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EVALUATION OF CLINICAL COURSE AND RISK FACTORS FOR POLYCYSTIC OVARY SYNDROME AMONG MARRIED AND UNMARRIED WOMEN

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ABSTRACT

Polycystic ovary syndrome (PCOs) is a frequently encountered endocrine disorder. It is still controversial that whether it's a single disorder or multiple associated pathologic conditions. It is significantly associated with reproductive morbidity, infertility, miscarriages, hyperandrogenism, cancers and other complications. For this study, 105 female subjects with PCOs were selected from Abbasi Shaheed Hospital and were divided in married and unmarried groups. Patients were asked for personal family history, disease and menstrual cycle and life style through a detailed questionnaire. Blood samples were taken for hematologic and biochemical findings. Data was compared between the groups for clinical course, risk factors and complications of the disease. In group I (married) 40.9% females were obese and 50% were overweight and in group II (unmarried) 62.5% females were obese and 18.75% were overweight. Oligomenorrhea, acne, hirsutism and acanthosis nigricans were higher in group II whereas testosterone levels, ovarian cysts, insulin resistance and psychological behavior disturbances were higher in group I. The mean menarche age was 12.83 ± 0.16 years in both the groups. Furthermore 99% group I females were infertile having no child history. This study concludes that PCOs is a widely spread very common endocrine disorder that may lead to infertility. However, physical exercises and life style modification are proven to be beneficial and preventive to a certain extent.

KEYWORDS: Endocrine disorder, Metabolic disorder, Infertility, Hyperandrogenism, Reproductive disorder.

INTRODUCTION

The *Polycystic Ovary Syndrome (PCOs*) is a prevalent and frequently encountered disorder with a prevalence of 6-7% women of premenstrual age worldwide (Codner and Escobar-Morreal, 2007). However in Pakistani women its prevalence is 20.7% in women of reproductive age group (Nazir *et al*., 1999). Because of the diversity in clinical findings it's still a controversy whether PCOs is a single disorder or multiple pathologic conditions (Lobo and Carmina, 2000; Zborowski *et al*., 2000) PCOs is also known as Stein-Leventhal syndrome because, it was first described by Stein and Leventhal in 1935, as pathogomonic ovarian findings and clinical trials of hirsutism, amenorrhea and obesity (Stein and Leventhal, 1935). Significantly PCOs is associated with infertility, abnormal uterine bleeding, miscarriage, reproductive morbidity and many other pregnancy complications as well (Oberfield, 2000).

A major clinical finding in PCOs is hyperandrogenism, manifested by hirsutism, acne and androgenic alopecia which contribute to chronic ovulation and menstrual dysfunction. Patients with PCOs present abnormal steroidogenic activity that ceases follicle maturation and ultimately leads to anovulation (Codner and Escobar-Morreal, 2007). Anovulatory infertility is presented in more than 75% cases of PCOs due to arrested antral follicle development. Excess androgen production contributes to irregular or absent ovulation causing irregular or absent menstrual periods and the women faces difficulty in becoming pregnant (Gorry *et al*., 2006). Also in women with PCOs, increased adrenal androgen concentrations are observed which suggests that they may have deregulated Hypothalamus-pituitary-adrenal axis. Rodin and colleagues proposed a subset of Women with PCOs having increased response of adrenal androgens and adrenocorticotropic hormone to corticotropin releasing hormone suggesting that increased catabolism of cortisol can cause hyperactivation of HPA axis with increased androgen formation (Gambineri *et al*., 2002). In PCOs the mechanism of exaggerated ACTH response to CRH is still unknown (Kondoh *et al*., 1999; Gambineri *et al*., 2002). PCOs is significantly associated with hyperinsulinemia, with a positive correlation seen between androstenedione, testosterone and insulin. Studies on a wide spectrum both in vivo and in vitro (in cultured theca cells) suggest that these women efficiently convert androgenic precursors to testosterone (Nelson *et al*., 2001).

PCOs women have higher rates of carbohydrate intolerance than age and weight matched control subjects, however lean women with PCOS have lower rates of carbohydrate intolerance as compared to the obese women with PCOs (Dunaif *et al*., 1987). Insulin plays a major role in developing hyperandrogenemia because it elevates the concentration of free testosterone levels. Peripheral Insulin resistance and hyperinsulinemia shows a high link with PCOs and obesity augments both the conditions. In women with PCOs, release of adiponectin (a lipid metabolism and glucose level regulatory hormone) produced by adipocytes, is coupled with insulin resistance. And so, the women having PCOs release lower levels of adiponectin as compared to women not having PCOs. This condition, in which insulin levels are at high, causes dyslipidemia (Lucidi, 2011). The two genes that evidential studies found to be involved in PCOs are steroid synthesis gene CYP11a and the insulin VNTR regulatory polymorphism. Difference in CYP11a could account for variation in androgen production in PCOs and, the subjects carrying class III alleles at insulin gene VNTR locus are more likely to be hyperinsulinaemic causing them to suffer from menstrual disorders (Frank *et al*., 1997). PCOs is usually thought to be a genetic ovarian disorder however the diversity of the syndrome depends upon its interaction with other genes and the environment (Gorry *et al*., 2006).

