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Review Article

Assessment of Endocrine, Metabolic, and Fibrinolytic Profile and Its Association with BMI in Polycystic Ovarian Syndrome

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Abstract: Polycystic ovarian syndrome is a typical endocrine disorder that occurs in women and has a significant impact on the reproductive, metabolic, endocrine, and fibrinolytic systems. It is a heterogeneous clinical condition caused by multiple factors, especially obesity. Furthermore, metformin is the classical treatment approach for PCOS, which has conflicted results. The current study aimed to find out the effect of the usage of metformin on metabolic, fibrinolytic, and reproductive profiles between obese women with PCOS and non-obese women with PCOS. A cross-sectional study was carried out on 200 women diagnosed with PCOS and divided into two groups based on BMI. Each group was further subdivided into three subgroups (A, B, and C) based on their prescribed treatment. In addition, 50 age-matched controls were selected to compare the outcome. The reproductive hormones, lipid profile, glycaemic index, and fibrinolytic profile were measured in each group and compared to find the desired association. The demographic variables did not show significant variation within or between the groups except BMI. Group IA has shown better metabolic variables, Group IB has an improved endocrine profile, and Group IC has a better fibrinolytic profile(p>0.01**). Group II B has shown a better metabolic and endocrine profile, whereas it is significantly higher in the fibrinolytic profile (p>0.01**). Cumulatively Group II has a drastic reduction in all variables than group I(p>0.01**) except few non-significant variables. Obese PCOS patients are at an increased risk for complications such as endometrial hyperplasia, metabolic syndrome, and vascular thrombosis. Metformin and OCP are highly beneficial as they reduce the risk of insulin resistance and glucose intolerance and improve ovarian functions for a better reproductive life.

Keywords: Polycystic ovarian syndrome, Metformin, Hyper Androgenism,

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1. INTRODUCTION

Polycystic ovarian syndrome (PCOS) is a heterogenic disorder in women of reproductive age. The prevalence of PCOS is 3-10% in different age group populations across the world [1] The clinical diagnosis of PCOS is a challenging assignment as PCOS overlaps with normal pubertal development. The prerequisite to diagnosing PCOS is to have a cautious evaluation of the clinical presentation of women's history, physical examination, and laboratory evaluation, emphasizing the accuracy and validity of PCOS. It must be correlated with both biochemical profile and radiographic ovarian assessment [2]. American Association of Clinical Endocrinologists (AACE) emphasizes the utmost imperative clinical concerns that provoke clinicians and their patients who are suffering from PCOS. Precise diagnosis of PCOS influences the likelihood of associated metabolic and cardiovascular risks and leads to proper treatment. PCOS is characterized by hyper and organism with ovarian dysfunction (Chronic anovulation) that leads to irregular menstruation, menorrhagia, and infertility. Therefore, AACE recommends the diagnosis of PCOS must be based on any two of the above-mentioned clinical presentations [3]. PCOS is also equally altered in women the metabolic profile results in insulin resistance, glucose intolerance, and hyperlipidaemia [4]. Furthermore, PCOS can result in an imbalanced hypothalamic pituitary ovarian axis that changes the secretion of pituitary hormones (Gonadotropins) and vitamin D [5]. In addition, PCOS impacts the fibrinolytic profile, which tends to cause augmented hemostatic mechanisms [6]. It is well documented in the previous literature that these profiles are significantly impacted in women with PCOS [7-9]. PCOS is caused by multifactorial conditions including genetic, environmental, metabolic, and altered hormonal profiles. Among these adipose tissue dysfunctions caused by morbid obesity have been implicated as a significant contributor to insulin resistance has been observed in PCOS[10]. Obesity contributes a significant role in the occurrence of PCOS. Approximately 50% of PCOS women who are overweight or obese have the abdominal phenotype. Obesity may play a pathogenic role in the development of PCOS [11]. However, the association between obesity and its effect on endocrine, metabolic, and fibrinolytic profiles was not well established especially in the Indian population. The symptoms and severity of PCOS vary with age, BMI, genetics, lifestyle factors, and geographic diversity [12]. Despite the surplus of relative information, the exact pathogenesis of PCOS still needs to be clarified. It may result in misinterpretation of clinical findings, which can misguide us in decision-making. However, the recent research scientific data especially the biochemical assessment of their interest provides new insights into adipose dysfunction that may constitute the association of different parameters and their disturbances in the pathogenesis of PCOS [13]. Metformin is the commonest drug often prescribed during PCOS which improves insulin sensitivity, endothelial activity, and ovulatory cycles [14]. Furthermore, the chronic PCOS often treated with OCP was well acknowledged [15]. However, the long-term safety of OCP use in PCOS has not been established, and the literature reveals conflicting data concerning the metabolic effects of OCP with outcomes in the development of diabetes [16-18]. There is no sufficient literature on the use of metformin and oral contraceptive pills (OCP) to reduce hyperandrogenic activity, improve ovulatory functions, and prevent metabolic and fibrinolytic complications in reproductive women with PCOS in the Indian population. Therefore, the current study aimed to evaluate the usage of metformin and OCP therapy on endocrine, metabolic, and fibrinolytic profiles in women with PCOS and its association with obesity and adipose tissue dysfunction.

