INTRODUCTION

Polycystic ovarian syndrome is the commonest endocrinopathy affecting women of reproductive age group with worldwide prevalence of 10 - 20% and occurs in higher frequency in South Asians; prevalence of 10 - 22.5% and 20 - 40% in India and Pakistan, respectively.1-6 Recent studies have shown that PCOS patients also demonstrated metabolic aberrations in addition to other endocrine abnormalities; most significant of these is presence of insulin resistance (IR). The reported prevalence of IR in PCOS women is 77% and hyperinsulinemia present in 60% women (fasting Insulin 18.5 ± 5.8 µIU/ml). Hyperandrogenism was present in 53.8% (n=49), whereas 38.5% (n=35) women had primary infertility or subfertility, while 65.9% (n=60) had menstrual irregularities; and higher frequencies were observed in women with IR. Eight subjects with IR and endocrine abnormalities were missed by fasting insulin.


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ABSTRACT

Objective: To assess the utility of HOMA-IR in assessing insulin resistance in patients with polycystic ovary syndrome (PCOS) and compare it with fasting insulin for assessing insulin resistance (IR).

Study Design: Observational study.

Place and Duration of Study: Section of Clinical Chemistry, Department of Pathology and Laboratory Medicine, The Aga Khan University Hospital, Karachi, from January 2009 to September 2012.

Methodology: Medical chart review of all women diagnosed with PCOS was performed. Of the 400 PCOS women reviewed, 91 met the inclusion criteria. Insulin resistance was assessed by calculating HOMA-IR using the formula (fasting glucose x fasting insulin)/405, taking normal value <2 in adults and hyperinsulinemia based on fasting insulin levels ≥12 µIU/ml.

Results: A total of 91 premenopausal women diagnosed with PCOS were included. Mean age was 30 ±5.5 years. Mean HOMA-IR of women was 3.1 ±1.7, respectively with IR in 69% (n=63) women, while hyperinsulinemia was present in 60% (n=55) women (fasting Insulin 18.5 ± 5.8 µIU/ml). Hyperandrogenism was present in 53.8% (n=49), whereas 38.5% (n=35) women had primary infertility or subfertility, while 65.9% (n=60) had menstrual irregularities; and higher frequencies were observed in women with IR. Eight subjects with IR and endocrine abnormalities were missed by fasting insulin.

Conclusion: Insulin resistance is common in PCOS and it is likely a pathogenic factor for development of PCOS. HOMA-IR model performed better than hyperinsulinemia alone for diagnosing IR.

Key Words: Women. Polycystic ovary syndrome. Insulin resistance. Fasting glucose. Fasting insulin.
assess the utility of HOMA-IR in assessing IR in women with PCOS and compare it with fasting insulin for assessing IR.

**METHODOLOGY**

An observational study was conducted at the Section of Clinical Chemistry, Department of Pathology and Laboratory Medicine of The Aga Khan University Hospital. Exemption was taken from Institutional Ethical Review Committee (2893-Pat-ERC-14).

Data of women diagnosed with PCOS from January 2009 to September 2012 was retrieved from electronic medical records. Those diagnosed with any other hormonal disorder were excluded. Clinical history regarding hyperandrogenism, oligomenorrhea, infertility and DM was obtained from medical records. Laboratory data of PCOS women aged between 18 to 45 years was also reviewed and only those simultaneously tested for fasting glucose and fasting insulin were finally included.

Hyperandrogenism was labelled if hirsutism, acne, *acanthosis nigricans* and/or high testosterone levels were present. Obesity was defined using World Health Organization (WHO) criteria on the basis of BMI (kg/m²); underweight as < 18.5, optimal weight 18.5 – 24.9, overweight 25 – 29.9, obesity ≥30, and morbid obesity ≥ 40.16

Fasting glucose <100 mg/dl was taken as normal, 101 – 125 mg/dl as impaired fasting glucose (IFG), and levels ≥126 mg/dl as diabetic. Fasting insulin levels ≥12 µIU/ml were taken as hyperinsulinemia. HOMA-IR was calculated using formula [(fasting glucose x fasting insulin)/ 405]. A cut off of < 2 was considered as normal. Plasma glucose was performed on Synchron CX9 chemistry analyzer (Beckman Coulter, USA) using manufacturer provided kits, by glucose oxidase method with analytical range of 0-700 mg/dl. For internal quality control, three level controls (low, normal, and high) are run with each batch of plasma glucose. Serum insulin levels were performed on Abbott Axsym Immunoassay Analyzer (Abbot Diagnostics, USA) using manufacturer provided kits by microparticle enzyme immunoassay. For internal quality control three level controls (low, normal, and high) are run with each batch of serum insulin. The laboratory participated in external quality assurance services of Bio-Rad (BioRad Laboratories, US) for plasma fasting glucose and serum insulin.