Women having PCOs are significantly prone to maternal pregnancy complications which include increased prevalence of early pregnancy loss (EPL), Pregnancy induced hypertensive disorders (PET), birth of small-for-gestational-age (SGA) babies and gestational Diabetes Mellitus (Homburg *et al*., 2006). These women also have greater risk of developing preeclampsia. As compared to normotensive pregnant women, women with PCOs also present other metabolic abnormalities linked to insulin resistance which includes gestational DM, hyperinsulinemia, hyperlipidemia and high levels of plasminogen activator inhibitor-1, leptin and TNF- α. This suggests that treating Insulin resistance may ameliorate PCOs (Seely, 2001). Normally PCOs women present with DM and are also obese that contributes in development of coronary artery disease (Legro *et al*., 2007). Insulin resistance appears to have a pivotal role in lipolysis causing dyslipidemia in women with PCOs (Deeks *et al*., 2010). In PCOs, when ovulation does not occur the lining is not shed and is exposed to higher levels of estrogen which increases the chances of cancer and studies have shown 2 to 3 fold increased Ovarian cancers in women with PCOs. Obesity and PCOs have a significant relationship and is still controversial that whether PCOs makes a woman obese or Obesity causes a women to develop PCOs. However obesity is reported in at least 30 percent cases and in some series the percentage is as high as 75 (Ehrmann, 2005). Acne and hirsutism are most common symptoms of PCOs because of the over production of androgens by ovarian cysts. Women who have PCOs suffer from depression, mood swings, anxiety and low self-esteem. It causes them to have negative body image and psychosexual dysfunction. Managing PCOs symptoms may help to relieve depression. (Coffey and Mason, 2003; Teede *et al*., 2010; Deeks *et al*., 2010).

MATERIALS AND METHODS

This study was conducted in Karachi and included females between the age of 15 ~ 45 year. The study was conducted on females of lower-middle socioeconomic class. A detailed questionnaire was prepared in accordance with the objectives of study. Subjects were thoroughly asked about menstrual history, oligomenorrhea, amenorrhea, dysmenorrhea, abnormal bleeding during periods and duration of menstrual cycle. The body mass index (BMI) of each subject was calculated by dividing the weight (kg) of the subject by the square of her height (m^2) to categorize the underweight and obese females. Patient's hospital reports were specially taken for laboratory investigations which include fasting blood glucose, insulin level, testosterone level and ultrasound reports for cysts. Patients were taken as hyperinsulinemic when the serum insulin level is >18 mlU/ml and as hyper-androgenic when the testosterone level is > 0.82 ng/ml. The diagnosis is based on the criteria approved in 2003 by European Society for Human Reproduction and Embryology (ESHRE) and the American Society for Reproductive Medicine (ASRM) (Lucidi, 2011).