2. MATERIALS AND METHODS

2.1 Study Design

It is a cross-sectional study carried out in a tertiary care hospital from 2018 to 2020. The entire study protocol was reviewed and approved by the Institutional Ethics Committee and an approval number (IEC Approval No.03/2019) was obtained before instituting the study. The sample size was calculated as 200 based on the outcome of a pilot study conducted earlier. Subjects who fulfilled the inclusion criteria received an explanation of the nature and purpose of the study, and informed consent was obtained from each subject as per the Declaration of Helsinki 1975 and later amendments.

2.2 Study Population

A total of 200 women with PCOS were selected for the study who were aged between 20-45 years and came to the outpatient department of the Gynaecology department of the host institute. The concerned clinicians made the diagnosis as per Rotterdam criteria and the New International Guidelines [19].

2.3 Inclusion Criteria

1. Age from Menarche to 45 yrs.
2. Diagnosis of PCOS based on revised Rotterdam criteria.

2.4 Exclusion Criteria

1. Current pregnancy or nursing
2. Subjects with renal disease, liver disease, gastrointestinal problems, and malnutrition.
3. Recent history of major surgeries, and trauma.

2.5 Selection Criteria

The participants were subjected to all general medical examinations, and a history of PCOS, duration, symptoms, manifestations, and drug usage were obtained by interviewing before inclusion in the study as per the protocol. Participants were excluded if they had any well-known psychiatric issues, a history of renal disorders, or other significant comorbidities.

2.6 Categorization of Participants

The participants were divided into groups based on BMI obese and non-obese women with PCOS. Body Mass Index (BMI) is defined as the body weight in kilograms divided by the square of the height in meters (kg/m^2. Obesity was described as a BMI≥25 kg/m^2, and non-obese as a BMI < 25 kg/m^2. The study population was divided into two groups as per the diagnostic criteria. Group I: Obese women with PCOS (n-100) and Group II: Non-obese women with PCOS(n-100). Each group was further divided into three subgroups based on the usage of metformin, OCP, and combined therapy (Metformin and OCP) as follows

Group I A: Obese women who are on metformin (n-26)
Group I B: Obese women who are on oral contraceptive pills (n-34)

Group IC: Obese women who are on both metformin and oral contraceptive pills(n-40)
Group II A: Non-obese women who are on metformin (n-32)
Group II B: Non-obese women who are on oral contraceptive pills (n-35)
Group II C: Non-obese women on both metformin and oral contraceptive pills (n-33).

2.7 *Quality Assessment*

It was a combined treatment trial executed by homogenous well-trained professionals in the OPD of the Gynaecology department of the host institute. The data obtained from each participant was organized as follows.

2.7.1 *Demographic Variables*

The participants were interviewed, and Socio-demographic profiles and Anthropometric data (Name, Age, Gender, Height, and Weight) were collected. Each participant's height and weight were estimated using a digital weight machine and a wall meter, and BMI was calculated using Quetelet's Index.

2.7.2 *Metabolic Variables*

The lipid profile includes total cholesterol, triglycerides, HDL, LDL and VLDL, as well as glycemic profile including Random Blood Sugar (RBS), Glycated Hemoglobin, and Insulin, were estimated using Beckman AU 480 analyzer [20].

2.7.3 *Endocrine Variables*

Serum LH and Testosterone values were estimated by "The ADVIA centaur CP". FSH assay using direct chemiluminometric technology (Kicklighter EJ, Norman RJ). Vitamin D levels were measured by SEIMENS CENTAUR CP using CLIA Method[21].

2.7.4 *Fibrinolytic Variables*

Fibrinogen, Plasminogen, and D dimer were measured by the semi-quantitative macro latex agglutination technique using a commercially available assay (Global Fibrinolytic Capacity STA Latest d-Di; Diagnostica Stago, Asnie¨res, France)[22].

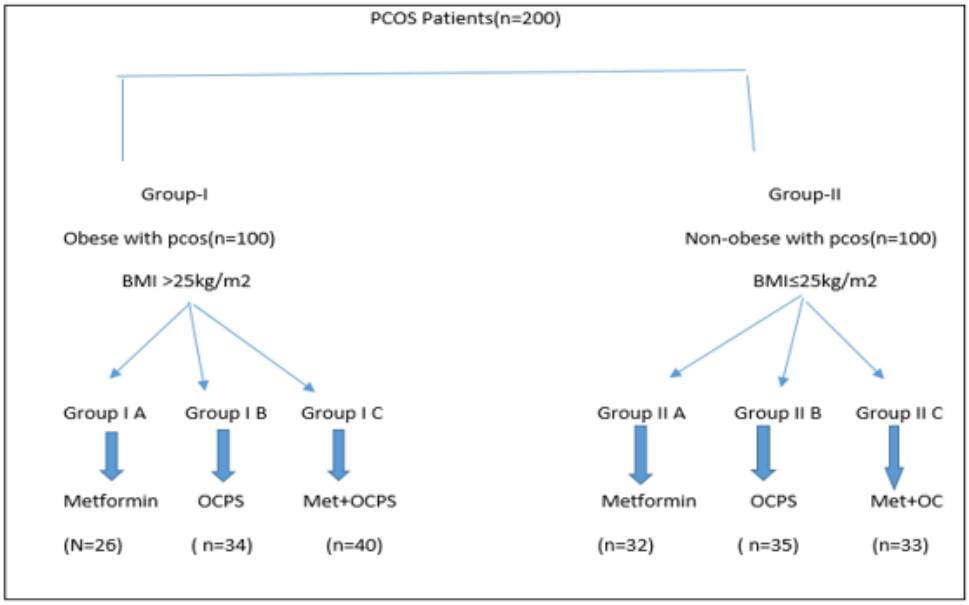

Fig 1: Flow chart of the study (PCOS-Polycystic ovarian syndrome. OCPS- Oral contraceptive pills, MI Body mass index)

