Journal of Clinical Medicine and Research Vol. 4(7), pp. 84-88, October, 2012
Available online http://www.academicjournals.org/JCMR
DOI: 10.5897/JCMR11.086
ISSN 2141-2235 ©2012 Academic Journals

Full Length Research Paper

Body mass index (BMI) related insulin resistance in polycystic ovarian syndrome among patients referred to gynecology clinic of Imam Reza Hospital, Tehran, Iran

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Accepted 18 September, 2012

Polycystic ovarian syndrome (PCOs) is one of the commonest endocrinopathies of women. The present work has been undertaken with an aim to study insulin resistance rate among army personnel families. Out of 108 women suffering from oligomenorrhea and hirsutism referred to gynecology clinic of Imam Reza hospital from 2009 to 2010, 58 patients with PCOs were evaluated for insulin resistance. Their disease was diagnosed clinically and confirmed by laboratory findings. The patients fasting blood sugar (FBS) was measured to be 81 to 103 with mean of 91.44 ± 6.52. Insulin level of their fasting blood (FBI) was 3.1 to 33 with mean of 10.95 ± 7.53. FBS/FBI ratio ranged from 2.87 to 31.6 with mean of 12.54 ± 7.98. The co-relational analysis reveals a positive relationship between insulin resistance and body mass index (BMI; normal, overweight and obese). There was a significant association between these two ordinal variables (Spearman's Correlation Coefficient is 0.59, P < 0.01). Leutinizing hormone/follicle stimulating hormone (LH/FSH) ratio is not significantly related with BMI (P = 0.65) and no significant relationship was observed between age groups and LH/FSH ratio (P = 0.76). The results achieved by two-way analysis of variance (ANOVA), that is, the F-values given in the Tests of Between-Subjects Effects indicate that the contribution of age group to ANOVA is not significant (F = 0.160, P = 0.852). The level of significance between BMI and FBS/FBI is 0.699 (F = 0.360). In addition to the main effects of both variables, there is no significant interaction. 6% of overweight and 39% of our obese patients were resistant to insulin, while no resistance to insulin was observed among cases with normal BMI.

Key words: Polycystic ovarian syndrome (PCOs), insulin resistance, diabetes, body mass index (BMI), infertility.

INTRODUCTION

Polycystic ovarian syndrome (PCOs) is one of the commonest endocrinopathies of women which is the most widely studied and is a controversial area in gynecologic endocrinology (Battaglia et al., 2008).

The current estimates suggest that PCOs affects 5 to 10% of reproductive age women (Fleischman and Mansfield, 2005; Chang and Coffler, 2007; Lam et al., 2004; Pfeifer, 2005). It is also the most common cause of female infertility (Legro et al., 2007) accounting for more than 40% of all cases. Some (Mastorakos et al., 2006; Aziz et al., 2005) believe that PCOs has substantial psychological, social and economic consequences and is associated with the development of a number of sequelae, including increased risk of glucose intolerance (gestational and type II diabetes).

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According to Angioni et al. (2008), approximately 40 to 50% of women affected by PCOs are overweight or obese, frequently presenting high insulin levels and reduced glucose-induced insulin metabolism, while Lam et al. (2004) stated that women with PCOs, both lean and obese, may be insulin resistant as reflected by fasting glucose/insulin ratio < 4.5. Insulin resistance in women with PCOs seem to be common in both obese and non obese women and there is strong evidence that women with PCOs are at an increased (3 to 7 times) risk of developing type 2 diabetes and possibly cardiovascular complications (Yavasoglu et al., 2009; Bener et al., 2007), abnormal gonadotropin secretion, hyperandrogenism or excessive production of androgens and insulin resistance (Chang and Coffler, 2007; Eisenhardt et al., 2006) and secondary oligomenorrhea or amenorrhea (Bartoszek, 2009).

Since majority of the patients referred to Imam Reza hospital, Tehran, Iran are army personnel or their families, this work has been undertaken with an aim to study insulin resistance rate among this group of patients.

MATERIALS AND METHODS

Case selection

Women (108) suffering from oligomenorrhea and hirsutism referred to gynecology clinic of Imam Reza hospital from 2009 to 2010 were the study cases.

