E-ISSN 2250-0944
ISSN 2250-1150
doi: 10.31838/ijprt/15.02.669

Research Article

Prevalence of Impaired Fasting Glucose and Associated Risk Factors In Patients with Polycystic Ovarian Syndrome in Pakistan

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Received: 09.03.2026, Revised: 02.06-2026, Accepted: 12.06.2026

ABSTRACT

Objective: To determine the frequency of impaired fasting glucose (IFG) and to assess its associated risk factors in patients with Polycystic Ovarian Syndrome attending the infertility clinic of Gynae department, Mardan Medical Complex, Mardan.

Study Design: Cross-sectional, descriptive study.

Place and Duration of Study: This study was conducted in the outpatient department of the Gynae unit at Mardan Medical Complex, Mardan from January 01, 2020 to October 01, 2020.

Materials and Methods: A total of 106 patients diagnosed with Polycystic Ovarian Syndrome were enrolled. Diagnosis of Polycystic Ovarian Syndrome was made based on the 2003 Rotterdam criteria (Table. 5). Height and weight were recorded to calculate BMI and venous blood sampling was performed for the measurement of Fasting blood sugar (FBS), Fasting plasma Insulin and HOMA-IR. The frequency of IFG was determined using the American Diabetes Association (ADA) criteria and its correlation with age, BMI and HOMA-IR was explored. WHO BMI cut-offs modified for the Asian population were used.

Results: The mean age of the participants was 28.6 ± 4.1 years. The frequency of IFG (Pre-diabetes) was found to be 16 % (n=17. IFG was significantly more common in patients aged > 30 years. Approximately 57% of the patients with IFG (FBS >100) were obese (BMI ≥30) and Mean BMI was significantly higher in elevated FBS group (32.7 vs 28.4, $p<0.001$). Approximately 76% of patients with FBS >100 had HOMA-IR >2.5 indicating insulin resistance, and a positive correlation was found between HOMA-IR and FBS ($r=0.62$, $p<0.001$).

Conclusion: A significant proportion of PCOS patients have impaired fasting glucose (Prediabetes), particularly those with advancing age, obesity and higher HOMA-IR.

Keywords: Polycystic Ovarian Syndrome, Impaired Fasting Glucose, Pre-Diabetes, BMI, HOMA-IR, Diabetes Mellitus.

INTRODUCTION

Polycystic ovary syndrome (PCOS) is the most common endocrine disorder in women of reproductive age and a leading cause of anovulatory infertility[1].

Ever since its initial description in 1935 by Stein and Leventhal[2], it has been a subject of considerable research owing to its association with multiple endocrine and gynecologic abnormalities. PCOS affects 5-20% of women in reproductive age worldwide[4], with common

manifestations including amenorrhea or oligo-amenorrhea, hirsutism, obesity, acne, androgenic alopecia and reproductive disorders[3].

PCOS however; is not a disease exclusive to fertility and adolescence period; rather it has lifelong implications. In adolescence, the main complications include menstrual irregularities, hirsutism, obesity, and acne. In reproductive age, infertility and ovulatory dysfunction becomes predominant while the complications of adolescence still persist. In later life, the syndrome increases the risk of type 2 diabetes, hypertension, dyslipidemia, cardiovascular diseases and even endometrial cancer and possibly breast cancer[1, 4].

Many women with PCOS demonstrate both basal and glucose-stimulated hyper-insulinaemia and are insulin resistant, independent of body mass index (BMI) [4, 5]. Approximately 75% to 95% of women with PCOS exhibit underlying insulin resistance, a key risk factor for impaired glucose tolerance and type 2 diabetes mellitus[6]. Data indicate that the incidence of metabolic syndrome, gestational diabetes mellitus, impaired glucose tolerance (IGT) and T2DM is increased in premenopausal women with PCOS compared with age-matched and BMI-matched controls[7].

A systematic review and meta-analysis reported that the prevalence of IGT (OR=3.26, 95% CI: 2.17–4.90) and T2DM (OR 2.87; 95% CI: 1.44–5.72) is signifiantly higher in patients with PCOS than in age-matched controls[7]. Moreover, the Asian population exhibited much higher risk of development of impaired glucose tolerance (5 fold) as compared to American (4 fold) and European population (3 fold) [8].

In Pakistan, PCOS is primarily viewed as a cause of gynecological morbidity and infertility. There is a relative scarcity of data regarding the risk of progression to IFG, overt diabetes mellitus, and its long-term impact. This study aims to determine the prevalence of impaired fasting glucose and type 2 diabetes mellitus in patients with PCOS in district Mardan. Identifying the strength of this association will thus highlight a critical, yet often overlooked, aspect of the PCOS spectrum in this ethnically high risk population.