3. STATISTICAL ANALYSIS

The data sets were expressed as Mean and standard deviation with 95% Confidence intervals (95%CI). All the data sets were analyzed using SPSS (Ver. 16). The normality of data was tested using the Smirnov Kolmogorov test. As the data sets were distributed normally, parametric tests were applied to determine the differences among subgroups using one-way ANOVA, post hoc analysis, and between groups using the independent 't-test. Finally, the association was estimated between desired variables using Pearson correlation. The statistical significance was taken as 0.05.

4. RESULTS

Table: 1 Baseline characteristics of patients with PCOS in obesity

Baseline characteristics	Group I A (*n*-26)	Group I B (*n*-34)	Group I C (*n*-40)	*p*-value
Age (yrs)	27.2 ± 2.86 (26.15- 8.32)	27.4 ± 2.02 (26.44 – 27.95)	27.7 ± 2.69 (26.92-28.93)	0.56
Height (cm)	158 ± 5.88 (156.32-0.78)	160 ± 5.99 (157.86-61.34)	159 ± 5.33 (156.83-60.71)	0.06
Weight (kg)	92.89 ± 7.17 (90.16 -.12)	89.05 ± 17.56 (82.47 -95.19)	85.03 ± 11.53 (81.62-88.9)	0.67
BMI (kg/m²)	28.64±3.08 (27.22-29.52)	29.5±2.782 (27.93-30.06)	29.34±2.42 (27.46-30.12)	0.52

Table -1 represents baseline characteristics in obese PCOS women. Data represented as Mean±SD, SD-Standard deviation, and mean age and BMI were insignificant. (p>0.05) Body mass index(BMI)

Table: 2 Metabolic profile variables among PCOS patients with obesity				
Metabolic variables	**Group I A**	**Group I B**	**Group I C**	***p*-value**
Serum Cholesterol	261 ± 47 (243- 279)	257 ± 27 (247 – 268)	258 ± 25 (249 - 266)	0.89
Triglycerides	102 ± 20.7 (94.6-100.67)	277± 47.91 (259-295)	142 ± 71.08 (119-164)	**<0.01****
HDL	39.62 ± 8.01 (39.87 - 46.67)	25.15 ± 5.99 (22.93 -27.69)	61.09 ± 15.63 (56.24-65.94)	**<0.01****
LDL	182 ± 18.28 (175-189)	168 ± 18.25 (161-175)	142 ± 19.31 (136-148)	**<0.01****
VLDL	22.1 ± 8.06 (18.96-25.24)	24.73 ± 7.48 (23.05-26.40)	28 ± 5.03 (26.41-29.58)	**<0.01****
HbA1C	6.24 ± 0.42 (6.04-6.80)	6.62 ± 0.25 (6.43-6.89)	7.55 ± 0.89 (6.44-8.54)	**0.05***
RBS	115 ± 36.24 (101-129)	160 ± 23.73 (152-169)	100.7 ± 23.77 (91-110)	**<0.01****
Insulin	41.72 ± 7.43 (38.89-44.55)	29.76 ± 4.73 (28.2-31.73)	33.34 ± 4.26 (31.99-34.68)	**<0.01****

Table 2 shows the metabolic variables among subgroups of group I, which are significantly different(p>0.01**) in group IA than in group IB and IC, except for cholesterol(p-0.89). High- density lipoproteins(HDL), Low -density lipoproteins(LDL), Very low-density lipoproteins(VLDL), Haemoglobin A1C(HBA1C), Random blood sugar(RBS).

Table:3 Endocrine profile variables among PCOS patients with obesity				
Endocrine profile variables	**Group I A**	**Group I B**	**Group I C**	***p*-value**
LH	11.59 ± 6.21 (9.23-13.27)	4.40 ± 3.97 (1.79 – 7.01)	37.52 ± 15.23 (32.71 – 42.33)	**<0.01****
FSH	6.68 ± 3.64 (5.26-8.11)	2.55± 2.04 (0.58-4.79)	19.47± 8.34 (16.83-22.11)	**<0.01****
Testosterone	48.84 ± 20.41 (41.05- 56.58)	85.27 ± 17.24 (79.43 -92.31)	79.12 ± 19.88 (72.84-85.39)	**<0.01****
Vitamin D	34.42 ± 8.24 (28.05- 42.31)	11.27 ± 8.52 (3.61 -17.79)	51.92 ± 10.35 (40.55-61.28)	**<0.01****

