A Study of Correlation between Abnormal Glucose Tolerance (AGT), Insulin Resistance (IR) and Abdominal Circumference (AC) in Young Girls with Polycystic Ovarian Syndrome at a Multi-Specialty Hospital in South Kolkata

Shubhasis Banerjee¹, Lipika Das Mukhopadhyay², Susmita Basu³

¹Department of Obstetrics and Gynaecology, Sri Aurobindo Seva Kendra (EEDF Hospital), Kolkata, West Bengal, India. ²Department of Obstetrics and Gynaecology, KPC Medical College & Hospital, Kolkata, West Bengal, India. ³Calcutta National Medical College & Hospital, Kolkata, West Bengal, India.

ABSTRACT

BACKGROUND

Polycystic ovarian syndrome is an array of metabolic, hormonal and reproductive dysfunction that affects women. It is an important cause of female infertility and also leads to other medical conditions including anxiety, depression, obesity, endometrial cancer, liver disease, cardio-vascular disease and type 2 diabetes mellitus which results from insulin resistance. Compared to the others, these patients may significantly develop low quality of life related to health.

METHODS

The current study analyses the data, retrospectively of female patients, in the age range of 16 - 28 years, who presented at the out-patient clinic of gynaecology & obstetrics, in a tertiary care multi-specialty hospital at South Kolkata. Data was collected over a six months period and was analysed using appropriate statistical method.

RESULTS

A total of fifty-seven cases was included in the study with a median age of 22 years and a median BMI of 24 Kg / m² (range 18 - 36). Insulin resistance was found in 25 patients (43.86 %), and impaired glucose tolerance was found in 6 patients (10.53 %). All patients of frank diabetes (post-prandial glucose > 140 mg %) were suffering from insulin resistance. Abdominal circumference was above the cut-off level (> 80 cm) in 28 patients (49.12 %).

CONCLUSIONS

From the current study, it is established that impaired glucose tolerance alone cannot be a good indicator of body's disturbed glucose metabolism and there is increased need to measure insulin resistance to diagnose prospective diabetic condition associated with PCOS.

KEY WORDS

Abnormal Glucose Tolerance, Insulin Resistance, PCOS, Polycystic Ovarian Syndrome

Corresponding Author:

*Dr. Shubhasis Banerjee,
Department of Obstetrics &
Gynaecology, SASK (EEDF Hospital),
1H, Gariahat Road, Kolkata - 700068,
West Bengal, India.
E-mail: banerjeeecolcutta@gmail.com*

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BACKGROUND

PCOS / PCOD (Poly-Cystic Ovarian Syndrome / Disorder) is a gynaecological disorder comprising of secondary amenorrhoea, hirsutism (with or without acne), obesity and ovaries with multiple small cysts (volume of one or both ovaries > 10 cc by USG).¹ It is one of the most common human endocrinopathies affecting 12-21 % of woman of reproductive age group. Up to 70 % of women with PCOS remain undiagnosed. The ovaries develop multiple tiny small cystic collections containing fluidic substance and may completely or partially fail to release ovums which may lead to infertility, primary or secondary.¹

Though the exact cause behind PCOS is unknown, but there are evidences which suggest that it may involve a combination of endocrine as well as genetic factors. In the past, it was found in numerous studies, repeatedly, that polycystic patients harbour elevated risk for conditions like hypertension, heart disease, dyslipidaemia, type 2 diabetes mellitus and other significant metabolic ordeal linked to insulin resistance.^{2,3,4} These patients develop lower QOL (Quality of Life)^{5,6} in terms of health, and are at higher risk for mental disorders like depression.⁷ Spitzer et al demonstrated overall occurrence of depressive spells as high as 12 % in a significantly large multi-centric study of OBG patients.⁸ Women with PCOS have a higher risk of cardiovascular sequelae, especially indigenous women who are already at increased baseline risk. Management of polycystic ovarian syndrome involves treatment of current conditions, as well as prevention of complications arising from it including frank diabetes. Thus, treatment of PCOS should include multi-disciplinary approach to provide management of psychological and fertility issues.

There is a range of symptoms in PCOS that women can experience depending on the age of the presentation. In younger women, reproductive symptoms predominate; whereas metabolic features are prevalent in older women. The onset of symptoms can be triggered by environmental factors and genetic predisposition. Ethnicity may also have impact over PCOS as some population groups have higher risk of PCOS; as for example, South-East Asian women are less likely to have hirsutism.^{9,10}

Attie et al.¹¹ established in a study that obesity associated with chronic inflammation triggers the action of adipocytokines which in turn may contribute to insulin resistance (IR). It was found that adipokines play an important role in paracrine and autocrine signalling. The liver communicates with adipose tissue through adipokines, lipoproteins and lipid particles.

