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ORIGINAL ARTICLE

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Mathematical indices of insulin resistance and body mass index in polycystic ovarian syndrome

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OBJECTIVE(S) : To find out the correlation between the mathematical indices of insulin resistance (IR) and body mass index (BMI) in polycystic ovarian syndrome (PCOS).

METHOD(S) : Sixty-six PCOS women were studied. BMI was calculated in each case and the mathematical indices of insulin resistance namely, fasting glucose: fasting insulin ratio (G:I), homeostatic model assessment (HOMA), and quantitative insulin sensitivity check index (QUICKI) were calculated from the values of fasting sugar and fasting insulin level. Patients were classified into three groups depending on BMI – Group A ($\leq$ 24 kg/m^2, n=22), Group B (25-29 kg/m^2, n=22), and Group C ($\geq$ 30 kg/m^2 ; n=22). Intra-group and inter-group correlation coefficients were calculated between these parameters.

RESULTS : Strong negative correlations between G:I and HOMA and strong positive correlations between G:I and QUICKI were found in each of the three groups. HOMA and QUICKI showed strong negative correlations in each of the three groups. There were moderate positive correlations between the respective indices among Group A and B. None of the indices showed any significant correlations with BMI, both intra-group and inter-group.

CONCLUSION(S) : Mathematical indices of insulin resistance have mild correlations with BMI in PCOS, in contrast to many other insulin resistant states and should be utilised cautiously in routine clinical practice in the management of PCOS.

Key words : insulin resistance, mathematical indices, bodymass index, polycystic ovarian syndrome

Introduction

Insulin resistance (IR) is a state in which a given concentration of insulin produces a less than expected biological effect. Apart from its effect on the carbohydrate metabolism, insulin has diverse functions to perform in other body systems. Significance of insulin resistance in polycystic ovarian syndrome (PCOS) has generated intense interest among reproductive endocrinologists and gynecologists, although insulin resistance is not a part of the diagnostic criteria of PCOS as per the revised guidelines of the PCOS consensus workshop group [1]. Again, among the different clinical states of IR, the degree of IR can vary from patient to patient. Ethnic factors may also be involved. Obesity is another factor believed to be involved independently in insulin resistance. It is a common experience of all gynecologists that women with PCOS do not respond equally to insulin-sensitising drugs like metformin. Not all people with impaired insulin sensitivity are necessarily suffering from a disorder and pregnancy is a perfect example of this.

There are many mathematical models to detect insulin resistance or insulin sensitivity. It would be helpful if one can evaluate insulin resistance or sensitivity in a clinical setting. This can help select the most appropriate candidates for insulin-sensitising drugs and subsequent planning of interventions.

In the present study, the three indices namely, fasting glucose: fasting insulin ratio (G:I), homeostatic model assessment (HOMA), and quantitative insulin sensitivity check index (QUICKI), were calculated to correlate with the body mass index (BMI) in PCOS patients.

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Materials and methods

Sixty-six cases of polycystic ovarian syndrome were studied. Each patient met the criteria for polycystic ovarian syndrome as recommended by Rotterdam ESHRE/ASRM sponsored PCOS consensus workshop group [1], and secondary causes such as non-classical 21-hydroxylase deficiencies, hyperprolactinemia and androgen secreting neoplasm were excluded.

All these patients were tested for fasting sugar and fasting insulin levels. BMI was calculated from height and weight measurements. Oral GTT glucose tolerance test (OGTT) was done if fasting glucose level exceeded 110 mg/dL to exclude diabetes mellitus or impaired glucose tolerance. There was only one patient that had fasting glucose level of 123 mg/dL but the oral glucose tolerance test was negative.

HOMA was calculated using the formula — HOMA = fasting insulin (μu/mL) x fasting glucose (mmol/L) / 22.5 [2].

QUICKI was calculated by the formula — QUICKI = 1 / [Log (fasting) insulin + Log (fasting) glucose] [2].

For each patient, fasting glucose: insulin ratio (G: I) was calculated.

The 66 cases were grouped as per the following criteria—

Group A — BMI $\leq$ 24 kg/m² (n=22)

Group B — BMI 25 - 29 kg/m² (n=22)

Group C — BMI $\geq$ 30 kg/m² (n=22)

Results

Table 1 shows the mean values of all the parameters noted in the study.

Table 2 shows the correlation coefficients between G:I - HOMA, G:I- QUICKI, HOMA-QUICKI, BMI-G:I, BMI-HOMA, and BMI-QUICKI in the three groups. There was strong negative correlation between G:I-HOMA and strong positive correlation between G:I- QUICKI in each of the three groups. There was strong negative correlations between HOMA-QUICKI. There was mild correlation between BMI and each of the three parameters in all the groups. Table 3 shows the correlation coefficients between the parameters inter-group. Group A and Group B showed moderate correlations among themselves but only mild correlation was seen between Group A and Group C, and between Group B and Group C.

Table 1. Mean values of the parameters.

