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A Study of Insulin Resistance, Polycystic Ovary Syndrome & Type-2 Diabetes Mellitus in Udaipur, Rajasthan

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Abstract
INTRODUCTION
Diabetes mellitus is a worldwide epidemic. Its prevalence and incidence are steeply growing with an estimated 425 million of people currently having diabetes. The great social burden of the disease is worsened by the huge number of people with prediabetes (i.e., impaired fasting glucose and/or impaired glucose tolerance) who are at high risk of developing it. In addition, one in two adults with diabetes (about 212 million of people) is undiagnosed.
MATERIAL AND METHODS
The study will be carried out jointly in the Department of Biochemistry and Department of Obstetric & Gynaecology, R.N.T Medical College & Hospital, Udaipur. A total of 170 subjects belonging to polycystic ovary syndrome will be classified. Women with PCOD should be interviewed of their name, address, age, socio-economic status, menstrual history. Diagnosed polycystic ovarian syndrome, age ranging from 18-40 years.
RESULT
In our study 63.53% study population is urban and 36.47% population is rural. The mean age of our study population is 24.75years. We calculated Hormonal profile of our study population. Here, mean LH is 90.39 mU/ml. Mean FSH is 23.24 mlU/ml. Mean Testosterone, Estrogen and Progesterone are 2.86 ng/ml, 59.82 and 2.87 respectively. We found that mean FBS is 95.83. Mean Insulin of our study population is 7.24 and mean HOMA IR is 31.25.
CONCLUSION
We found that PCOS women had significantly high levels of LH, LH/FSH, TT, fasting insulin levels and HOMA-IR when compared to the control group and non-PCOD-D group which denotes their role in PCOS.

Keywords: *PCOS, Hormonal profile, T2DM1.*

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I. Introduction

Diabetes mellitus is a worldwide epidemic. Its prevalence and incidence are steeply growing with an estimated 425 million of people currently having diabetes [AA1]. The great social burden of the disease is worsened by the huge number of people with prediabetes (i.e., impaired fasting glucose and/or impaired glucose tolerance) who are at high risk of developing it. In addition, one in two adults with diabetes (about 212 million of people) is undiagnosed. Several risk factors for the development of the disease have been well recognized. Some risk factors are gender specific, such as gestational diabetes mellitus (GDM) and polycystic ovary syndrome (PCOS). PCOS is defined by its reproductive features of hyperandrogenism, chronic oligoanovulation, and/or polycystic ovarian morphology [AA2]. Its prevalence is 5–15%, depending on the diagnostic criteria applied [AA3].

Tis hormonal disturbance is a critical factor associated with the syndrome. Various studies proved the presence of PCOS in women who are diagnosed with T2DM (Type 2 Diabetes Mellitus) though this is not clearly explored area in terms of molecular biology [D3, 4]. PCOS is associated with metabolic abnormalities, including insulin resistance (IR) and β-cell dysfunction [AA2]. Sometimes hyperglycemia may induce the excess production of ROS (reactive oxygen species) which eventually results in the malfunction of the mitochondria [5]. Cells and their cellular organs i.e. mitochondria play a vital role in the production of ATP required in a number of cellular processes, for instance glucose metabolism. T2DM has an association with maternal mitochondrial inheritance in addition to PCOS [6]. During glucose metabolism, some researchers suggested that the production of insulin might signifcantly vary as per the functioning of mitochondria [D7–9]. The result of IR is hyperinsulinemia, which has a central role in the pathogenesis of androgen excess in PCOS. Indeed, insulin acts as a cogonadotropin to increase luteinizing hormone (LH)-induced androgen synthesis in theca cells [AA4] and can enhance gonadotropin-releasing hormone (GnRH)-mediated gonadotropin secretion [AA5]. Insulin also reduces hepatic sex hormone binding globulin (SHBG) synthesis, thereby increasing the levels of bioavailable androgens [AA6].

The defect of insulin action was quantified in PCOS using the euglycemic clamp [AA7]. Insulin action was reduced by 35–40% in both lean and obese women with PCOS compared to control women of similar age and body composition [AA8].

Recent studies in daughters of women affected by PCOS have found evidence for pancreatic β-cell dysfunction prior to menarche [AA9]. Genetic analyses showed that metabolic abnormalities such as obesity and IR contribute to the pathogenesis of PCOS [AA10]. Women with PCOS have a higher cardiometabolic risk compared with women without ovarian problems [AA11].

In women with PCOS, dysglycemia typically consists of impaired glucose tolerance [AA12], its prevalence being of almost 30% in both adult women [AA13] and affected adolescents [14]. For this reason, PCOS is associated with a two times increased risk for type 2 diabetes (T2D) [AA15].