Table: 3 shows LH, FSH, and Vitamin-D levels were drastically decreased in group IB whereas Testosterone was less in group IA than in the other two groups respectively, which has a statistical significance(p>0.01**) Leutinizing hormone (LH), Follicle stimulating hormone(FSH)

Table: 4 Fibrinolytic profile variables among PCOS patients with obesity				
Fibrinolytic variables	**Group I A**	**Group I B**	**Group I C**	***p*-value**
Fibrinogen	504.3 ± 44.84 (486-526)	503.5 ± 48.41 (476 – 522)	619.2 ± 50.54 (583 – 654)	**<0.01****
Plasminogen	22.31 ± 3.65 (5.26-8.11)	21.23± 3.47 (0.58-4.79)	49.12± 17.25 (16.83-22.11)	**<0.01****
D Dimer	52.24 ± 9.41 (41.05- 56.58)	54.56 ± 7.24 (48.43 -62.31)	65.83 ± 19.88 (49.84-79.39)	**<0.01****

Table: 4 represents Fibrinogen, Plasminogen. and D dimer are significantly higher in group IC than in the other two subgroups (p>0.01**).

Table: 5 Baseline characteristics of PCOS in non-obese patients				
Baseline characteristics	**Group II A(*n*-32)**	**Group II B(*n*-35)**	**Group II C(*n*-33)**	***p*-value**
Age (yrs)	33.13 ± 5.72 (30.96- 35.31)	31.05 ± 5.92 (28.8 – 33.21)	33.73 ± 5.73 (32.02-35.44)	0.13
Height (Cm)	162 ± 5.16 (158.16-167.23)	164 ± 5.9 (158.72-167.41)	159 ± 7.77 (152.24-165.82)	0.97
Weight (Kg)	63.06± 5.89 (90.16 -95.12)	65.16 ± 7.74 (82.47 -95.19)	59.94 ± 5.42 (81.62-88.9)	0.07
BMI (Kg/M2)	24.82±1.58 (24.22-25.52)	24.5±1.52 (23.93-25.06)	24.68±1.42 (24.46-25.12)	0.70

Table: 5 shows the mean age and BMI of the participants within groups and between the groups were not significant (p>0.05) BMI-Body mass index.

Table:6 Metabolic profile variables among PCOS non-obese patients				
Metabolic variables	**Group II A**	**Group II B**	**Group II C**	***p*-value**
Serum Cholesterol	183 ± 22.01 (174- 191)	209 ± 19.93 (201 – 216)	222 ± 39.95 (210 - 235)	**<0.01****
Triglycerides	114 ± 27.95 (104-125)	170± 12.29 (161-185)	184 ± 33.32 (174-193)	**<0.01****
HDL	26 ± 8.06 (22.72 – 27.27)	45.5 ± 8.90 (43.26 -47.73)	19.95 ± 8.56 (17.15-22.75)	**<0.01****
LDL	73.34± 24.56 (64-82)	123± 14.56 (118-134)	200 ± 29.88 (191-210)	**<0.01****
VLDL	14.79 ± 3.84 (13.34-16.26)	22.83 ± 3.38 (21.59-24.07)	31.58 ± 6.72 (29.46-33.7)	**<0.01****
HbA1C	5.47 ± 0.41 (5.32-5.69)	6.39 ± 0.21 (6.28-6.49)	6.86 ± 0.48 (6.71-7.01)	**<0.01****
RBS	76.27 ± 11.21(71.81-80.7)	104± 9.21(100-108.26)	185 ± 41.91(172-191)	**<0.01****
Insulin	21.35 ± 12.45 (16.61-20.01)	42.96 ± 6.91(40.68-45.28)	35.82 ± 8.25 (33.32-38.43)	**<0.01****

Table 6: Represents the data of Metabolic variables of subgroups that all variables are significantly decreased in group IIA (p.0.01**) except HDL, even less in group IIC. But, Group IIC has significantly higher metabolic variables than the other two groups.

Table:7- Endocrine profile variables among PCOS with non-obese patients				
Endocrine variables	**Group II A**	**Group II B**	**Group II C**	***p*-value**
LH	12.11 ± 4.45 (10.03-14.18)	3.80 ± 2.13 (1.59 – 6.08)	26.28 ± 2.14 (25.67 – 27.09)	**<0.01****
FSH	6.02 ± 3.17 (4.81-7.23)	2.23± 1.70 (0.81-2.53)	13.65± 2.04 (13.05-14.29)	**<0.01****
Testosterone	44.30 ± 24.57 (34.95- 53.65)	82.71 ± 21.45 (74.71 -90.71)	109.18 ± 59.68 (79.07-135.92)	**0.04***
Vitamin D	39.17 ± 8.24 (36.05- 42.31)	14.31 ± 8.52 (9.61 -18.97)	60.85 ± 10.35 (50.54-69.32)	**<0.01****

Table 7: Endocrine profile variables among PCOS with non-obese patients, which shows the hormonal variables are significantly reduced in Group IIB, whereas Testosterone is elevated than in the other two groups(p>0.01**).