Parameter	Group A (n=22)	Group B (n=22)	Group C (n=22)	All the groups (n=66)
Age (years)	20.72 ± 3.23	23.22 ± 5.54	23.81 ± 04.29	22.59 ± 4.59
BMI (kg/m^2)	21.90 ± 1.79	26.23 ± 1.52	32.40 ± 02.38	26.98 ± 4.72
Fasting glucose (mg/dL)	85.81 ± 7.53	86.90 ± 8.24	91.09 ± 11.46	87.93 ± 9.38
Fasting insulin μu/mL	11.50 ± 4.93	18.02 ± 4.99	18.43 ± 11.67	15.98 ± 8.37
G:I ratio	9.05 ± 4.73	5.21 ± 1.53	06.28 ± 02.79	6.85 ± 3.63
HOMA	2.47 ± 1.15	3.84 ± 1.02	04.18 ± 02.80	3.50 ± 1.96
QUICKI	0.33 ± 0.02	0.31 ± 0.01	00.31 ± 00.02	0.32 ± 0.02

Discussion

Insulin resistance is a term, which has a broad clinical spectrum and heterogeneities in the manifestations. Degree of insulin resistance can also vary among different clinical states. The concept of insulin resistance is easy to understand but quantitative assessment of insulin sensitivity, which is the reverse of resistance, and the ability to determine exactly who is insulin resistant is more difficult in a clinical setting. However, this assessment of insulin resistance or insulin sensitivity is of great importance in the study of epidemiology and pathophysiology of major public health problems and in following the clinical course of patients on various therapeutic regimens.

Table 2. Correlation coefficients between the indices in the three groups.

	Group A (n=22)	Group B (n=22)	Group C (n=22)
G:I and HOMA	-0.77	-0.81	-0.73
G:I and QUICKI	0.90	0.73	0.88
HOMA and QUICKI	-0.94	-0.96	-0.87
BMI and G:I	0.09	0.18	-0.28
BMI and HOMA	-0.03	-0.03	0.09
BMI and QUICKI	0.07	0.02	-0.18

Table 3. Correlation coefficients between the indices in the three groups.

	Group A (n=22)	Group B (n=22)	Group C (n=22)
G:I and HOMA	-0.77	-0.81	-0.73
G:I and QUICKI	0.90	0.73	0.88
HOMA and QUICKI	-0.94	-0.96	-0.87
BMI and G:I	0.09	0.18	-0.28
BMI and HOMA	-0.03	-0.03	0.09
BMI and QUICKI	0.07	0.02	-0.18

Insulin sensitivity can be influenced by age, ethnicity etc and obesity is considered an important independent cause of insulin resistance. Nestler et al [3] have suggested that all women with PCOS should be considered as insulin resistant. But this recommendation does not take into consideration the large differences in insulin sensitivity among women with PCOS. As already mentioned, obesity as an independent factor for insulin resistance, can influence the phenotype of the syndrome and can worsen the endocrine and metabolic parameters [4] .

The parameters that have been studied in the present work have already been assessed by various workers and correlated with the Euglycemic-Hyperinsulinemic Clamp Studies that is considered the gold standard method for the assessment of insulin resistance though it is not suitable for routine clinical work [5-7] .

The present work shows that the inter-relationships between the three parameters viz., G:I, HOMA, QUICKI, follow the same trend as reported by various other authors [8,9]. But we fail to find any significant correlations between Group B and Group C (Table 3). It should be remembered that these pure mathematical models carry a risk in extrapolating conclusions from calculations to in vivo phenomenon [8].

The present study shows a marginal fall in QUICKI value between Group A and Group B or Group A and Group C but no difference between Group B and Group C. Katz et al [8] have found that QUICKI may not be a reliable method to accurately include the wide spectrum of insulin sensitivity in different insulin-resistant populations. Abassi and Reavan [9] had also found that QUICKI is less efficient in cases of mild insulin resistance. Strong correlations between HOMA and QUICKI as found by us have also been reported by other workers [8,9].

We are aware that the study does not include a control group but it was not the aim of the study to determine the normal values for insulin resistance indices. The objective was to evaluate the relationships between these mathematical indices and BMI in cases of PCOS. For this purpose, it is of no importance whether the values of these indices lie within the normal range or not. The present work fails to find any significant correlations between these indices and BMI in all the three groups. This is in contrast to other insulin resistant states like diabetes mellitus and hyperlipidemia. It may be possible that only glucose and insulin are not involved in the pathogenesis of PCOS but other factors like free fatty acids and androgens are also involved. It is also possible that not only the total amount of body fat represented by BMI, but also fat tissue distribution may be important in the pathogenesis of insulin resistance. Cibulo et al [10] have reported that the insulin resistance/sensitivity parameters correlated with BMI and not with the waist: hip ratio.

Kaufman et al [11] have suggested that a single screening test for PCOS related insulin resistance should be individualized for different racial or ethnic populations. Skrha et al [12] have found very strong associations between BMI and the insulin sensitivity indices. Thus if BMI is excluded, it is not possible to assess the insulin resistant state by the three mathematical indices in cases of PCOS.

Hence these indices should be utilised carefully by a gynecologist in the treatment of PCOS and should not be considered a surrogate of BMI for assessment of insulin resistance.

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