The statistical analyses were performed using the SPSS version 19. Mean and standard deviations of age, fasting insulin and fasting glucose and HOMA-IR were derived. Frequencies with percentages were derived for gender, IR, hyperandrogenism, oligomenorrhea, and infertility. Mean comparison of HOMA-IR, fasting insulin, fasting glucose, BMI, hyperandrogenism and infertility/ subfertility was done by independent t-test, statistical significance was attributed to p < 0.05.

**RESULTS**

A total of 91 women with mean age of 30 ±5.5 years were included in the final analysis. Mean BMI was in the overweight range, 27.9 ±4.8 kg/m². Average fasting insulin and HOMA-IR were high 14.27 ±7.1 µIU/ml and 3.1 ±1.7, respectively. Average fasting glucose was normal 87±10 mg/dl with IFG in 14% (n=13) women.

![Flow chart showing distribution of PCOS women in groups with and without insulin resistance.](image-url)
Biochemical parameters of all women are summarized in Table I. Hyperandrogenism was present in 53.8% (n=49, mean HOMA-IR 3 ±1.5), obesity in 29% (n=26, HOMA-IR 3.5 ±1.8) while 38.5% (n=35) women had primary infertility/subfertility (HOMA-IR 3.5 ±1.7) and menstrual irregularity in 65.9% (n=60, HOMA-IR 3 ±1.5).

Insulin resistance based on HOMA-IR was observed in 69% (n=63) of the women and these women have higher frequencies of hyperandrogenism, menstrual abnormality, infertility/subfertility and obesity compared to the subjects without IR, shown in Figure 1. Impaired fasting glucose was observed in 14 women, 10 among them had IR (mean HOMA 4.4 ±2.7). Sixty percent (n=55) women had hyperinsulinemia and all had IR based on HOMA values (mean 4 ±1.6), while 8 women with high HOMA-IR levels had normal insulin levels. Mean levels of biochemical parameters of women with and without IR based on HOMA-IR and hyperinsulinemia are reported in Table I.

DISCUSSION

There is scarcity of data regarding IR prevalence in PCOS subjects in Pakistan and this study provided the frequency of IR in a representative sample of our PCOS population. In present study, we report high frequency of IR in women with PCOS; based on HOMA-IR. The PCOS women with IR had higher frequencies of menstrual irregularity, hyperandrogenism, infertility or subfertility and obesity. In the present study, HOMA-IR performed better than the hyperinsulinemia for diagnosing IR. Eight women with high HOMA-IR levels had normal insulin levels; of them, 6 subjects had hyperandrogenism and menstrual irregularity, 2 subjects had IFG, while subfertility/ infertility was present in 3 and BMI ≥ 30 kg/m² in 2 women.

The presently reported findings are consistent with the findings of Hussain et al. done in Pakistani women with PCOS who revealed 63% prevalence of IR.10 Similar, findings were reported by Moghetti et al., in Caucasian subjects with PCOS with 71% women with PCOS having IR.17 Another study by Tabassum et al. however, reported 34.7% in PCOS subjects had IR. The differences in findings could have been due to different criteria used for IR and their sample size was small (n=46).8 A recent study done in Pakistan also reported IR to be positively correlated with metabolic syndrome, which again is a cluster of disorders leading to increased risk of developing IFG, IGT, type 2 DM, gestational diabetes and increased cardiovascular risk.18,19 So identifying IR in women with PCOS is important; and strategies designed to reduce IR should be adopted in such patients to decrease the risk of aforementioned endocrine abnormalities.

There were some limitations to this study. The main limitation was that data for the study were not collected prospectively. Secondly, the ideal method for insulin resistance measurement, hyperinsulinemic-euglycemic clamp technique was not used.

CONCLUSION

Frequency of IR among PCOS women is high and they are prone to develop other endocrine abnormalities related to IR. Moreover, the surrogate measure for IR assessment, HOMA-IR is more accurate than fasting insulin for evaluating PCOS women.

REFERENCES

women of polycystic ovary syndrome: A study from Pakistan. 


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