Table:8 Fibrinolytic profile variables among PCOS with non-obese patients				
Fibrinolytic variables	**Group II A**	**Group II B**	**Group II C**	***p*-value**
Fibrinogen	327 ± 91.38 (292-361)	455 ± 128 (407 – 503)	604 ± 102 (572 – 637)	**<0.01****
Plasminogen	15.06 ± 2.52 (14.1-16.02)	22.57± 5.07 (20.67-24.46)	52.37± 16.55 (47.07-57.52)	**<0.01****
D Dimer	7.77 ± 1.89 (5.64- 9.34)	25.55 ± 18.12 (18.78 -32.31)	64.35± 33.14 (53.84-74.81)	**<0.01****

Table 8 represents the data of Fibrinolytic profile variables among non-obese PCOS patients, which shows Fibrinogen, Plasminogen, and D-dimer are more statistically significant in group IIB than the other two groups, which have reduced.

Table:9 Comparison of Baseline, Metabolic, Endocrine, and Fibrinolytic variables between obese and non-obese women with PCOS			
	Obese group (*n*-100)	**Nonobese group (*n*-100)**	***p*-value**
Baseline characteristics			
Age	31.45 ± 3.55	32.75 ± 5.73	0.24
Height	159 ± 5.86	162 ± 6.47	0.12
Weight	88.6 ± 12.99	64.42 ± 6.42	**<0.01****
BMI	30.16 ± 2.35	24.67± 1.48	**<0.01****
Metabolic profile			
Cholesterol	257 ± 33.47	188 ± 32.48	**<0.01****
Triglycerides	179 ± 15.86	159 ± 18.46	**0.05***
HDL	44.08 ± 18.92	39.37 ± 13.49	**0.05***
LDL	161 ± 25.41	140 ± 59.49	**0.03***
VLDL	25.39 ± 6.44	24.09 ± 8.63	0.46
RBS	145± 39.99	133 ± 55.78	0.38
HbA1C	7.77 ± 3.29	6.32 ± 1.87	**0.04***
Insulin	34.7 ±7.17	32.05±12.55	**0.49**
Endocrine Profile			
LH	20.06± 18.45	15.47 ± 10.37	**0.03***
FSH	10.68 ± 9.97	7.87 ± 5.68	**0.05***
Testosterone	82.53 ± 24.52	72.46 ± 36.57	**0.02***
Vitamin D	23.37 ±13.25	40.60 ± 20.54	**<0.01****
Fibrinolytic profile			
Fibrinogen	550 ± 98.46	479 ± 157	**<0.01****
Plasminogen	33.27 ± 17.6	30.12 ±20.31	0.87
D Dimer	58.58 ± 27.12	30.54 ± 15.46	**<0.01****

Table: 9 -represents the Comparison of Baseline, Metabolic, Endocrine, and Fibrinolytic variables between obese and non-obese women with PCOS, all variables of group II are significantly lowered than group I. VLDL, RBS, and Plasminogen did not show any statistical variation(p>0.05). Association of BMI with all variables not shown any statistical correlation.

The study participants were divided into obese and non-obese women with PCOS. The obese women were divided into IA (n-6), IB (n-34), and IC (n-40), whereas non-obese women were divided into IIA (n-32), IIB (n-35), and IIC (n-33) respectively, based on the protocol. The mean age of the participants within and between groups was insignificant, as shown in tables -1 & 5 (p>0.05). The demographic variables, like weight within subgroups of groups I and II, were insignificant, as depicted in table - 9. However, Group I's BMI (30.16 ± 2.35) is significantly higher than Group II BMI (24.67± 1.48, p>0.01**). Table -2 shows the metabolic variables among subgroups of group I, which are significantly different (p>0.01**) in Group IA than in group IB and IC, except for cholesterol(p-0.89). The triglycerides, VLDL, and HbA1C, decreased in Group IA, whereas HDL and insulin were reduced in group IB. In addition, RBS and LDL were shown to have a significant reduction in group IC. Table – 3 shows LH, FSH, and vitamin – D levels were drastically decreased in group IB. In contrast, Testosterone was less in group IA than in the other two groups, respectively, which has a statistical significance (p>0.01**). Fibrinolytic variables like fibrinogen, Plasminogen, and D dimer are significantly higher in group IC than in the other two subgroups (p>0.01**), as shown in Table - 4. Table – 6 reveals that the metabolic variables of group II subgroups significantly decreased in group IIA (p>0.01**) except for HDL, even less in group IIC. But, group IIC has significantly higher metabolic variables than the other two groups. The hormonal variables are significantly reduced in group IIB whereas Testosterone is elevated than in the other two groups (p>0.01**), as shown in Table - 7. Fibrinogen,

Plasminogen, and D – dimer was shown to be statistically significant group IIB than the other two groups, which have reduced as shown in table – 8. Table – 9 compares all variables between two major groups evaluated cumulatively. All variables of group II are significantly lower than group I, including demographic, metabolic, endocrine, and fibrinolytic variables. However, VLDL, RBS, and Plasminogen showed no statistical variation (p>0.05). We have also evaluated the association of BMI with all variables, which had not shown any statistical correlation.

