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COMPARATIVE STUDY ON POLY CYSTIC OVARIAN SYNDROME IN NORMAL, OVERWEIGHT AND OBESE WOMEN OF SELECTED POPULATION

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ARTICLE INFO	ABSTRACT
	Objectives: To investigate the levels of C- reactive protein, liver enzymes and TBARS levels in the women with Polycystic Ovary Syndrome (PCOS) and controls divided according to body mass index (BMI) and their association with features of this syndrome. **Methods**: Twenty one PCOS women and 10 healthy women were studied. Patients and controls were subdivided into three groups, Group 1 Healthy women with BMI 18.5- 24.99(n=10), Group 2 PCOS with BMI 25-29.9(n=11) and Group 3 PCOS with BMI >29.9(n=10).Clinical history, height and weight were obtained from the participants. **Results**: Serum CRP, Plasma TBARS, and liver marker enzymes were significantly elevated in both overweight and obese PCOS compare to normal healthy women. **Conclusion**: An increase in oxidant status, inflammatory response and liver marker enzymes was found in women with PCOS, and this increase was related to Body mass Index.

INTRODUCTION

Polycystic ovary syndrome (PCOS) is a common endocrine and metabolic disorder affecting 6–10% of women of reproductive age, and it accounts for 70–80% of anovulatory female infertility (Ghazeeri *et al*., 2003). The European Society of Human Reproduction and Embryology/American Society for Reproductive Medicine criteria, includes three main phenotype characteristics of this condition which are hyperandrogenism, polycystic ovaries, and ovulatory dysfunction (Rotterdam 2004). Globally, prevalence estimates of PCOS are highly variable, ranging from 2.2% to as high as 26% (Katulski *et al.,* 2015). Presence of Insulin Resistance in PCOS is significantly associated with the an increased risk of type 2 diabetes mellitus, cardiovascular disease (Solomon *et al.,* 2015), and also non-alcoholic fatty liver disease (NAFLD) (Tan *et al*., 2010). Women with PCOS are also at an increased risk of pregnancy complications such as impaired glucose

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tolerance, gestational diabetes mellitus, pregnancy-induced hypertension and pre-eclampsia, and small for gestational age (SGA) children. Thus, the metabolic abnormalities of PCOS can affect the woman's health as well as that of her children (Katulski *et al.,* 2015). The wide variation in prevalence might be due to heterogeneous presentation of symptoms, diagnostic criteria practiced, limitations in diagnosis, age groups, and ethnic populations studied. Therefore, it is essential to consider these factors before diagnosis and/or management is initiated. Oxidative stress and chronic inflammation are closely inter-related; indeed, extensive evidence supports the concept of a vicious cycle, whereby inflammation induces generation of reactive oxygen species (ROS), while oxidative stress promotes and aggravates inflammation (Hulsmans*.,* 2010). C-reactive protein (CRP) is an acute-phase protein, which is measured in the serum and is widely used in the routine clinical practice for the monitoring of bacterial infections, as well as the efficacy of the antimicrobial therapy. CRP serves not only as a marker of severe infection but also of low-grade chronic inflammation, as it constitutes a useful screening marker of intravascular inflammatory processes (Du Clos, 2000). 10 of 14 (71%) female patients in childbearing years

with histologically diagnosed NAFLD also had revealed PCOS (Brzozowska 2009). The main aim of this cross-sectional study was to evaluate the serum concentrations of (CRP), Alanine transaminase, Aspartate transaminase and TBARS in a selected population of normal weight women without PCOS, PCOS Women of BMI >25 and >29.

MATERIAL AND METHODS

The study protocol was approved by the Institutional Human Ethical committee (IHEC/16 – 17/BC – 02). A Written informed consent was obtained from all the participants of the Study. Twenty one women with diagnosed PCOS (eleven over weight and ten obese) according to Rotterdam criteria between 19 and 32year of age and10 normal weight control subjects between 19 and 32 year of age volunteered to participate in the study. Detailed history about their menarche, menstrual pattern, menstrual loss, dysmenorrhoea, past and present medical and surgical problems, general physical examination especially their height in meters and weight in kilograms for body mass index were obtained. None of the patients had clinical evidence of recent or acute infection.