Insulin resistance and abnormal glucose tolerance is prevalent in patients of PCOS in varied degrees.¹² Therefore, a screening Oral Glucose Tolerance Test (OGTT) along with serum insulin level test is highly recommended independent of the obesity pattern of PCOS patients.

During initial assessment of women for PCOS, few points to be considered which are further addressed in the guideline.¹³ After menarche, it may take up to 2 years for the menstrual cycle to be regular. Irregular cycles persisting into the third-year post-menarche should be investigated for PCOS. Ultrasound is not a reliable diagnostic tool in the diagnosis of PCOS in adolescent and young women, as up to 70 % of young women may have polycystic ovaries on ultrasound.¹⁴ Initial

investigations must exclude other causes of same presentation. Hormonal assessment should consider thyroid function tests, serum prolactin and follicle stimulating hormone (FSH) levels.

METHODS

The current study is representing analysis of data, retrospectively, on female patients, suffering from PCOS, aging between 16 - 28 years who attended in the Out-Patient-Department of Gynaecology & Obstetrics, in a tertiary care multi-specialty hospital at South Kolkata, over six months periods (6th October' 2019 - 5th March 2020). PCOS was diagnosed using Rotterdam criteria. (2003).^{15,16,17} The patients were assessed by clinical and psychological examination and evaluation of hormonal levels as advised, to diagnose PCOS according to the criteria which requires the presence of the two of the following: oligo / anovulation, hyperandrogenism (Clinical-hirsutism or less commonly male pattern alopecia or Biochemical-raised FAI or testosterone), or polycystic ovaries on ultrasound. Oligo / anovulation is usually seen in women with menstrual cycle greater than 35 days apart or conversely with shorter cycle (< 21 days); even a woman with regular cycle may be anovulatory. Ovulatory status is best diagnosed with luteal phase progesterone assessment. Hyperandrogenaemia is best diagnosed with free testosterone or Free Androgen Index (FAI). Polycystic ovaries on ultrasound scan are diagnosed when at least 10 small antral follicles are seen in each ovary. A unilateral polycystic ovary is equally significant.

Conventionally, BMI (Body Mass Index)¹⁸ is defined as a ratio of weight in Kg to height in m². Abdominal circumference was measured with a metric tape (twice, to get an average). Care was taken to avoid errors in reading by asking the subjects to wear a light cloth during measurement. As recommended by Legro et al,¹⁹ abdominal circumference is measured at the maximum circumference between lower margin of the 10th rib and the highest point of iliac crest. Obesity is defined when BMI is ≥ 23 kg / m². An abdominal circumference of ≥ 80 cm (32 inch) was also considered as above cut-off level.^{20,21} Hirsutism was assessed by mFG score.²² Nine different body places were observed for hair growth pattern, hirsutism is considered if mFG score > 9. To know the follicular status of ovary, ultrasound study was done on patients. Married women underwent Trans-Vaginal Sonography (TVS), whereas Trans-Abdominal Sonography (TAS) was preferred in girls who were not married yet. Few biochemical assessments were also included in the study, e.g. serum testosterone level (electro-chemiluminescence method), insulin level (Elecys 2010, Roche), and serum glucose level (2 hours after meal). Hormonal tests are recommended to be done on the second or the third day of an induced bleeding. AGT screening is based on oral glucose tolerance test and WHO criteria using 75 gm oral glucose intake followed by measurement of plasma glucose and insulin after 2 hours.²³ Insulin resistance was diagnosed as a ratio of Post-Prandial Blood Sugar (PPBS): Post-Prandial Insulin (PPI). Conventionally, IR is defined when the ratio is ≤ 1.0 .²⁴

In this study, post-prandial blood glucose estimation is preferred over measuring fasting glucose, because of two

reasons. Firstly, it is easier to diagnose impaired glucose tolerance if challenged with specific amount of glucose before performing the test. Secondly, by measuring post-prandial insulin and making a ratio of PPBS: PPI (the insulin resistance), one can get clear idea about body's ability to neutralize glucose after each meal.

Written consent was taken from all the participants of the study. They were enlightened regarding the goal of the study. Patients were informed that there would be no requirement of any extra tests or procedures.

Permission was obtained from the Ethical Committee of the multi-specialty hospital where the first author conducted the study. All procedures carried out, followed the revised Helsinki declaration-2008²⁵ for the ethical standards to be maintained for research on mankind.

Statistical Analysis

Statistical analysis of collected data was done using SPSS software (version 13.0, IBM Corporation). Inter-group comparison was done using Chi-square test. A p-value < 0.05 was considered as significant in terms of analysis.

RESULTS

A total of fifty-seven cases were included in this study with a median age of 22 years (range 16 - 28 years); a median BMI of 24 kg / m² (range 18 - 36). Insulin resistance was found in 25 / 57 patients (43.86 %), and impaired glucose tolerance was found in 6 / 57 patients (10.53 %).