Inclusion criteria

Patients were included in the study on the basis of criteria such as presence of hyperandrogenism (hirsutism or hyperandrogenemia) with either oligo/amenorrhea or polycystic ovaries (≥12 small cyst with 9 to 2 mm in diameter or an increased ovarian volume >10 ml or both) and missing exclusion criteria.

Exclusion criteria

Patients were excluded from the study on the basis of the presence of hyper prolactinemia, thyroid abnormalities, late onset congenital adrenal hyperplasia (CAH), androgen secreting tumors and treatment in past 6 months for PCOs.

Patients (50) were excluded from the study on the basis of our exclusion criteria. At last, the study was carried out with 58 patients with PCOs who were evaluated for insulin resistance related to their BMI.

Patients were checked for hirsutism, hyperandrogenemia (total testosterone concentration and dehydroepiandrosterone sulfate (DHEAS)) and oligomenorrhea or polycystic ovaries. Sonography was performed as a diagnostic tool for determining the specificities of ovarian cyst, if present, on the basis of criteria like ≥12 cysts (2 to 9 mm in diameter) or an increased ovarian volume (>10 ml) or both (Cunningham et al., 2010).

Experimental

The height and weight of every patient was measured and recorded on their first visit and BMI was calculated. Patients were grouped according to their BMI into 3 groups of normal with BMI of 20 to 24.9, overweight (25 to 29.9) and obese (≥30). A questionnaire was filled by every patient, which included information regarding history of menstruation like interval and duration, history of infertility, presence of galactorrhea and weight changes. Laboratory investigations were requested for every patient on third day of their period including total testosterone concentration, leutinizing hormone (LH), follicle stimulating hormone (FSH), LH/FSH ratio, fasting blood sugar (FBS), fasting blood insulin (FBI), 17-Hydroxyprogesterone (17-OHP), DHEAS, thyroid stimulating hormone (TSH) tests and the results were recorded in their files.

All the patients' laboratory tests were done in the hospital laboratory. Patients with increased or decreased TSH, patients with 17-OHP level more than 200 ng/dl or those with testosterone level higher than 200 ng/dl and DHEAS more than 700 µg/dl were excluded from the study.

The insulin resistance was diagnosed according to the criteria laid down in William's Gynecology (Cunningham et al., 2010). Multiple testing and screening approaches have been proposed to assess the presence of insulin resistance (Fritz and Speroff, 2011). The gold standard for evaluating insulin resistance has been hyperinsulinemic euglycemic clamp. Homeostatic model assessment-insulin resistance (HOMA-IR) [glucose (mg/dl)], [insulin (µU/ml)]/405 is another method of measuring insulin resistance (Speroff, 2011). As hyperinsulinemic euglycemic clamp is not practical in a clinical setting and HOMA-IR is used in larger epidemiologic studies, so we used fasting serum glucose to insulin ratio to calculate insulin resistance. We also considered values less than 4.5 as insulin resistant cases. A consent form was signed by every patient.

Statistical Package for Social Sciences (SPSS) 17 was employed for analytical purposes. In order to statistically analyze our data, we applied both descriptive and inferential statistics. Descriptive statistics contains minimum, maximum, mean and standard deviation for each variable. In the inferential part, we used Chi-Square test, Spearman and Pearson correlation coefficients, and Phi and Cramer V and linear regression to find out the relationship between all the variables. A two-way analysis of variance (ANOVA) test is also used to find out the effects of BMI and age group on FBS/FBI. The level of significance was considered as 0.01.

RESULTS

In this study, our patient's age varied from 14 to 38 years with mean of 23.67 ± 6.34. Patients BMI was calculated which ranged from 23 to 36. Most of our cases, that is, 35 cases (60.34%), aged 20 to 27 years. They had the highest mean BMI (38 kg/m^2) as well. The lowest study cases belong to age group ≥28, that is, 18.96% of all study cases with mean BMI of 33 kg/m^2 (Table 1).

As regard the relationship between BMI (normal, overweight and obese) and age, no significant relationship was observed (P = 0.63). Patients were checked for hyperandrogenism in the clinic. Hirsutism was observed in 32 (55%) patients, while hyperandrogenemia was noticed in 45% of the cases.