MATERIALS AND METHODS

This was a cross sectional study. 250 cases with Polycystic Ovarian Syndrome were initially recruited from the outpatient department of the Gynecology and obstetrics unit of Mardan Medical Complex Teaching Hospital, Mardan. Among those, a sample of 106 was randomly selected, based on their consent and availability for further testing to determine the frequency of IFG and diabetes mellitus.

Inclusion Criteria: Cases aged 20 - 40 years with menstrual cycle irregularities (anovulation or oligo ovulation), elevated serum testosterone levels and ultrasonic features suggestive of Polycystic Ovarian Syndrome, as per the 2003 Rotterdam criteria (Table. 5) were included.

Exclusion Criteria: Women with active pregnancy, previous history of Cushing syndrome or hyperprolactinemia, and those taking medicines that change the hormonal or biochemical profiles, were excluded through appropriate clinical evaluation and laboratory testing.

Informed written consent was obtained from the head of the concerned Gynecology and Obstetrics unit as well as the study participants. A comprehensive questionnaire was used to collect the socio demographic data, menstrual, marital and reproductive history. Clinical assessment included measurement of height, weight, body mass index (BMI), pulse and blood pressure. Fasting venous blood samples were obtained for the measurement of fasting blood sugar, fasting plasma insulin and HOMA-IR.

American Diabetes Association (ADA) criteria[3] was used to define IFG and diabetes mellitus:

- Normal: Fasting blood sugar < 100 mg/dl
- Impaired Fasting Glucose: Fasting blood sugar ≥100 and <126 mg/dl)
- Diabetes mellitus: Fasting blood sugar ≥ 126 mg/dl (on multiple occasions)

Modified WHO BMI criteria for Asian population were applied:

1. Normal weight (18.5-24.9 kg/m²)
2. Pre-obese (25-29.9 kg/m²)
3. Obesity Class-I (30-34.9 kg/m²)
4. Obesity class-II (35-39.9 kg/m²) and
5. Obesity class-III (> 40 kg/m²).

Statistical Analysis: Data were analyzed using SPSS version 22. The frequencies and percentages were calculated. The frequency of IFG and Diabetes mellitus was determined and its association with BMI, age and HOMA-IR was explored using appropriate statistical tests, including the Pearson Chi-Square test and the correlation analysis.

RESULTS

The demographic and metabolic characteristics of the study population are shown in table 1-3. The mean age of the participants was 28.6 ± 4.1 years. Key findings are as follows:

1. Of the total 106 participants, 16 % (n=17) had IFG (Pre-diabetes) as per the ADA criteria. An additional 2.8% (n=3) had diabetes mellitus, making the total dysglycemia prevalence 19.8%
2. Approximately 57% of the patients with IFG (FBS >100) were obese (BMI ≥30) and Mean BMI was significantly higher in elevated FBS group (32.7 vs 28.4, p<0.001). Moreover, Obese patients (BMI ≥30) were 2.7 times more likely to have FBS >100 mg/dL (p<0.001).
3. Approximately 76% of patients with FBS >100 had HOMA-IR >2.5 (indicating insulin resistance) suggesting a strong link with insulin resistance. Besides, Obese patients (BMI ≥30) with FBS >100 had highest HOMA-IR (4.2 ± 2.3). Notably, normal-BMI patients with FBS >100 still showed elevated HOMA-IR (2.9 ± 1.5), suggesting the influence of additional factors beyond obesity.
4. Patients with IFG were significantly older than those with normal glucose (mean age 28.6 vs. 26.2 years, p=0.012). Patients >30 years had 2.4 times higher prevalence of IFG (22.2% vs. 9.4%, *p=0.047*).

Table 1: Distribution of Patients with Elevated Fasting Blood Sugar (>100 mg/dL)

Blood Sugar Range (mg/dL)	Number of Patients	Percentage of Total (n=106)
101-110 (Prediabetic)	14	13.2%
111-125 (Prediabetic)	4	3.8%
>125 (Diabetic)	3	2.8%
Total >100	**21**	**19.8%**

Table 2: Correlation between Elevated Fasting Blood Sugar and Body Mass Index

Metabolic Parameter	Patients with FBS >100 (n=21)	Patients with FBS ≤100 (n=85)	p-value
Mean BMI (kg/m²)	32.7 ± 5.2	28.4 ± 4.1	<0.001*
BMI Categories:			
- Normal (18.5-24.9)	2 (9.5%)	29 (34.1%)	
- Overweight (25-29.9)	7 (33.3%)	38 (44.7%)	
- Obese (≥30)	12 (57.1%)	18 (21.2%)	<0.001*

Table 3: Correlation of HOMA-IR with Metabolic Parameters

Parameter	Patients with FBS >100 (n=21)	Patients with FBS ≤100 (n=85)	p-value	Correlation (r)
Mean HOMA-IR (before)	3.8 ± 2.1	2.1 ± 1.3	<0.001*	0.62**
HOMA-IR >2.5	16 (76.2%)	29 (34.1%)	<0.001*	-