Despite the very clear association between PCOS and dysglycemia, few studies have explored the continuum of glycemic alterations leading from minor glucose abnormalities to overt diabetes. The purpose of this study to assess the hormonal profile of PCOD women with T2DM.

II. Material And Methods

The study will be carried out jointly in the Department of Biochemistry and Department of Obstetric & Gynaecology, R.N.T Medical College & Hospital, Udaipur. A total of 170 subjects belonging to polycystic ovary syndrome will be classified. All PCOD women were underwent a complete history and physical examination. Women with PCOD should be interviewed of their name, address, age, socio-economic status, menstrual history.

Inclusion criteria:

1. Diagnosed polycystic ovarian syndrome, age ranging from 18-40 years. **2.** Women with PCOD Willing to have physical examinations like Weight, Height, BMI, W/H ratio, Blood Pressure. 3. Polycystic ovary syndrome (PCOS) associated with Diabetes. 4. Polycystic ovary syndrome (PCOS) associated with Obesity.

Exclusion criteria: 1. Women with diagnosed adrenal hyperplasia. 2. Women with diagnosed androgen secreting neoplasm. 3. Women with hyperprolactinemia and other infertility cause.

III. Result

The study will be carried out jointly in the Department of Biochemistry and Department of Obstetric & Gynaecology, R.N.T Medical College & Hospital, Udaipur. A total of 170 subjects belonging to polycystic ovary syndrome will be classified. We found that majority (44.71%) of patients are of age group 21-25 years followed by 32.94% population in 26-30 years. 14.12% study population are in less than 20 years age group and 8.24% population are of >30 years age group. The mean age of our study population is 24.75years. In our study 63.53% study population is urban and 36.47% population is rural.

Table 1: Distribution of study population according Weight and W/H ratio.

Parameter	Mean	SD
Weight	45.04	5.95
W/H Ratio	0.79	0.03

In table 1, we found that mean weight of our study population is 45.04kg and mean waist to height ratio is 0.79cm. In our study mean BMI for overweight category is 23.8 followed by 20.64 in Normal category and 16.32 in underweight category.

Table 2: Distribution of study population according diet.

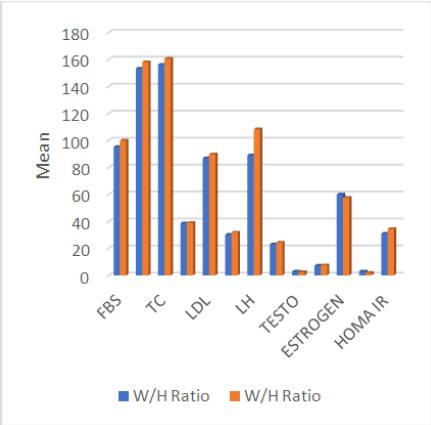
Diet	No. of Patients	Percentage
Vegetarian	120	70.59
Occasional Non-Vegetarian	24	14.12
Non-Vegetarian	16	9.41
Vegetarian/ FF	7	4.12
Non-Vegetarian/ FF	3	1.76
Total	170	100.00

In our study majority (70.59%) patients are vegetarian followed by 14.12% study population of Occasional Non-Vegetarian. 9.41% study population are non-vegetarian followed by 4.12% and 1.76% population of vegetarian/FF and Non-vegetarian/FF.

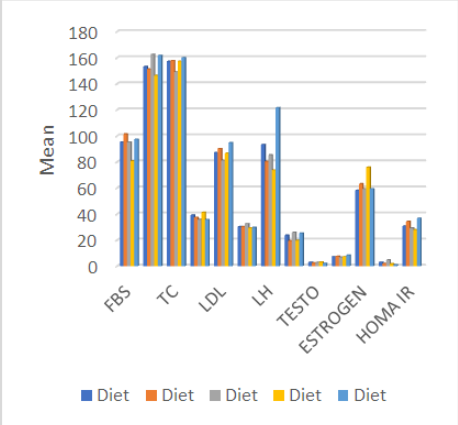
Table 3: Distribution of study population according Hormonal Profile.