To find out the association between hyperinsulinemia and hyperandrogenemia, as these two variables are closely linked, we used Phi and Crammer's V test. Our analysis reveals P > 0.05, indicating that their relationship is not significant.

Amongst patients with hyperandrogenism, amenorrhea and/or oligomenorrhea was noticed in 94% of the cases.

Table 1. Age distribution, BMI, FBS and FBI of the study cases.

Age group (years)	No. in each group	Mean BMI	Mean FBS	Mean FBI
≤19	12	28	81.69 ± 3.81	5.14 ± 3.12
20 - 27	35	38	138.73 ± 8.93	19.29 ± 2.30
≥28	11	33	78.46 ± 4.91	8.43 ± 2.11
Total	58	33	91.44 ± 6.52	10.95 ± 7.53

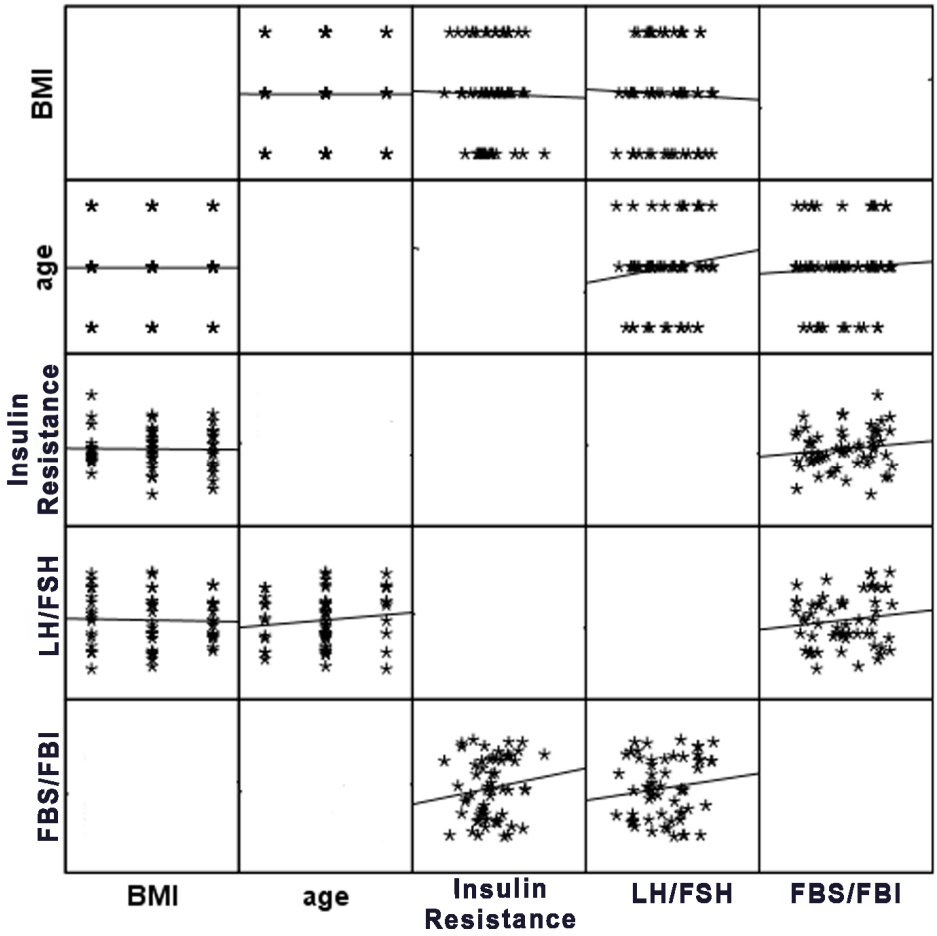

Figure 1. Linear regression scattered plot for all correlations.

Sonographic findings indicate that 45 out of 58 (77.58%) cases had polycystic ovaries. Insulin resistance is defined as a reduced glucose response to a given amount of insulin. We used fasting glucose/insulin ratio as an index of insulin resistance in women with PCOs. The patients FBI level was 3.1 to 33 with mean of 10.95 ± 7.53. Sugar level of their fasting blood was measured to be 81 to 103 with mean of 91.44 ± 6.52. FBS/FBI ratio ranged from 2.87 to 31.6 (Table 1).