Table 4: Age Distribution in IFG (Pre-diabetic) vs. Normal Glucose Patients

Parameter	Pre-diabetic (FBS 100-125) (n=18)	Normal Glucose (FBS <100) (n=85)	p-value
Mean Age (years)	28.6 ± 4.1	26.2 ± 3.8	0.012*
Age Categories:			
- ≤25 years	4 (22.2%)	38 (44.7%)	
- 26-30 years	10 (55.6%)	39 (45.9%)	
- >30 years	4 (22.2%)	8 (9.4%)	0.047*

Table 5: 2003 Rotterdam Criteria for PCOS

Criteria	Description
Oligo- or Anovulation	Irregular or absent periods (e.g., cycles >35 days).
Hyperandrogenism	Clinical signs (hirsutism, acne, alopecia) and/or high androgen levels in blood tests.
Polycystic Ovaries (PCOM)	Ultrasound showing ≥12 follicles (2-9 mm) and/or ovarian volume >10 mL in at least one ovary.

*A diagnosis of PCOS is made if any two of these three criteria are met, provided other conditions that can cause similar symptoms (such as thyroid disorders, hyperprolactinemia, or adrenal hyperplasia) have been ruled out.

DISCUSSION

This study aimed to determine the prevalence of impaired fasting glucose (pre-diabetes) and overt diabetes mellitus in patients with polycystic ovarian syndrome. We found a 16 % prevalence of IFG in a cohort of Pakistani women with PCOS. This finding is consistent with Younas B et.al [9] who reported IGT prevalence at 16.7 % in women with PCOS from Karachi. Our results also align closely with studies by zhou et al.[10] and Wang P et al.[11] in Chinese cohorts, who reported IFG prevalence of 12.6 % and 18.7 %, respectively. This is however; much lower than the 37.4% prevalence of IGT reported by Anwar B et. al [12] from Abbotabad. This discrepancy may be partly due to their use of the Oral Glucose Tolerance Test (OGTT) as a diagnostic test, which has a higher sensitivity for detecting IGT in PCOS patients[6]. Similarly, a meta-analysis published by Al khalifa et al.[13] reported a higher global pooled prevalence of prediabetes in PCOS at 32.5%. This discrepancy may be attributable to the relatively young mean age of our population, ethnic variations in insulin resistance, or a different distribution of PCOS phenotypes.

We observed a strong association between obesity and IFG. This observation is well-supported by the existing literature [14-15]. Jane K et al identified advancing age, high BMI and increased waist: hip ratio as significant independent risk factors for IFG in PCOS [14]. Likewise, we found that obese patients (BMI ≥ 30 kg/m^2) were 2.7 times more likely to have IFG as compared to non-obese PCOS patients. This finding converges with the results from Sadeghi et al. [15]. Furthermore, the high prevalence of insulin resistance (HOMA-IR >2.5) among our pre-diabetic patients aligns with the established pathophysiological role of insulin resistance in PCOS [16]. Notably, we found elevated HOMA-IR in pre-diabetic patients even with normal BMI, echoing the complex interplay between insulin resistance and hyper-androgenism, described by Moghetti & Tosi et al. [17]. It may also be explained by the genetic predispositions outlined by Khan et al. [18].

We found a higher prevalence of impaired fasting glucose in the older subset of our PCOS cohort which aligns perfectly with contemporary meta-analyses and large cohort studies conducted within the last decade, which consistently identify age as a primary modulator of dysglycemia risk in PCOS [19-21]. Local studies in age-matched non-PCOS populations report IFG prevalence of 11 % to 19.2 % [22-24]. Similarly, global statistics from the international diabetes federation (IDF) exhibit wide regional variations, from 4.8 % in Europe to 15.6 % in North America, with the prevalence being lowest in the 20-39 years age group and increasing progressively after the age of 40 years[25].

CONCLUSION

The 16% prevalence of IFG (prediabetes) in PCOS patients in our study is significant enough to warrant regular screening and intervention. However, this frequency is comparable to that reported in local and global age- and BMI-matched controls. Given the established escalation of risk after 40 years of age, we recommend more vigilant screening for prediabetes and diabetes in older PCOS patients.

Limitations of the Study

The gold standard for the screening of dysglycemia in PCOS is the 2-hour Oral Glucose Tolerance Test (OGTT). Due to resource constraints and unforeseen challenges, only fasting blood sugar (FBS) and HOMA-IR were used. Inclusion of other complementary tests like 2-hour Oral glucose tolerance test and HbA1c would have provided more comprehensive metabolic profile but was not feasible due to patient's preference and funding constraints.

Conflict of Interest(s): None

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