Relational Analysis of Anthropometric Measurements, Biochemical Parameters, Clinical Profile and Hormonal Levels Of Obese Versus Non Obese Women with PCOS in Kashmir Valley

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ABSTRACT:

BACKGROUND:

During the past decade, our understanding of pathophysiology of PCOS (Polycystic Ovarian Syndrome) has undergone a remarkable Evolution. Despite our familiarity with this disease, Polycystic ovarian Syndrome (PCOS) Is considered as Multisystem Endocrinopathy. Some of it’s fundamental characteristics remain poorly recognized and understood. The present Study focuses on relational and Comprehensive analysis of the Anthropometric Measurements, Biochemical Parameters, Clinical Profile and Hormonal Levels of Obese versus Non obese women with PCOS (Polycystic ovarian syndrome) in Kashmir valley. Obesity was found to be one of the important factors that contribute to the development of long term risk of PCOS. In addition, increased obesity and abdominal adiposity further aggravate the clinical, hormonal and metabolic parameters in PCOS and if treated, can reverse most of these abnormalities to a clinically significant degree. Our study suggests that anthropometric parameters (Especially BMI and WHR) are significantly correlated with lipid profile in PCOS patients confirming the importance of early treatment of obesity to prevent further complications in the future. We wanted to study anthropometric measurements, the hormonal status and biochemical parameters in females diagnosed with PCOS. Study the correlation between them and compare them with controls. The present study on 146 patients including both obese and non obese PCOS cases and 70 controls revealed that Ferriman Gallway(FG) score of the obese PCOS was more as compared to non obese and normal controls. Hirusitism, acanthosis nigricans and alopecia was seen significantly raised in PCOS women in comparison to non obese PCOS and controls, giving an indication of risk of hypertension in obese women. Fasting blood glucose level and one hour (1hour) glucose level was almost same for all three groups but two hour (2 hour) blood glucose levels were raised in obese cases in comparison to the non obese PCOS and controls. Hormonal analysis of our subjects revealed that lutenizing hormone (
LH) and (FSH) value, values of obese PCOS, non-obese PCOS and controls were almost same but testosterone levels was raised in PCOS cases but much raised in obese PCOS cases.

Index Terms: Polysyctic ovarian syndrome, BMI, Obesity, FG Score

1. INTRODUCTION:
Polycystic ovary syndrome [PCOS] is among the most common endocrine disorder, affecting more than 10 – 12% of women of reproductive age, mostly 18 – 45 years of age. Prevalence of PCOS in Kashmir is 41% among infertile which is significantly high. Most of the women with PCOS are hirsute with central obesity and overweight or obese by BMI standards. Several clinical features of PCOS are expressed differently in affected women. Women with PCOS are at a higher risk for a number of illness such as high blood pressure, diabetes mellitus, cardiovascular problems and cancer of the uterus, ovary and breast.

It has been suggested that PCOS may represent an early manifestation of the metabolic syndrome with cluster of abnormalities. PCOS women are characterized by using a high prevalence of numerous metabolic abnormalities, which are strongly motivated by the presence of obesity. Several research have absolutely confirmed that period abnormalities are more common in overweight than normal weight PCOS girls. With this background we have investigated clinical, hormonal and biochemical profile of PCOS Kashmiri women and normal healthy controls. Further we made a relational comparative analysis of all the parameters studied between obese PCOS and non-obese PCOS cases.

2. AIMS AND OBJECTIVES:-
A: To study the Anthropometric measurements, Biochemical parameters, clinical profile and hormonal levels of PCOS kashmiri women patients and controls.
B: To make a relational analysis between Anthropometric, biochemical clinical and hormonal profile of obese versus non-obese PCOS women.

3. SUBJECTS:- This was a case control study involving a total of 146 PCOS Cases and 70 Controls. Among 146 PCOS cases 76 were obese (BMI<30) and 70 were non-obese (BMI>21) Subjects were recruited from different Higher Secondary Schools, High Schools and different departments of University of Kashmir. The Controls had no history of any endocrinological disorder.