Hormonal Profile	Mean	SD
LH (mU/ml)	90.39	45.6
FSH(mlU/ml)	23.24	17.8
TESTO(ng/ml)	2.86	2.13
ESTROGEN	59.82	19.28
PROGEST	2.87	3.29

In table 3, we calculated Hormonal profile of our study population. Here, mean LH is 90.39 mU/ml. Mean FSH is 23.24 mlU/ml. Mean Testosterone, Estrogen and Progesterone are 2.86 ng/ml, 59.82 and 2.87 respectively. We found that mean FBS is 95.83. Mean Insulin of our study population is 7.24 and mean HOMA IR is 31.25. In graph 1, we calculated various biochemical, lipid profile and hormonal parameter according to W/H Ratio of our study group. We found significant difference in FBS, VLDL, LH, Testosterone and Progesterone. There is no-significant difference between these parameters as p value is >0.05.



Graph 29: Correlation of various hormonal and biochemical factors with W/H Ratio. In graph 2, we calculated various biochemical, lipid profile and hormonal parameter according to Diet of our study group. There is no-significant difference between these parameters.



Graph 2: Correlation of various hormonal and biochemical factors with Diet.

IV. Discussion

A number of endocrine abnormalities such as dyspidemia, hyperglycemia and hyperinsulinemia and other such metabolic syndrome occur in PCOS patients [D15, 16]. Since insulin resistance and mitochondrial dysfunction has a correlation between each other, it plays a major role in the pathogenesis of PCOS. In glucose metabolism, the mitochondrial function plays a critical role due to which T2DM has the potential pathogenic roles in PCOS. In a number of diseases, the researchers identifed point mutations in the functional genes that encode mt-tRNAs [D17, 18].

We found that majority (44.71%) of patients are of age group 21-25 years followed by 32.94% population in 26-30 years. 14.12% study population are in less than 20 years age group and 8.24% population are of >30 years age group. The mean age of our study population is 24.75years. A recent study by Kumar A N et al [B] found that age range of PCOS patients are 19-35 years. The mean age of controls was 26.7 ± 3.4 years and for PCOS patients, it was 25.6 ± 3.9 years (P=0.06). Out of 80 PCOS women recruited for the study, 42 women were in the age range of 20 to 25 years, 29 women were 25 to 30 years of age, and 9 women were 30 to 35 years of age. These finding are agreed with Naidu et al. (B2), Zhang et al. (B16).

In table 1, we found that waist to height ratio is higher as age group increased. 0.84 W/H ratio is found in >30years age group followed by 0.8 in 26-30 years age group. Mean W/H ratio for 21-25 years and 15-20 years age group is 0.78 and 0.76 respectively. Here, we also calculated various biochemical, lipid profile and hormonal parameter according to W/H Ratio of our study group. We found significant difference in FBS, VLDL, LH, Testosterone and Progesterone. There is no-significant difference between these parameters as p value is >0.05. A similar study by Sachdeva G et al [I] found that waist circumference mean values were for all women 79.5 cm (SD=9.46), women with PCOS 80.49 cm (SD=9.47), controls 76.6 cm (SD=8.9), with a p-value of 0.017. However, there were significant differences in the waist-circumference categories (normal, overweight, obese); mainly, the obese status n=40 (25.2%) compared to the obese of the control group n=4 (7.4%), p-value=0.018. Codner E et al [E] found that waist-to-hip ratio were higher in PCOS women than in DM1PCOS and controls. Women with DM1PCOS had higher waist-to-hip ratio than the control group, despite similar BMI.

Insulin resistance and hyperinsulinemia are factors that play an important role in the pathogenesis of PCOS. In the present study we have shown predominant insulin resistance, hypothyroidism, dyslipidemia, and an increased LH/FSH ratio in women with POCS compared to control women (B2, 5, 6). The direct effect of testosterone adipocytes has been investigated and induction of androgen receptor mediated insulin resistance via testosterone was established (B27). Hyperandrogenism is due to increased LH and low-to-normal FSH levels. Due to the increase in LH and estrogen, FSH is

negatively inhibited. Theca cell hyperplasia ensues, leading to hyperandrogenemia that clinically presents as hirsutism. BMI has a negative association with the baseline levels of LH in PCOS patients. We observed similar association in the present study, which supported results from previous studies (B27, 28). A similar study by Saeed N A H et al [D] found that PCOS women had signifcantly high levels of LH, LH/FSH, TT, fasting insulin levels and HOMA-IR when compared to the control group and non-PCOD-D group which denotes their role in PCOS. The mutations were mostly observed in PCOS study sample individuals though they were found in HC group (two mutations) and non-PCOS no diabetic group (one mutation). A similar study by Codner et al [E] found that total testosterone levels are similar in both groups of hyperandrogenic women but that diabetic women exhibit lower levels of androstenedione, LH/FSH, and follicle number than nondiabetic PCOS women. In addition, SHBG levels in women with PCOS and DM1 were within normal range.

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