/10.1093/humrep/deh098

WEINER J. S., LOURIE J. A., 1981: *Practical human biology*: Academic press.

WELT C. K., ARASON G., GUDMUNDSSON J. A., ADAMS J., PALSDOTTIR H., GUDLAUGSDOTTIR G., CROWLEY W. F., 2006: Defining constant versus variable phenotypic features of women with polycystic ovary syndrome using different ethnic groups and populations. *The Journal of Clinical Endocrinology & Metabolism* 91, 11: 4361–4368. DOI: 10.1210/jc.2006-1191

WILD R. A., CARMINA E., DIAMANTI-KANDARAKIS E., DOKRAS A., ESCOBAR-MORREALE H. F., FUTTERWEIT W., DUMESIC D. A., 2010: Assessment of cardiovascular risk and prevention of cardiovascular disease in women with the polycystic ovary syndrome: a consensus statement by the Androgen Excess and Polycystic Ovary Syndrome (AE-PCOS) Society. *The Journal of Clinical Endocrinology & Metabolism* 95, 5: 2038–2049. DOI: 10.1210/jc.2009-2724

YILMAZ M., ISAOGLU U., DELIBAS I. B., KADANALI S., 2011: Anthropometric, clinical and laboratory comparison of four phenotypes of polycystic ovary syndrome based on Rotterdam criteria. *Journal of Obstetrics and Gynaecology Research* 37, 8: 1020–1026. DOI: 10.1111/j.1447-0756.2010.01478.x

ZHANG H. Y., ZHU F. F., XIONG J., SHI X. B., FU S. X., 2009: Characteristics of different phenotypes of polycystic ovary syndrome based on the Rotterdam criteria in a large scale Chinese population. *BJOG: An International Journal of Obstetrics & Gynaecology* 116, 12: 1633-1639. DOI: 10.1111/j.1471-0528.2009.02347.x

Raminder Kaur[1]*
Maninder Kaur[1]
Vanita Suri[2]
[1]Department of Anthropology,
Panjab University
Chandigarh, India
E-mail: reetkaur1792@gmail.com
E-mail: maninderkaur_1@yahoo.in
[2] Department of Gynaecology and
obstetrics, PGIMER, Chandigarh,
India
E-mail: Surivanita@yahoo.co.in

*Corresponding author.