5. DISCUSSION

The current study was initiated to reveal the effect of BMI and drug dosage on metabolic, endocrine, and fibrinolytic variables among women with PCOS. PCOS patients reported classical manifestations with reproductive changes like anovulation, amenorrhoea, and menorrhagia. The masculinizing features are alopecia, hirsutism, acne, and hyperandrogenism[23]. The metabolic changes are impaired insulin resistance, glucose intolerance, and hyperlipidemia. The endocrine changes are elevated LH, FSH & Testosterone, and a significant reduction in vitamin D[24]. In addition, the thrombotic tendency also increases which elevates the relevant parameters[25]. All variables mentioned above are significantly higher in obese women compared with non-obese women with PCOS confirming their association with BMI and the occurrence of PCOS. The effective medicine to treat PCOD for preventing further consequences is the usage of metformin and OCP. Our study results outline that women with PCOS have a better outcome with metformin in obese patients and combined metformin and OCP therapy is effective in non-obese patients, which is similar and in the same trend as the previous studies conducted on PCOS[26,27]. PCOS is multifactorial in the onset of clinical manifestations. However, in obesity, PCOS is remarkably high, especially at an early age.Saxena et.al (2012) postulated the relationship between BMI and PCOS. The weight and BMI innately have insulin resistance which increases intrinsic insulin secretion as a compensatory mechanism and is the main cause of the etiopathogenesis of PCOS. Hyperinsulinemia influences the hypothalamic-pituitary-gonadal axis to elevate gonadotrophins (LH, FSH), resulting in irregular anovulatory cycles[28]. Bathena et.al (2011) has reported that the liver decreases the synthesis of androgen-binding protein due to insulin resistance elevating the free androgen. As a result, it enters the ovary to produce the weak androgens that are responsible for masculinizing features (Hirsutism, Acne) in PCOS. Furthermore, these hormones are converted to estrogen due to aromatase activity, increasing the endometrial cells to cause endometrial hyperplasia. The results of the present study with elevated LH FSH and testosterone levels especially in obese women are similar to previous studies that altered hormonal regulations[29]. Obesity is a significant contributor to the pathogenesis of PCOS which results in metabolic manifestations. Our results have shown that all metabolic variables are significantly higher especially hypercholesterolemia and hyperlipidemia, especially elevated LDL. Our results are in the same trend as Diamanti et.al (2012) stated that impaired glucose tolerance and diabetes mellitus were more common in the obese PCOS group than in the non-obese group, with rates of 41.9% and 8.06%, respectively [30]. In addition, women with PCOS experience issues with hemostasis regulation. An elevated plasma propensity to produce thrombin and impaired fibrinolysis due to elevated plasma levels of fibrinolytic inhibitors are both linked to a diagnosis of PCOS[31]. In addition, it increases the risk of vascular thrombosis and cardiovascular morbidities. Adali E et al. (2010) and Sampson et al. (1996) reported similar findings to our study on prothrombotic hyperactivity and cardiovascular disease[32,33]. However, it is debatable whether the hemostatic changes seen in women with PCOS are primarily related to the elevated BMI PCOS or whether they are primarily related to PCOS as with elevated testosterone levels as reported by Pruller et al. (2012) in their study outcomes[34]. Our study also reports that metformin is highly effective in treating women with PCOS, especially those with high BMI compared with normal BMI. But the previous studies (Eloise et al. 2020) have shown uncertain results that insulin resistance, glucose intolerance, and altered lipid profile variables can be improved. In contrast, OCP has produced better results in optimal fibrinolytic and reproductive hormones[35]. However, combined usage of metformin and OCP did not provide beneficial results, which could be attributed to other confounding factors involved in the disease process of PCOS. The current study has shown the pathway for effectively controlling BMI, which could restore metabolic variables and hormonal imbalance in women with PCOS.

6. LIMITATIONS

There are certain limitations to the current study. We did not choose healthy volunteers as a separate control group as a reference to compare the extent of severity and usefulness of the drug therapy. We had also yet to focus on radiographic examination, which could provide additional information for new insights into the outcome. The duration and severity of PCOS were not considered in the statistical analysis.

7. CONCLUSION

The present study has revealed that obesity significantly impacts PCOS, and metformin has shown more promising results than OCP and combined usage. It is more effective to treat patients with normal BMI than obese women with PCOS. Further studies are warranted to strengthen the outcome and to provide new insights into PCOS with appropriate treatment modalities to reduce comorbidities.

8. ETHICAL CONSIDERATIONS

The research proposal of this study was studied and approved by the Institutional Ethics committee of the host institution.

9. ACKNOWLEDGMENT

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10. AUTHORS CONTRIBUTION STATEMENT

Dr B.Vijayalakshmi designed the study and gave the article structure, and Dr Yogananda reddy. I provided inputs for the study, and A.Swathi gathered data and wrote and modified the article. Finally, all three authors discussed and analyzed the results and contributed to the final version of the manuscript.

11. CONFLICT OF INTEREST

Conflict of interest to declared none.