As some of our data are quantitative like FBS/FBI ratio and LH/FSH ratio, we used Pearson's correlation and for qualitative readings we used Spearman s linear regression correlation (Figure 1).

Resistance to insulin on the basis of FBS/FBI ratio showed that 6% of the overweight and 39% of the obese cases were resistant to insulin; none of our studied cases with normal BMI were resistant to insulin and none of our cases who were resistant to insulin had type II diabetes mellitus.

The co-relational analysis reveals a positive relationship between insulin resistance and BMI (normal, overweight and obese). There was a significant association between these two ordinal variables (Spearman's Correlation Coefficient is 0.59, $P < 0.01$). Pearson's correlation between BMI (Scale variable) and FBS/FBI ratio indicates that the relationship is significant

(P = 0.013) and as Pearson's correlation coefficient is -0.4 indicating a reverse relationship between these two variables with medium intensity.

The LH/FSH ratio is not significantly correlated with BMI (P = 0.65) and no significant relationship was observed between age and LH/FSH ratio (P = 0.76).

The results achieved by two-way ANOVA, that is, the F-values given in the Tests of Between-Subjects Effects indicate that the contribution of age group to ANOVA is not significant (F = 0.160, P = 0.852). The level of significance between BMI (normal, overweight and obese) and FBS/FBI is 0.699 (F = 0.360). In addition to the main effects of both variables, there is no significant interaction.

DISCUSSION

PCOs is one of the common causes of infertility due to anovulation in 35 to 94% of women (Yavasoglu et al., 2009). In our study also, 54 (93.1%) patients missed regular menstruations and only 6.89% (4 cases) had regular menstruations.

It has been inferred that hyperinsulinemia, compensatory to insulin resistance, contributes to the hyperandrogenism, because most women with PCOs appear to have increased insulin resistance. We observed clinical hyperandrogenism signs like acne, hirsutism, and hair fall in 33 out of 58 (56.89%) patients. Sonographic findings of our cases revealed 45 out of 58 (77.58%) had polycystic ovaries and no PCOs was detected in 13 (22.41%) cases.

Many researchers (Fruzzetti et al., 2008; Diamanti-Kandarakis et al., 2007; Berneis et al., 2007; Cupisti et al., 2008) believe that obesity is more prevalent in women suffering from PCOs. According to Angioni et al. (2008), a high proportion of women with PCOs are obese, while in this study only 10 (17.24 %) patients were obese.

The fasting glucose/insulin (G/I) ratio has been widely used as an index of insulin resistance (Fritz and Speroff, 2011; Angioni et al., 2008). According to Angioni et al. (2008), G/I ratio lower than 4.5 implies a 95% sensitivity and 84% specificity for insulin resistance.

Ketel et al. (2009) reported that androgen and LH concentrations were increased in both normal-weight and obese women suffering from PCOs, while FSH was slightly lower in the normal weight women with PCOs as compared to the normal weight controls. In their study, LH/FSH ratio of 33 (56.89%) patients was above 2 and in 25 (43.1%) cases the ratio was less than 2. In our study, no relationship was found between LH and BMI in cases with LH/FSH ratio greater than 2. Also, no relationship was found between hirsutism and insulin resistance in cases with LH/FSH ratio greater than 2.

Areej and Catherine (2008) reported insulin resistance accompanied by compensatory hyperinsulinemia, a common finding in both lean and obese women with PCOs. According to them, insulin resistance is most marked in obese cases with 70% incidence. In our study also, 45% of patients with BMI more than normal (39% of the obese and 6% of overweight patients) were resistant to insulin.

Conclusions

Considering the side effects of insulin resistance in patients with PCOs and significant relationship between BMI and insulin resistance, weight loss of obese and overweight patients with PCOS is strongly recommended. As good sum of money is to be spent for treatment, it is wise to screen for impaired insulin tolerance in women with PCOs, especially those who are obese or overweight.

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