Collection of blood sample

Venous samples were collected from each subject after a 12-hfast and used for assay of CRP and Thio Barbituric Acid Reactive Substances (TBARS). Aliquots of serum and plasma was   immediately stored at $-20^{o}C$ until analysis. Blood was stored at $4^{o}C$ for further analysis. CRP analysis was carried out by the method of (Ridker *et al*., 2000). Plasma TBARS was measured by the method of Bishayee and Balasubramaniam (1971).
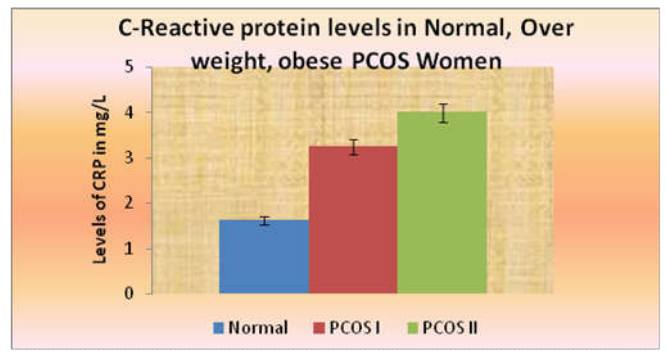
Values are expressed by mean □SE, Significant at 5% level, p<0.05

Figure 1. Levels of C-Reactive protein in normal, overweight and obese PCOS Women
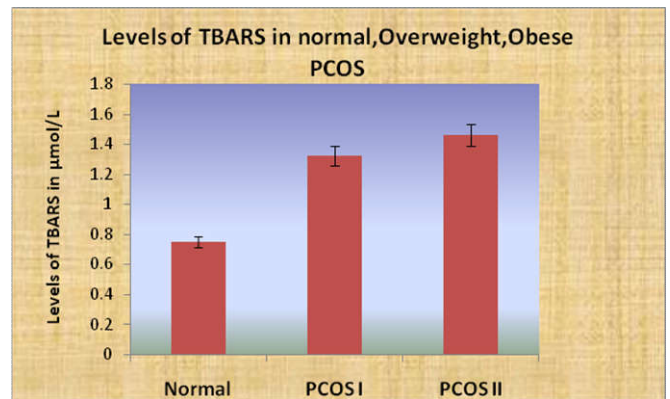
Values are expressed by mean ± SE Significant at 5% level, p<0.05

Figure 2. Levels of Liver marker enzymes in normal, overweight and obese PCOS Women

Table 1.

| Parameter	Group 1 Healthy women with BMI 18.5-24.99 n = 10	Group 2 PCOS with BMI 25-29.9 n = 11	G1 vs G2		Group 3 PCOS with BMI >29.9 N=10 't' value	G2 vs G3	
			't' value	p value		't' value	p value
Age	24+4.3	26.09+4.60	.567[ns]	.586	24.72+4.43	1.632[ns]	.141
Weight in Kg	51+4.18	61.36+4.37	5.428**	.001	72.4+3.13	10.356**	.000
Height in m^2	2.31+0.12	2.29+0.10	.517[ns]	.619	2.31+0.10	.425[ns]	.682
BMI	21.75+2.11	26.71+2.33	5.601**	.001	31.23+1.29	8.569**	.000

* - significant at 5% level

** - Significant at 1% level

As partate amino transferase (AST) was carried out by the method of Reitman and Frankel (1957) and Alanine aminotransferase (ALT) was measured by the method of King (1965). BMI was calculated by standard formula Kg/m^2.

RESULTS

Table 1 show that values of the demographic characters in Group 1 and group 2 did not differ significantly among the groups. Women in Group 2 and group 3 showed highly significant difference in the mean values of weight, BMI, (p<0.001). Figure I show that mean values CRP is significantly increased in group 2 and group 3 as compared to their matched controls (Group 1).

Figure 2 shows that mean values TBARS is significantly increased in group 2 and group 3 as compared to their matched controls (Group 1). Figure 3 shows that mean values of AST and ALT is significantly increased in group 2 and group 3 as compared to their matched controls (Group 1).
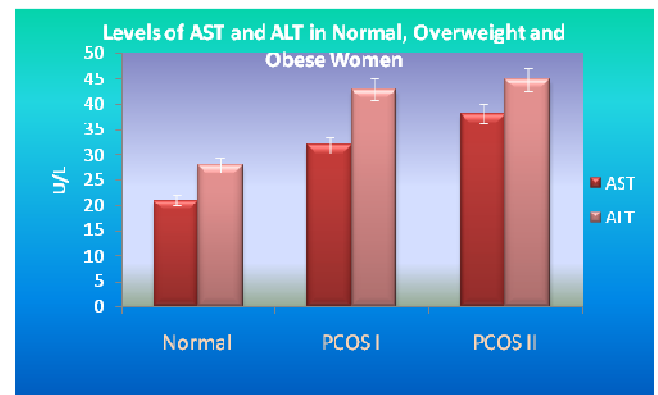
Values are expressed by mean ±SE, Significant at 5% level, p<0.05