4. METHODOLOGY:-
4(I) HISTORY AND GENERAL EXAMINATION:-
All the women fulfilling the Rotterdam 2003 criteria for a diagnosis of PCOS as well as controls were made to fill a questionnaire involving the details of menstrual history like extent of hair growth, weight gain, acne and family history.
Anthropometric assessment of all women was done like measurement of height, weight, waist hip circumference ratio and detailed systemic examination. Hirsutism assessment was done using modified Ferriman-Gallway Score. A score of 8 out of a total of 36 is taken as significant. Moderate to severe acne was taken as a clinical feature of hyperandrogenemia. All patients were subjected to trans
abdominal ultrasonography (USG) to measure Ovarian Volume and morphology.

4 (II) SAMPLING AND INVESTIGATIONS:-
The blood samples were taken under aseptic conditions for the biochemical and hormonal analysis. The biochemical investigations involve [ TG], Total Cholesterol, Oral Glucose Tolerance test (OGTT). The Oral Glucose Tolerance test was performed after 10-12 hours overnight fasting with 75 grams of oral anhydrous glucose load dissolved in 300ml of water.

Samples were estimated on a semi automated biochemical analyser [ERBA- Manheim , Germany] by using Commercially available kits.

The blood samples for hormonal assay were collected on 2\textsuperscript{nd} Or 3\textsuperscript{rd} day of the follicular phase of either spontaneous or progesterone induced menstrual cycle.

The hormone estimation included:-

➢ T4 – to rule out hypothyroidism.
➢ TSH – to rule out hypothyroidism.
➢ PRL – to rule out prolactinoma.
➢ LH.
➢ FSH
➢ Testosterone.

Hormonal assay was done by radioimmunoassay [ T4, Testosterone ] and immuno-radiometric assays [TSH, LH and FSH] using commercial kits in duplicate and according to supplier protocol.

4(III) STATISTICAL ANALYSIS :-

Results were statistically analysed and data was expressed as mean ± SD. A P. Value of <0.05 was used as a criteria for statistical significance. For the analysis, Statistical Software Graph Pad Prism Version 5.0 was used.

1. RESULTS:-

All the Anthropometric parameters are compared in table 1. The mean BMI for obese PCOS, non obese PCOS and normal controls was 30.76 ± 1.73, 21.32 ± 2.73 and 24.1 ± 2.1 respectively and was very significant [ P = 0.0001]. Mean waist circumference of obese PCOS was increased in comparison to non – obese PCOS and normal controls. Systolic and Diastolic blood pressure was blood pressure was also seen to be increased in obese PCOS women.

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Mean ± SD n=76 (Obese)</th>
<th>Mean ± SD n =70 ( Controls)</th>
<th>P – Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean Age (years)</td>
<td>24.18 ± 5.28</td>
<td>21.03 ± 4.80</td>
<td>0.019</td>
</tr>
<tr>
<td>Age of Menarche (years)</td>
<td>12.28 ± 2.13</td>
<td>12.25 ± 1.88</td>
<td>0.970</td>
</tr>
</tbody>
</table>

TABLE.1 RELATION OF ANTHROPOMETRIC PARAMETRE BETWEEN OBESE PCOS AND NON PCOS AND CONTROLS .
Clinical examination of the cases revealed that 61 [79.53%] of obese PCOS and 49 [71%] of Non obese PCO Subjects were hirsute. 61 [79.53%] of obese PCOS and 47 [67%] of non obese PCOS cases had acne. 14 [18.66%] of obese PCOS and 9 [12%] of Non obese PCOS cases had Acanthosisnigricans. 52 [68%] of obese PCOS and 40 [57%] of non PCOS cases presented with alopecia.