12. REFERENCES

1. Wolf WM, Wattick RA, Kinkade ON, Olfert MD. Geographical prevalence of polycystic ovary syndrome as determined by region and race/ethnicity. Int J Environ Res Public Health. 2018 Nov;15(11):2589. doi: 10.3390/ijerph15112589, PMID 30463276.
2. Roe AH, Dokras A. The diagnosis of polycystic ovary syndrome in adolescents. Rev Obstet Gynecol. 2011;4(2):45-51. PMID 22102927.
3. Goodman NF, Cobin RH, Futterweit W, Glueck JS, Legro RS, Carmina E et al. 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. Endocr Pract. 2015 Nov 1;21(11):1291-300. doi: 10.4158/EP15748. DSC, PMID 26509855.
4. Escobar-Morreale HF. Polycystic ovary syndrome: definition, aetiology, diagnosis and treatment. Nat Rev Endocrinol. 2018 May;14(5):270-84. doi: 10.1038/nrendo.2018.24, PMID 29569621.
5. Rossmanith WG, Wirth U, Benz R, Wolf AS. Endocrine dynamics during pulsatile GnRH administration in patients with hypothalamic amenorrhea and polycystic ovarian disease. Gynecol Endocrinol. 1989 Jan 1;3(1):21-34. doi: 10.3109/09513598909152449, PMID 2658471.
6. Targher G, Zoppini G, Bonora E, Moghetti P. Hemostatic and fibrinolytic abnormalities in polycystic ovary syndrome. Semin Thromb Hemost. 2014;40(5):600-18. doi: 10.1055/s-0034-1384512, PMID 25000958.
7. Słopień R, Lewandowski K, Kolacz E, Zawilska K, Warenik-Szymankiewicz A. Comparison of fibrinolytic and metabolic system parameters in obese patients with polycystic ovary syndrome and women with simple obesity. Gynecol Endocrinol. 2006 Jan 1;22(11):651-4. doi: 10.1080/09513590601005805, PMID 17145652.
8. Glueck CJ, Goldenberg N. Characteristics of obesity in polycystic ovary syndrome: etiology, treatment, and genetics. Metabolism. 2019 Mar 1;92:108-20. doi: 10.1016/j.metabol.2018.11.002, PMID 30445140.
9. Falsetti L, Gambera A, Andrico S, Sartori E. Acne and hirsutism in polycystic ovary syndrome: clinical, endocrine–metabolic and ultrasonographic differences. Gynecol Endocrinol. 2002 Jan 1;16(4):275-84. doi: 10.1080/gye.16.4.275.284, PMID 12396556.
10. Ciampelli M, Fulghesu AM, Lanzone A. Comment on "Prevalence and predictors of risk for type 2 diabetes mellitus and impaired glucose tolerance in polycystic ovary syndrome". J Clin Endocrinol Metab. 1999 Aug 1;84(8):2974-5. doi: 10.1210/jcem.84.8.5939-3, PMID 10443707.
11. Wijeyaratne CN, Seneviratne Rde A, Dahanayake S, Kumarapeli V, Palipane E, Kuruppu N et al. Phenotype and metabolic profile of South Asian women with polycystic ovary syndrome (PCOS): results of a large database from a specialist Endocrine Clinic. Hum Reprod. 2011 Jan 1;26(1):202-13. doi: 10.1093/humrep/deq310, PMID 21098627.
12. Norman RJ, Dewailly D, Legro RS, Hickey TE. Polycystic ovary syndrome. Lancet. 2007 Aug 25;370(9588):685-97. doi: 10.1016/S0140-6736(07)61345-2, PMID 17720020.
13. Boumosleh JM, Grundy SM, Phan J, Neeland IJ, Chang A, Vega GL. Metabolic concomitants of obese and non-obese women with features of polycystic ovarian syndrome. J Endocr Soc. 2017 Dec 1;1(12):1417-27. doi: 10.1210/js.2017-00323, PMID 29264465.
14. Al-Zubeidi H, Klein KO. Randomized clinical trial evaluating metformin versus oral contraceptive pills in the treatment of adolescents with polycystic ovarian syndrome. J Pediatr Endocrinol Metab. 2015 Jul 1;28(7-8):853-8. doi: 10.1515/jpem-2014-0283, PMID 25781525.
15. Panidis D, Georgopoulos NA, Piouka A, Katsikis I, Saltamavros AD, Decavalas G et al. The impact of oral contraceptives and metformin on anti-Müllerian hormone serum levels in women with polycystic ovary syndrome and biochemical hyperandrogenemia. Gynecol Endocrinol. 2011 Aug 1;27(8):587-92. doi: 10.3109/09513590.2010.507283, PMID 20836726.
16. Gambineri A, Patton L, Altieri P, Pagotto U, Pizzi C, Manzoli L et al. Polycystic ovary syndrome is a risk factor for type 2 diabetes: results from a long-term prospective study. Diabetes. 2012 Sep 1;61(9):2369-74. doi: 10.2337/db11-1360, PMID 22698921.
17. Dumesic DA, Lobo RA. Cancer risk and PCOS. Steroids. 2013 Aug 1;78(8):782-5. doi: 10.1016/j.steroids.2013.04.004, PMID 23624028.
18. Dokras A. Noncontraceptive use of oral combined hormonal contraceptives in polycystic ovary syndrome—risks versus benefits. Fertil Steril. 2016 Dec 1;106(7):1572-9. doi: 10.1016/j.fertnstert.2016.10.027, PMID 27817838.
19. Eshre R, ASRM. Revised 2003 consensus on diagnostic criteria and long-term health risks related to polycystic ovary syndrome (PCOS). Hum Reprod. 2004 Jan;19(1):41-7. doi: 10.1093/humrep/deh098, PMID 14688154.
20. Kumar S, Banerjee A, Mahto M, Ranjan A, Singh M, Takhelmayum R. Evaluation of relationship between hyperuricemia and lipid profile. Evaluation. 2018 Jun;4(6).
21. Park J, Lee S, Kim Y, Choi A, Lee H, Lim J et al. Comparison of four automated carcinoembryonic antigen immunoassays: Advia Centaur XP, ARCHITECT I2000sr, Elecsys E170, and Unicel Dxi800. Ann Lab Med. 2018 Jul;38(4):355-61. doi: 10.3343/alm.2018.38.4.355, PMID 29611386.
22. Yildiz BO, Haznedaroğlu IC, Kirazli S, Bayraktar M. Global fibrinolytic capacity is decreased in polycystic ovary syndrome, suggesting a prothrombotic state. J Clin Endocrinol Metab. 2002 Aug 1;87(8):3871-5. doi: 10.1210/jcem.87.8.8716, PMID 12161525.
23. Franks S. Polycystic ovary syndrome. N Engl J Med. 1995 Sep 28;333(13):853-61. doi: 10.1056/NEJM199509283331307, PMID 7651477.
24. Dunaif A, Book CB. Insulin resistance in the polycystic ovary syndrome. Clin Res Diabetes Obes. 1997:249-74.
25. Godtfredsen ACM, Sidelmann JJ, Gram JB, Andersen M, Glintborg D. Fibrin lysability is associated with central obesity and inflammation in women with polycystic ovary syndrome. Acta Obstet Gynecol Scand. 2020 Aug;99(8):1078-84. doi: 10.1111/aogs.13825, PMID 32048272.

