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Case Series

Insulin resistance by homeostatic model assessment in patients of polycystic ovarian syndrome

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ABSTRACT

Polycystic ovarian syndrome (PCOS) is one of the common endocrine disorders of reproductive age and affects approximately 6-16% of general population. Considering high incidence (70-95%) of insulin resistance in women with high BMI, 30-75% of population is found to have insulin resistance inspite of being lean. So, it is worth proving insulin resistance irrespective of BMI. Of amongst different tests to diagnose insulin resistance, homeostatic model assessment of insulin resistance (HOMA-IR) has been proved to be useful as a screening test for insulin resistance. This is a retrospective observational study of 4 months from April 2022 to July 2022 and included 18 patients diagnosed with PCOS. We studied their BMI, fasting glucose, fasting insulin and HOMA-IR. Out of total patients screened, the prevalence of insulin resistance was 72.22% as calculated by HOMA-IR test. No prevalence of HOMA-IR was observed in underweight cases. Out of normal weight cases, 83.33% cases were found to have Insulin resistance. Of the overweight and obese cases, 100% were found to have insulin resistance. Majority of women with PCOS have insulin resistance and consequent hyperinsulinemia. Insulin resistance is directly proportional to weight gain in PCOS patients. Lifestyle modification and administration of insulin sensitizers like Metformin is useful in reducing insulin resistance in overweight and obese patients. In patients with normal BMI who prove to have insulin resistance with raised HOMA-IR test are also benefited from medical therapy.

Keywords: Polycystic ovarian syndrome, Insulin resistance, HOMA-IR, BMI

INTRODUCTION

Polycystic ovarian syndrome (PCOS) is one of the most common endocrine disorders of reproductive age group and affects approximately 6-16% of the general population.[1] It is characterized by androgen excess and oligo-ovulation or anovulation, after the exclusion of other causes of hyperandrogenism.

According to European society for human reproduction and embryology (ESHRE) and American society for reproductive medicine (ASRM), presence of any two of the following three criteria can be used for diagnosis of PCOS (a) polycystic ovarian morphology on ultrasound (b) oligo-ovulation and/or anovulation; and (c) clinical or biochemical evidence of hyperandrogenism, provided other etiologies (congenital adrenal hyperplasia, androgen-secreting tumors, Cushing syndrome) have been excluded. The presence of 12 or more follicles in each ovary, measuring 2-9 mm in diameter, with or without increase ovarian volume (>10 ml) is considered as morphological diagnostic criteria based on ultrasonography.[2]

In addition, many patients with PCOS demonstrate presence of insulin resistance, accompanied by compensatory hyperinsulinemia. Insulin resistance is frequently observed in obese women and also in lean patients with PCOS. PCOS remains one of the important causes of anovulatory infertility and insulin resistance adds to the problem of ovulation induction in these

patients. The American diabetes association (2019) recommends initial diabetes mellitus screening and then periodic testing in obese or overweight women and adolescents diagnosed with PCOS.[3] Overall, insulin resistance and the compensatory hyperinsulinemia affects about 65–70% of women with PCOS. Administration of insulin sensitizing agents cause improvement in the clinical, endocrinologic, and metabolic features in PCOS patients.[4]

Considering high incidence (70-80%) of insulin resistance in obese patients (BMI>30), there is (20-25%) of population found to have insulin resistance inspite of being lean (BMI<25).[5] So, while considering optimization of patients with PCOS, it is worth proving insulin resistance irrespective of their BMI.

Of amongst different tests to diagnose insulin resistance, homeostatic model assessment of insulin resistance (HOMA-IR) has been proved to be useful as a screening test for insulin resistance. It is an index used to determine if insulin resistance is present in a patient. HOMA-IR index is simple to use and requires very little data. It is used widely because of its simplicity and non-invasive nature. This study was designed to evaluate the prevalence of insulin resistance in PCOS patients, according to the homeostatic model assessment (HOMA-IR).

The aim and objective of this case series to determine the prevalence of insulin resistance in patients with polycystic ovarian syndrome (PCOS). To determine the pattern of BMI according to WHO criteria in patients of PCOS, determine the prevalence of insulin resistance in each BMI group and to assess the need for HOMA-IR test in patients of PCOS with normal BMI.

CASE SERIES

This case series was conducted at tertiary care hospital from April 2022 to July 2022. Study Population: Eighteen PCOS patients were selected from the Gynecology outpatient department (OPD). Diagnosis was based on menstrual irregularities and ultrasonographic criteria, including, ≥12 follicles in each ovary (2–9 mm in diameter) and/or increased ovarian volume (>10 cc). Anthropometric and clinical assessment. BMI was calculated from recorded height and weight. Patients were classified into BMI categories using WHO criteria.

Patients fasted for 8 hours before blood sampling. Fasting venous blood (5 ml) was collected in a plain vial. Fasting glucose was measured using the glucose oxidase-peroxidase method.

Fasting insulin levels were estimated using ELISA-based kits. HOMA-IR was calculated using the formula, HOMA-IR=Fasting insulin (mIU/l) ×Fasting glucose (mg/dl)/ 405. A HOMA-IR value >2 was considered indicative of insulin resistance. BMI Classification (WHO Criteria). Underweight: BMI < 18.5 kg/m². Normal weight: BMI 18.5–24.9 kg/m². Overweight: BMI 25–29.9 kg/m². Obese: BMI≥30 kg/m²

Table 1: Distribution of cases according to BMI.