Table 2. RELATION OF CLINICAL PARAMETRES OF OBESE PCOS AND NON OBESE PCOS

<table>
<thead>
<tr>
<th>Parametres</th>
<th>Obese PCOS n = 76</th>
<th>Non Obese PCOS n = 70</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hirsutism</td>
<td>79.53 %</td>
<td>71 %</td>
</tr>
<tr>
<td>Acne</td>
<td>79.53 %</td>
<td>67 %</td>
</tr>
<tr>
<td>Acanthosis</td>
<td>18.66 %</td>
<td>12 %</td>
</tr>
<tr>
<td>Alopecia</td>
<td>68 %</td>
<td>57 %</td>
</tr>
</tbody>
</table>

Luteinizing Hormone [LH] levels and FSH levels of Obese PCOS and non obese were raised as compared to Controls [10.06 ± 2.92 ,10.508 ± 1.53, 7.01 ± 3.05 IU/L], [7.03±- 2.73,7.89±2.53, 5.53±2.01] IU/L, respectively. However the testosterone levels were much raised in obese PCOS in
comparison to non obese PCOS and controls [ 63.1 ±21.24, 61.79±2.13, 26.32± 9.01] mg/dl respectively.

**TABLE:- 3 RELATION OF HORMONAL PARAMETERS OF OBESE , NON OBESE AND PCOS AND CONTROLS.**

<table>
<thead>
<tr>
<th>Parameters</th>
<th>Mean ± SD n = 76 (Obese)</th>
<th>Mean ± SD n=70 (Non obese)</th>
<th>Controls n=70</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>LH (IU/L)</td>
<td>10.06 ± 2.92 IU/L</td>
<td>10.508 ± 1.53 IU/L</td>
<td>7.01 ± 3.05 IU/L</td>
<td>0.0001</td>
</tr>
<tr>
<td>FSH (IU/L)</td>
<td>7.03 ± 2.73 IU/L</td>
<td>7.89 ± 1.53 IU/L</td>
<td>5.53 ± 2.01 IU/L</td>
<td>0.0005</td>
</tr>
<tr>
<td>TESTOSTERONE (mg/ml)</td>
<td>63.1 ± 21.24 mg/dl</td>
<td>61.79 ± 2.13 mg/dl</td>
<td>26.32 ± 9.01 mg/dl</td>
<td>0.019</td>
</tr>
</tbody>
</table>

Biochemical Variables estimated are shown in Table 4. Fasting Blood Glucose levels and one hour blood glucose levels in obese PCOS, Non obese PCOS and controls were within normal range i, e [89.36±10.91, 87.01±10.12, 87.99±10.219] mg/dl 1130.38±16.132, 124.22±14.53, 125.33±17.01 ]mg/dl respectively. However two hour blood (2h) blood glucose levels of obese PCOS was slightly raised in comparison to Non obese PCOS and controls [116.09 ±14.99,106.07±14.33, 103.23±10.29 ] mg/dl respectively. Cholesterol levels were also found to be raised in obese PCOS as compared to that of Non obese PCOS and controls. [174.13±28.01, 140.01±24.13, 143.13 ± 18 ] mg/dl. However serum triglyceride levels were in normal range in obese PCOS, Non obese PCOS and controls. [ 136.1 ± 27.01, 125.31±21.01, 109.09±24] mg /dl.