		IR Present (%)	IR Absent (%)	Significance	OR (95 % CI)	AOR (95 % CI)
Abdominal Circumference	Obese	14 (50.0)	14 (50.0)	$\chi^2 = 0.843$ $dF = 1$ $p = 0.358$	1.636 (0.570-4.696)	1.187 (0.339-4.154)
	Normal	11 (37.9)	18 (62.1)			
Blood Glucose Level	IGT	5 (20.0)	20 (80.0)	$\chi^2 = 0.2641$ $dF = 1$ $p = 0.104$	7.750 (0.842-71.317)	7.619 (0.693-83.793)
	NGT	1 (3.12)	31 (96.88)			

Table 1. Factors Affecting Insulin Resistance (IR) in PCOS Patients (n = 57)

Chart 1. Blood Glucose (PPBS)

Chart 2. Abdominal Circumference

All patients of frank diabetes (post-prandial glucose > 140 mg %) were suffering from insulin resistance. Abdominal

circumference was above cut-off level (> 80 cm) in 28 / 57 patients (49.12 %).

Chart 3. Insulin Resistance

DISCUSSION

The majority of PCOS patients suffer from insulin resistance. Their body needs higher insulin level to titrate the same amount of glucose comparing a normal person. It is a symptom of PCOS and at the same time, it is the most powerful physiological reason to cause the array of disorders. Thus, testing for insulin resistance helps to differentiate it from other similar conditions like PCOS.²⁶

Insulin resistance may be observed in both obese and non-obese PCOS patients. By observing insulin resistance, one can differentiate patients who lack an insulin related symptom; as for example, patients with adrenal PCOS²⁷ and a considerably large group of patients having amenorrhoea because of disturbed hypothalamus-pituitary axis but have wrongly diagnosed as 'lean PCOS'. There is evidence from research that demonstrates an increasing rate of PCOS correlated with weight gain, over previous 10 years²⁸. Another study portrays a proportionate increase of polycystic disorder to rising occurrence of type-II diabetes.²⁹

Conventional treatment strategy for insulin resistance includes exercise, weight loss and medications like metformin which improves insulin sensitivity at cellular level.³⁰ It is observed that resistance training may also be effective in few cases.³¹ Combined OCPs (Oral Contraceptive Pills) are among other drugs that is being widely used in the treatment of PCOS, but studies revealed that this drugs can alter body's usual response to blood glucose and can actually induce insulin resistance which is the major cause of PCOS.³²

Increased dietary intake of fructose also contributes to insulin resistance. Though low amount of fructose from fruits does not induce insulin resistance, but substantially higher content of fructose in junk foods has a more adverse effect. It is obvious that body's metabolic response to higher and lower quantity of sugar is very different.³³

Subclinical deficiency of magnesium and inositol may contribute to insulin resistance. A meta-analytical study, conducted in 2018, which included ten different RCTs (Randomized Controlled Trials), proved that inositol has some certain role in improvement of insulin resistance which means gross improvement in symptoms like ovulation dysfunction, irregular menstrual cycles, hormonal misbalance and mental health.³⁴ Another study revealed that supplementation with trace minerals like Mg has some positive effect on symptomatic relief of polycystic disease.³⁵

Delayed menstruation is a sign of altered ovarian activity.^{36,37} Traditionally, PCOS is one of the causative factors for type 2 diabetes. Insulin resistance is considered an important problem in the pathogenesis of PCOS.

Our study reveals, there are non-obese PCOS women who demonstrated impaired glucose tolerance and deranged insulin levels though having normal fasting sugar levels. Those patients had not developed frank diabetes, but at increased risk of developing diabetes in later life. Thus, they may get benefited from serial monitoring of blood glucose and metformin therapy. Findings of this study are in line with other studies of regarding PCOS. All of these study demonstrated that results of impaired glucose tolerance tests were not adequate to establish risks associated with metabolism.^{2-5,23} In this study, it is found, abdominal obesity contributed to higher post-prandial insulin level, which is consistent with prior literatures.³⁸ We have found higher PPI levels in the high BMI group which is consistent with prior studies.³⁹

CONCLUSIONS

There have been reports of conversion of NGT (Normal Glucose Tolerance) to AGT and subsequently, AGT to T2DM (Type 2 Diabetes Mellitus) in population with PCOS as well as in healthy subjects. Results of this study showed, post-prandial insulin levels to be increased in abnormal glucose tolerant (AGT) patients in comparison to (NGT) patients. In PCOS patients, it is difficult to find out prospective frank T2DM without measuring serum insulin level and comparing them to insulin resistance. Insulin resistance is an integral part of most patients in PCOS. The overall risk of conversion from NGT to AGT or T2DM in women with PCOS is higher in the presence of obesity.

Data sharing statement provided by the authors is available with the full text of this article at jemds.com.

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