BMI	No. of cases	%
Underweight (< 18.5)	4	22.23
Normal weight (18.5 - 24.9)	6	33.33
Over weight (25 - 29.9)	6	33.33
Obese (> 30)	2	11.11
Total	18	100

Table 2: Distribution of HOMA-IR according to BMI.

BMI	No. of cases	%
Underweight (n=4)	0	0
Normal weight (n=6)	5	83.33
Over weight (n=6)	6	100
Obese (n=6)	2	100

Table 3: Correlation between BMI and HOMA (IR).

	Mean±SD	P value
BMI	23.61±1.07	<0.0001***
HOMA (IR)	3.55±0.62	

***Statistically important

Data were analyzed using mean±standard deviation (SD). Pearson correlation was used to assess the relationship between BMI and HOMA-IR. A p value <0.0001 was considered statistically significant. 18 cases of PCOS were observed and were studied for their BMI according to WHO criteria. Out of which, 22.23% cases were underweight, 33.3% cases were having normal weight, 33.33% were overweight and obesity was observed in 11.11% cases (Table 1).

After distributing these patients into their BMI group, prevalence of insulin resistance by HOMA-IR levels was studied in each BMI group. There was no prevalence of insulin resistance in underweight cases. Out of normal weight cases, 83.33% cases were observed with Insulin resistance. 100% of overweight and obese patients were found to have insulin resistance.

Of the patients with normal BMI, 83.33% were found to have raised HOMA-IR levels suggestive of insulin resistance, hence the need for this test in PCOS patients with normal BMI is justified (Table 2). Correlation between BMI of PCOS patients and HOMA-IR test was studied. In the present study, statistically significant correlation was observed between the BMI and HOMA-IR measurements (p<0.0001) (r2=0.89).

DISCUSSION

Hyperinsulinemia appears to be an important factor that induces excess androgen production by theca cells and also as a co-gonadotropin, causing increase in LH stimulus

seen in a majority of women with PCOS. The above outlines the importance of insulin resistance, compensatory hyperinsulinemia and its consequences, the majority of which have negative effects on both metabolic and reproductive health of a woman. Hence, it is necessary to assess the prevalence of insulin resistance in patients of PCOS and its early diagnosis so as to initiate treatment for the same.

According to a study conducted by Catherine Marin et al. prevalence of insulin resistance in PCOS patients by HOMA-IR was 64%, whereas in our study the prevalence of insulin resistance was approximately 72.22%. Patients with insulin resistance are more obese and have a greater degree of android body fat distribution. Although insulin resistance is a common abnormality in PCOS, it does not seem to be a universal feature. It is important to have race, BMI, and age-specific values, particularly for large commercial laboratories and reference centres, for diagnosing insulin resistance.[6]

Our study was carried out at a tertiary care centre in a rural set-up. Using the HOMA-IR calculation to estimate insulin resistance, in our study, the insulin resistance appears to be independent of obesity and is also present in patients with normal BMI. We calculated HOMA-IR values by HOMA-IR calculator which is available online as "Omni Calculator" and on entering patient's fasting glucose and insulin values, it directly gives the value of HOMA-IR. More recently, Matthews et al, have developed a computerized HOMA model (The HOMA2 calculator), which seems to have increased accuracy, particularly in patients with glucose intolerance.[7]

Options for treating insulin resistance/hyperinsulinemia include lifestyle modifications, exercise, diet and weight loss, or administration of insulin sensitisers like Metformin or Thiazolidinediones (TZDs). Given the high prevalence of obesity in women with PCOS, efforts to achieve weight reduction are an important component of treatment of the disorder. When effective, often as part of an organized program of lifestyle modification together with exercise and diet, weight loss has been shown to reduce hyperandrogenism, increase ovulation and rates of conception, together with improving the metabolic functions.[8]

Present evidence would support every effort to reduce hyperinsulinemia and its consequences both before and during puberty in hyperandrogenaemia girls. Importantly in PCOS metformin for up to six months reduced hirsutism and, in most studies, significantly reduced androgen levels, with reductions in testosterone being between 25–50%.[9] According to John Marshall et al. all patients with PCOS, irrespective of their BMI should be treated for insulin resistance.[10] Our study is indicated towards treatment of patients within normal BMI range with raised HOMA-IR levels.

CONCLUSION

In patients with PCOS, the prevalence of IR was approximately 72.22% according to the HOMA-IR measurement. A majority of women with PCOS have insulin resistance and consequent hyperinsulinemia. The latter commonly leads to hyperandrogenaemia with negative effects on reproductive function. Treatment of insulin resistance, either by lifestyle changes or Metformin, leads to improvement in reproductive and metabolic abnormalities and reduces future development of diabetes and arterial disease. Along with lifestyle modification with exercise and dietary advice, administration of Metformin can be useful in reducing insulin resistance in overweight and obese patients. Normal BMI patients who prove to have insulin resistance with raised HOMA-IR test may also benefit from medical therapy.

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