**TABLE:- 4 RELATION BETWEEN BIOCHEMICAL PARAMETERS OF OBESE PCOS , NON OBESE PCOS AND CONTROLS.**

<table>
<thead>
<tr>
<th>Parameters</th>
<th>Mean ± SD n=76 (Obese)</th>
<th>Mean ± SD n=70 (Non obese)</th>
<th>Controls n=70</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Blood fasting glucose</td>
<td>89.36 ± 10.91</td>
<td>87.01 ± 10.12</td>
<td>87.99 ± 10.0.219</td>
<td>0.829</td>
</tr>
<tr>
<td>Blood glucose 1hr</td>
<td>130.38 ± 16.132</td>
<td>124.22 ± 14.53</td>
<td>125.33 ± 17.01</td>
<td>0.950</td>
</tr>
<tr>
<td>Blood glucose 2hr</td>
<td>116.09 ± 14.99</td>
<td>106.07 ± 14.33</td>
<td>103.23 ± 10.29</td>
<td>0.0130</td>
</tr>
<tr>
<td>Cholesterol mg/dl</td>
<td>174.13 ± 28.01</td>
<td>140.01 ± 24.14</td>
<td>143.13 ± 17.9</td>
<td>0.0036</td>
</tr>
</tbody>
</table>
2. DISCUSSION:
A combination of many genetic and environmental risk factors lead to the occurrence of PCOS, that include obesity, lack of physical exercise, and a family history of someone with PCOS. PCOS has a multifactorial epidemiology and a synergistic effect of dietary environmental, genetic and lifestyle factors is being associated with its development. The contributing factors are not the same in different populations of the world and obesity is considered as a common risk factor. Our results demonstrated that the obese PCOS subjects had higher BMI, waist and hip circumference and compared to Non obese PCOS subjects. Also, the obese PCOS patients exhibited higher levels of hyperandrogenism. Significant correlation of BMI with waist and hip circumference in the present study further suggested that these parameters are important determinants of obesity in PCOS. Hyperandrogenism could be clinical (with hirsutism, alopecia, acne) or subclinical with only increase in the levels of serum testosterone and DHEA. The prevalence in PCOS varies from 21% to 86%. In our study 79.53 obese and 71% Non obese women and 18.66% controls had hirsutism. Also the mean FG score was higher in obese PCOS women than Non obese which was much higher than controls. Hirsutism is actually assessed through the (FG) Ferrima Gallway Score, which evaluates the presence of terminal hair in the upper lip, chin, chest, upper and lower back, upper and lower abdomen, thighs and arms. There was clear cut difference in occurrence of hirsutism between PCOS cases and controls and obese PCOS cases hirsutism was more than in non obese PCOS cases. Obese PCOS women had more FG Score that means their hair growth was more in comparison with non-obese PCOS women.

In our study, we demonstrated that the testosterone levels were raised in most of the PCOS cases. The levels of testosterone for all the PCOS cases was 59.5mg/dl. However, levels were higher in obese cases than non-obese ones. 17.06% of obese PCOS and 11% of non-obese PCOS cases had acanthosis nigrians which is closely related to insulin resistance. It represents acanthosis nigrians skin disorder commonly associated with hyperinsulinemia and insulin resistance. It prevalence in women with PCOS is not fully established and may vary from 5 to 5% depending on the case reported by the various studies. The frequency of the association between PCOS, acanthosis nigrians and Obesity has not been completely investigated but available data based solely on clinical skin examination indicate that it seems to be very high. Also 79.03% of obese PCOS and 66% of non-obese PCOS cases had acne. Sebaceous glands are also androgen dependent structures, with sebocytes being highly sensitive to androgen signalling, which is exacerbated in PCOS, leading to the development of acne and seborrhea. Androgens stimulate sebocyte proliferation especially in the mid back, forehead, and chin and secretion of sebum, a mixture of lipids including glycerides, squalene, free fatty acids [FFA], and cholesterol. Local bacteria further complicate the process by secreting lipolytic enzymes which break down Tri glycerides

<table>
<thead>
<tr>
<th>Triglycerides</th>
<th>136.15 ±76.59</th>
<th>125.36 ± 20.9</th>
<th>109.21 ± 23.8</th>
<th>0.0031</th>
</tr>
</thead>
</table>

| Triglycerides | 136.15 ±76.59 | 125.36 ± 20.9 | 109.21 ± 23.8 | 0.0031 |
produced in the sebocyte. The resulting FFA that are released into sebaceous ducts by apocrine glands are responsible for the characteristic odour observed in these patients.