RESULTS AND DISCUSSION

Mean age of group I (married) was 30 ± 1.21 years and group II (unmarried) was 22 ± 0.94 years, whereas mean age of menarche of both groups was 12 ± 0.161 years. Individuals belonging to middle class, lower middle class and lower class socioeconomic status of group I were 31.8%, 13.6% and 54.50%, respectively (Table 1) and, in group II there were 7.60%, 23% and 69.20%, respectively. Married as well as unmarried women were characterized Oligomenorrhea and Dysmenorrhea (Table 2). Subjects had prominent signs and symptoms of PCOs. Obesity, Acne, mood swings, sleep Apnea were found to be higher in group II (Fig. 1). Mean BMI of group I and II was 3.3 ± 0.138 and 3.77 ± 0.122 Kg/m^2 (P=0.033) respectively which is statistically not significant (Table 5). Mean testosterone level in group I was 2.74 ± 1.66 and in group II was and 1.28 ± 0.31 ng/mL (P=0.432), however, mean insulin level of group I and II was 26.96 ± 4.10 and 30.23 ± 4.48 mL/U (P=0.606) respectively, which is statistically not significant. Blood glucose fasting in group I was 100.45 ± 10.22 and in group II was 100.6 ± 13.7 mg/dL (P=0.99) (Table 4). Women with PCOs usually have fewer than six to eight menstrual cycles per year. Some women have normal cycles, which may become irregular if the women become obese (Barbieri *et al*., 2011). In this study, the married female had 81.8% oligomenorrhea and unmarried female had 84.6% (Table 3). It has also been suggested by some studies that a family history of Diabetes Mellitus worsens insulin secretion and glucose tolerance in PCOs (Ehrmann *et al*., 1995). In our study the family history of Diabetes in group I subjects was 40.8% and in group II subjects about 92.29% (Fig. 3). Our study also suggests that chronic infections may be involved in the etiology of PCOs. Such chronic infections may induce inflammation and oxidative stress, which in turn may contribute to insulin resistance, ovarian dysfunction and other characteristics of PCOs. Studies have shown relationship of pathogen (Chlamydia Pneumonia) infection in mice that resulted in increased ovarian size and a greater number of antral follicles. In our study 22.7% married and 30.7% unmarried women showed history of infection (viral or bacterial). When found in conjunction with hyperandrogenism the acanthosisnigricans' condition is termed as HAIR-AN syndrome (Hyperandrogenic-insulin resistant acanthosis nigricans). It occurs in 2 to 5% of hirsute women. The majority of women with PCOs i.e. 70% are insulin resistant but hyperinsulinemia is far more severe in women with HAIR-AN syndrome. In our study 45.4% married and 50% unmarried females had these kinds of patches (Fig. 4).

High risk of sleep apnea is reported in subjects of PCOs. This may be due to the increased BMI. Another probable reason of increased prevalence of sleep apnea in people with PCOs is the effect of testosterone on blood vessels. Sleep apnea may occur in almost 50% of women with PCOs (Legro, 2007). Through our study we found that in married group 27.2% and in unmarried group 6.25% women had sleep apnea problem (Fig. 4). PCOs and fatigue both are linked to endocrine imbalances, this study also include 95.4% married and 76.9% unmarried females with fatigue problem. Many

studies found that women with PCOs are highly susceptible to develop depression or depressive symptoms. Depression is associated with increased BMI and increased insulin resistance. In our study married females showed 72.7% and unmarried females showed 50% problem of depression and anxiety. Due to the many symptoms of hyperandrogenism and insulin resistance, they were psychologically disturbed; also about 63.6% married and 50% unmarried females were socially inactive. Aggression was reported in about 95.4% married and 62.5% unmarried women (Fig. 2). According to a study nearly 80% of women with hyperandrogenism have polycystic ovaries (Driscoll, 1994). According to our study 54.5% married females had cyst in right ovaries whereas in unmarried females 31.2% had cyst in right ovary and 53% of married females had cyst in left ovary whereas 37.5% of unmarried females had cyst in left ovary.

Limitations of the study: This study was conducted in a local government hospital and most of the patients belonged to lower socioeconomic status. This study was conducted in a short time span and could not include a large number of populations.

Table 1. Demographic profile.

Variable	Married (%) N=66	Unmarried (%) N=39
Middle	31.80	7.60
Lower middle	13.60	23
Lower	54.60	69.20

Table 2. Menstrual history of patients.

Variable	Married (%)	Unmarried (%)
Oligomenorrhea	81.8	84.6
Dysmenorrhea	81.8	92.3
Heavy bleeding	54.5	69.2

Table 3. Life style and habits of the patients.

Habits	Married (%)	Unmarried (%)
Smoking	0	0
Junk food	77.2	56.25
Walk	36.3	62.5
Oil intake heavy	81.8	75
Oil intake normal	27.2	25
Plenty of water intake	68.1	50

Table 4. Mean biochemical estimations of the patients.

Variable	Married (%)	Unmarried (%)	P-value
Testosterone	2.74 ± 1.66	1.28 ± 0.31	0.432
Insulin	26.96 ± 4.10	30.23 ± 4.48	0.606
Blood glucose fasting	100.45 ± 10.22	100.6 ± 13.7	0.99

Table 5. Anthropometric measurements of patients.

Variable	Married (%)	Unmarried (%)	P-value*
BMI	3.3 ± 0.138	3.77 ± 0.122	0.033
Weight	77.59 ± 3.18	94.31 ± 4.19	0.003
Height	5.2 ± 0.45	5.4 ± 0.48	0.32

* p – value < 0.05 significant (calculated by Independent t-test)