26. Yang YM, Choi EJ. Efficacy and safety of metformin or oral contraceptives, or both in polycystic ovary syndrome. Ther Clin Risk Manag. 2015;11:1345-53. doi: 10.2147/TCRM.S89737, PMID 26366087.
27. Essah PA, Arrowood JA, Cheang KI, Adawadkar SS, Stovall DW, Nestler JE. Effect of combined metformin and oral contraceptive therapy on metabolic factors and endothelial function in overweight and obese women with polycystic ovary syndrome. Fertil Steril. 2011 Aug 1;96(2):501-504.e2. doi: 10.1016/j.fertnstert.2011.05.091, PMID 21733508.
28. Saxena P, Prakash A, Nigam A. Effect of metformin therapy on 2-h post-glucose insulin levels in patients of polycystic ovarian syndrome. J Hum Reprod Sci. 2010 Sep;3(3):139-42. doi: 10.4103/0974-1208.74156, PMID 21234175.
29. Bhathena RK. Insulin resistance and the long-term consequences of polycystic ovary syndrome. J Obstet Gynaecol. 2011 Feb 1;31(2):105-10. doi: 10.3109/01443615.2010.539722, PMID 21281021.
30. Diamanti-Kandarakis E, Dunaif A. Insulin resistance and the polycystic ovary syndrome revisited: an update on mechanisms and implications. Endocr Rev. 2012 Dec 1;33(6):981-1030. doi: 10.1210/er.2011-1034, PMID 23065822.
31. Srinag L, Maruthy KN, Kareem SK, Siva Kumar AV, Kumar K, Preetham Gurja J. Impact of overweight on cognition and psychomotor skills among children with overweight. Obes Med. 2020 Jun 1;18:100191. doi: 10.1016/j.obmed.2020.100191.
32. Adali E, Yildizhan R, Kurdoglu M, Bugdayci G, Kolusari A, Sahin HG. Increased plasma thrombin-activatable fibrinolysis inhibitor levels in young obese women with polycystic ovary syndrome. Fertil Steril. 2010 Jul 1;94(2):666-72. doi: 10.1016/j.fertnstert.2009.03.037, PMID 19368913.
33. Sampson M, Kong C, Patel A, Unwin R, Jacobs HS. Ambulatory blood pressure profiles and plasminogen activator inhibitor (PAI-1) activity in lean women with and without the polycystic ovary syndrome. Clin Endocrinol (Oxf). 1996 Nov;45(5):623-9. doi: 10.1046/j.1365-2265.1996.00863.x, PMID 8977761.
34. Prüller F, Raggam RB, Posch V, Almer G, Truschnig-Wilders M, Horejsi R et al. Trunk weighted obesity, cholesterol levels and low grade inflammation are main determinants for enhanced thrombin generation. Atherosclerosis. 2012 Jan 1;220(1):215-8. doi: 10.1016/j.atherosclerosis.2011.09.035, PMID 22035573.
35. Fraison E, Kostova E, Moran LJ, Bilal S, Ee CC, Venetis C et al. Metformin versus the combined oral contraceptive pill for hirsutism, acne, and menstrual pattern in polycystic ovary syndrome. Cochrane Database Syst Rev. 2020 Aug 13;8(8):CD005552. doi: 10.1002/14651858.CD005552.pub3, PMID 32794179.