A significant higher prevalence of Obesity, dyslipidemia and hypertension has been reported for Indian PCOS women. In our study we demonstrated that BMI for obese PCOS cases was higher than non-obese PCOS cases. A study reported that mean BMI for Indian PCOS women 27.5 Also waist circumference for obese group was higher than non-obese group. As per National Cholesterol Education Programme Adult Treatment Panel III [ NC EP ATP III] 2001 criteria waist circumference of greater than 88 cm represents central obesity. Also as per European Group for study of Insulin Resistance [EGIR] 1999 criteria waist circumference of greater than 80 cm represents central obesity. There is emerging evidence that women with PCOS have an elevated risk of being overweight and obese and have increased longitudinal weight gain compared with Community controls. A recent meta analysis has reported increased prevalence of overweight or Obesity, [1.96 Risk ratio; 95.6% confidence interval ( CI) 1.53 - 2.60] For women with PCOS compared with controls. Indeed Women with PCOS may have specific physiological or intrinsic barriers to maintain a healthy weight such as insulin resistance Hyperinsulinimia, Hyperandrogenism, which can contribute to weight or abdominal fat gain, reduce energy expenditure and increase food intake. We observed an increase in the levels of cholesterol in the obese PCOS in comparison to non obese PCOS cases and controls. As per International Diabetes Federation [IDF ] 2006, serum cholesterol > 200mg/dl is diagnosed as dyslipidemia. In our study, 14.13% obese cases had dyslipidemia, but no single case of dyslipidemia was seen in Non PCOS and control group. There was also an increase in the levels of triglycerides in the obese PCOS in comparison to non obese PCOS patients and controls as per International Diabetes Federation [IDF] 2006 serum triglycerides > 150 mg/dl is diagnosed as dyslipidemia. The present study show that 17.11% obese PCOS and 5.5% Non obese cases had dyslipidemia. There was an increase in both systolic and diastolic blood pressure in obese PCOS cases in comparison to Non obese PCOS cases and controls. As per International Diabetes Federation [IDF] systolic blood pressure of greater than 130 mm Hg is diagnosed as systolic hypertension and diastolic blood pressure of 85 mm Hg is diagnosed as diastolic hypertension.

Although the role of obesity in PCOS is not very clear. It is a Major feature of PCOS that may contribute to PCOS pathogenesis by aggravating the intrinsic insulin resistance that culminates as metabolic syndrome. Diabetes mellitus, insulin resistance, Impaired Glucose tolerance and dislipidemia are very common in PCOS. In our study we found that levels of fading blood sugar in obese PCOS non obese PCOS and controls were not much different. As per Modified US National Cholesterol Education Programe Adult Treatment Panel III [ NCEP ATP III] Criteria, fasting Glucose equal to or greater than 104 mg / DL is diagnosed as Impaired fasting Glucose. 9.33 obese PCOS 5% non obese PCOS and 3% controls had fasting Glucose equal to or greater than 104 mg/ DL and hence Impaired fasting Glucose. The 1st hour blood Glucose for obese, non obese and control group was 130.59mg/dl, 124.44mg/dl, 124.74mg/dl, respectively which was statistically insignificant. However, the 2nd hour blood glucose levels for obese, non-obese and control were 117.39mg/dl, 106.47mg/dl, 104.56mg/dl respectively which was statistically significant. According to world Health Organization (WHO) Criteria, the person with 140–199mg/dl two hour (2h) glucose has impaired glucose tolerance. Among obese PCOS cases, 5.66% and in non-obese PCOS cases 3.23%
have impaired glucose tolerance. Hormonal profile of our PCOS patients revealed imbalance of sex hormones indicating that bit is a polyendocrinial disorder. LH, FSH greater than 2 has been a golden mark in PCOS diagnosis for a long time. The mean of follicle stimulating hormone for obese PCOS, non obese PCOS and controls was 6.9 IU/L, 7.57 IU/L AND 5.3 IU/L respectively. The mean of lutinising hormone for obese PCOS, non obese PCOS cases and controls is 9.98 IU/L, 9.58 IU/L, 6.66 IU/L respectively. For most of the cases LH/FSH ratio was greater than 2.

CONCLUSION:
The present study revealed significant differences in hormonal and biochemical parameters among the obese and non obese PCOS cases. We conclude that the obese PCOS cases have higher levels of cholesterol, triglycerides, hyper androgenism as compared to non obese PCOS cases. Obese PCOS also show more impaired glucose tolerance and insulin resistance. Hence we conclude that obese PCOS cases are at high risk of developing secondary Complications like insulin resistance diabetes, infertility and other metabolic disorders. Further large scale studies are warranted to establish our findings as well as to check physiological and metabolic parameters and preventive strategies among obese PCOS cases.

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