Figure 3. Levels of Liver marker enzymes in normal, overweight and obese PCOS Women

DISCUSSION

In the present study, presence of higher BMI indicates presence of deranged lipid metabolism and higher CRP levels

indicates chronic low grade inflammation in PCOS group. In the present study, CRP levels were significantly different between obese PCOS and overweight PCOS and also between normal PCOS and obese PCOS, this indicating that chronic inflammation in PCOS could be because of or accentuated by increased body weight. PCOS patients may represent the largest group of women at high risk for the development of early-onset cardiovascular disease (CVD) and/or diabetes. C-reactive protein (CRP) is a strong independent predictor of future CVD and/or stroke (Boulman *et al.,* 2004). Previous studies have found that the measurement of CRP compared with screening based on lipid levels may provide an improved method of identifying women at risk for CVD (Ridker 2000). The PCOS is a proinflammatory condition and its low grade chronic inflammation causes metabolic derangements and ovarian dysfunction. promoters like adipokines and vasoactive substances, these interfere with insulin action (Gonzalez *et al.,* 2006) and also diet induced inflammation results in over activity of androgens and inflammation of ovaries in PCOS (onzález *et al.,* 2009), so obesity places a major role in the development of PCOS.

Adipose tissue is a known source of IL-6 and TNF- α, which stimulates CRP synthesis in the liver (Moshage *et al.,* 1988). Raise in CRP levels indicates the inflammatory process. Insulin resistance and compensatory hyperinsulinemia are also related to increased de novolipogenesis (synthesis of free fatty acids in the liver) which is another contributor to hepatic fat accumulation. Data from human studies suggest that liver fat accumulation may contribute to insulin resistance and the metabolic syndrome. Metabolic dysfunction in PCOS patients leads to increased risk for cardiovascular disease with aging, particularly after menopause. However, all these components are worsened when obesity is present (Diamanti *et al.,* 2012). In most previous studies, in which BMI and age matched controls were not included, increased se-rum aminotransferases, and especially ALT, and an increased prevalence of NAFLD were found in PCOS women. (Schwimmer*,* 2005). Another study found that 41% (17/41) of women with PCOS had concomitant NAFLD as diagnosed by hepatic steatosis and abnormal ALT levels, whereas the incidence of NAFLD in the weight and age matched non-PCOS control group was only 19% (Vassilatou *et al.,* 2010). Elevated alanine aminotransferase (ALT) serum levels are a common finding in PCOS. Moreover, in PCOS women with abnormal ALT, insulin sensitivity is markedly decreased (P < 0.001). 55% (48/88) of PCOS women had both hepatic steatosis and high Insulin scores Cerda *et al* 2007; Setji *et al.,* 2006).

The above findings suggest that women with PCOS probably are at an increased risk for developing NAFLD and conversely, women with NAFLD may be at risk for having PCOS. In addition, it is reasonable to propose that women with central obesity are at a higher risk for both NAFLD and PCOS. However, for reasons yet unknown, some women develop obesity and never develop PCOS, whereas others develop obesity and then develop PCOS and/or NAFLD. Below, we will review the molecular genetics and environmental interactions in PCOS and try to dissect these facets for possible interplay between PCOS, NAFLD and metabolic syndrome. Non-alcholic fatty liver disease is considered as the hepatic manifestation of metabolic syndrome. Similarly, it seems appropriate to consider polycystic ovary syndrome as the ovarian manifestation of metabolic syndrome.

Both these conditions can co-exist and may respond to similar therapeutic strategies.

Conclusion

An increase in oxidant status was found in women with PCOS, and this increase was related to central obesity, age, blood pressure, serum glucose, insulin and triglyceride levels and insulin resistance. In contrast, antioxidant status was observed to be insufficient. These findings suggest that increased oxidative stress may contribute to the increased risk of cardiovascular disease in women with PCOS. CRP levels are elevated in patients with PCOS and may be a marker of early cardiovascular risk in these patients. High CRP levels may explain why some PCOS women may possibly be at an increased risk for the development of early-onset CVD. Consequently, whether treatment regimens directed toward lowering CVD risk factors should be more aggressive for those PCOS women with increased CRP levels, awaits further clinical experience.

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