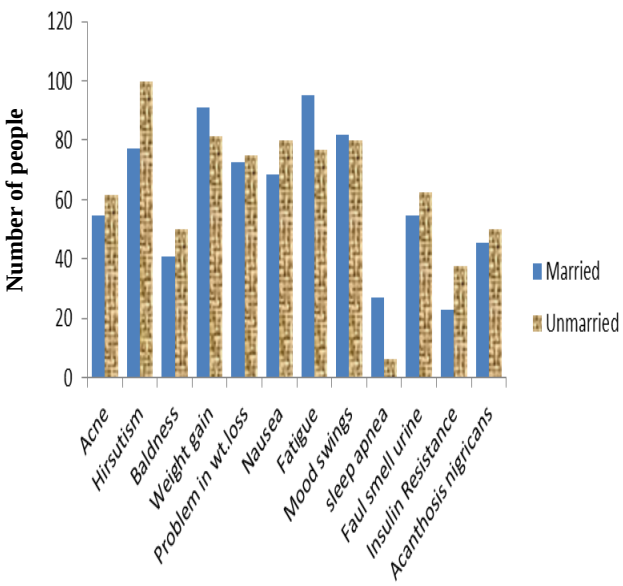

Fig. 1. Physical sign and symptoms of married and unmarried groups.

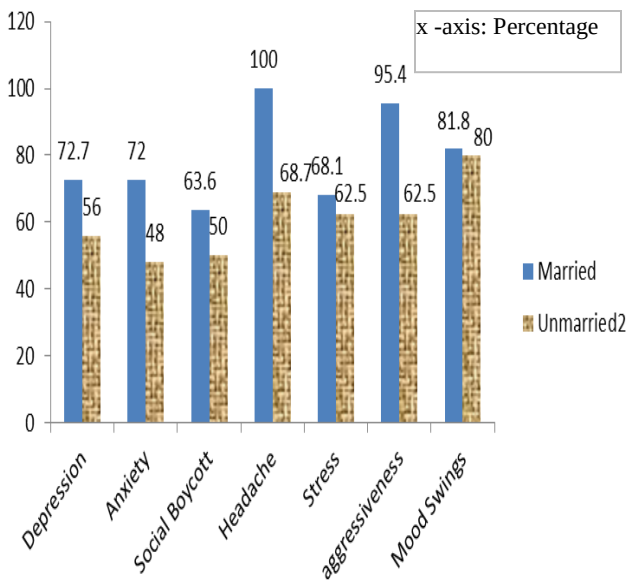

Fig. 2. Psychological sign and symptoms of the two groups.

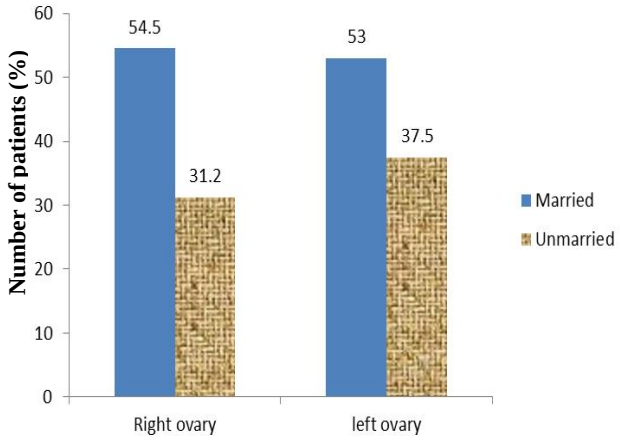

Fig. 3. Presence of cyst in married and unmarried groups.

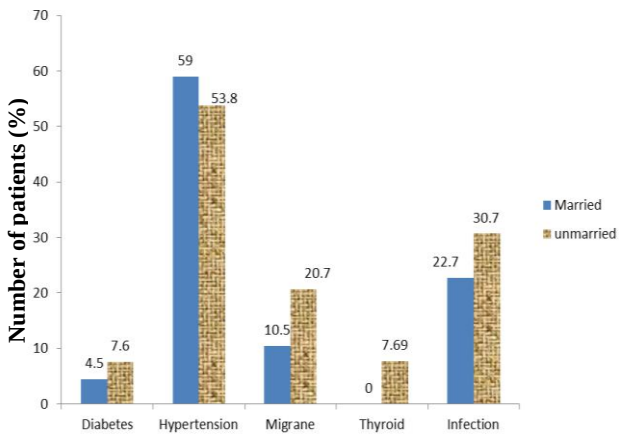

Fig. 4. Medical history of the groups.

CONCLUSION

It maybe concluded that PCOs has becoming a common endocrine problem in our females that may lead to infertility. Numerous genetic, psychological and environmental factors are responsible for this syndrome. Many body systems are affected in polycystic ovary syndrome resulting in severe complications including menstrual dysfunction, hirsutism, obesity, infertility and metabolic syndrome. Management of PCOs can be accomplished through lifestyle modifications. Physical exercises in this condition can be beneficial and preventive to a certain extent.

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