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Research Article

Oxidative stress versus inflammation, a better predictor of cardiovascular disease risk in polycystic ovary syndrome

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ABSTRACT

Background: Polycystic ovary syndrome (PCOS) is also known as hyperandrogenic anovulation (HA) or Stein-Leventhal syndrome. PCOS has a diverse range of causes that are not entirely understood, but there is evidence that it is largely a genetic disease. Aim of the study was to evaluate better predictor of cardiovascular disease risk in women with polycystic ovary syndrome.
Methods: 50 diagnosed patients of PCOS and 50 age matched healthy females were included in this study. Cases were diagnosed based on new Rotterdam criteria formulated by the American Society for Reproductive Medicine (ASRM). Fasting Blood samples were collected. Serum High sensitivity-C reactive protein (hs-CRP) and Malondialdehyde (MDA) were estimated.
Results: Results were analyzed using unpaired t-test and p-value was calculated. Statistically non-significant increased levels of serum hs-CRP in PCOS cases as compared with controls were observed. MDA was found to be significantly increased in cases as compared to controls. ROC curve analysis shows MDA as a more specific predictor of cardiovascular disease risk in PCOS compared to hs-CRP.
Conclusions: Increase in the serum MDA level indicates increased formation of reactive oxygen species and lipid peroxidation which leads to increased oxidative stress and this may increase cardiovascular disease risk in PCOS. hs-CRP a marker of chronic inflammation was not significantly increased in PCOS.

Keywords: PCOS, hs-CRP, MDA

INTRODUCTION

Polycystic ovary syndrome (PCOS) is also known as hyperandrogenic anovulation (HA) or Stein-Leventhal syndrome. PCOS has a diverse range of causes that are not entirely understood, but there is evidence that it is largely a genetic disease. PCOS is not only a reproductive problem but a complex endocrine, multifaceted disease with several health complications. Cardiovascular disease representing an important long-term squeal of it. PCOS is now thought to be a pro-inflammatory state, and emerging data suggests that chronic low-grade inflammation underpins the development of metabolic aberration and ovarian dysfunction in the disorder.[1,2] The evidence in support of the presence of chronic inflammatory state in the majority of women with PCOS is incontrovertible.

Study of oxidative stress in PCOS is important since cardio-metabolic risk factors along with insulin resistance seen in these women are associated with endothelial dysfunction an early reversible marker of atherosclerosis.[3] Oxidative stress is also known to independently contribute to endothelial dysfunction and increased cardiovascular risk in these women.[4] Polycystic ovary syndrome (PCOS), is the most common female endocrinopathy in up to 10% in reproductive age and appears to be related with an increased cardiovascular

disease risk.[5] The European society of Human Reproduction and Embryology/American Society for Reproductive Medicine (ESHRE/ASRM) defines PCOS as, the presence of two out of the following three criteria: (i) oligo- and/or anovulation; (ii) hyperandrogenism (clinical and/or biochemical); (iii) polycystic ovaries, with the exclusion of other etiologies (2004). This syndrome is characterized by chronic anovulation and hyper-androgenism.[6] Women with PCOS are insulin resistant and have increased risk for CHD and type 2 diabetes, but currently there are no data on markers of inflammation in women with PCOS. Low grade chronic inflammation as reflected by increased hs-CRP concentrations independently predicts those at risk for coronary heart disease (CHD) and type 2 diabetes.[7]

Reactive oxygen species (ROS) are formed continuously as a consequence of both biochemical reactions and external factors. Malon-dialdehyde (MDA) is one of the stable end products of lipid peroxidation that serves as a biomarker of oxidative stress.[8] Although there are many studies investigating the association of oxidant and antioxidant status with various other conditions, there are limited studies examining their relationship to cardiovascular risk factors in women with PCOS. The current study is aimed to evaluate the serum levels of hs-CRP and MDA and to find a better predictor of cardiovascular disease risk in PCOS.

METHODS

This study was conducted in the Department of Biochemistry at Lokmanya Tilak Municipal medical college and general hospital. Approval from institutional ethical committee was taken. 50 PCOS cases and 50 age matched healthy controls were taken for this study. This sample size was calculated from desired CI of the study and estimated prevalence of the condition.

hs-CRP was measured by immunoturbidimetric method and MDA by the modified method of Sadasivdu et al colorimetrically.[9,10] Subjects with known cardiovascular pathology or taking medications affecting cardiovascular functions like beta blockers, sympathomimetic drugs and women smokers were excluded from this study.

RESULTS

Table 1 shows a significant (p=0.0001) increased levels of MDA in the PCOS patients (2.97±0.71 nmol/ml) as compared to healthy controls (1.63±0.46 nmol/ml). MDA levels show statistically significant increase in cases compared to controls (p=0.0001). It shows a non-significant (p=0.0688) increased levels of hs-CRP in the PCOS patients (0.89±0.73 mg/dl) as compared to healthy controls (0.69±0.19mg/dl).

Table 1: Serum MDA, hs-CRP, in controls and cases.

Parameter (nmol/ml)	Controls	Cases	*p* value	Statistical significance
MDA	1.63±0.46	2.97±0.71	0.0001*	HS
hs-CRP	0.69±0.19	0.89±0.73	0.0688	NS

**p* value statistically significant; HS-Highly Significant.

Table 2: Pearson correlation between serum MDA and hs-CRP in controls and PCOS.

Correlations	MDA	
	Cases	Control
hs-CRP [Pearson Correlation Sig. (2-tailed)]	-0.121	-0.222
N	50	50

Table 3: ROC curve analysis of MDA with hs-CRP.

Area	Std. Error[a]	p-value	Asymptotic 95% confidence interval	
			Lower Bound	Upper Bound
0.951	0.021	0.001	0.911	0.992
Test result variable(s):hs-CRP				
Area	**Std. Error[a]**	**p-value**	**Asymptotic 95% confidence interval**	
			Lower Bound	Upper Bound
0.48	0.061	0.728	0.361	0.598

Table 2 shows no significant correlation between hs-CRP and MDA in PCOS cases (r=-0.121) as compared to control group (r= -0.222). Table 3 shows the Receiver Operating Characteristic (ROC) Curve analysis for hs-CRP and MDA shows that, the test for MDA is having high sensitivity and specificity and area under curve for

MDA (0.951) is more and is a good diagnostic predictor of cardiovascular disease risk in PCOS whereas for hs-CRP, sensitivity, specificity and area under curve (0.48) is less and is a poor diagnostic predictor of cardiovascular disease risk in PCOS.

DISCUSSION

In the present study mean hs-CRP was increased in PCOS cases as compared to healthy controls and it was not statistically significant. This is in accordance with the previous studies done by Mohlig M, et al whose findings showed neither hs-CRP nor IL-6 were significantly elevated in lean or obese PCOS women compared with age-matched lean or obese controls.[11]

Our findings are contradictory to the study done by Kelly CCJ et al, who showed that low grade chronic inflammation as reflected by increased C-reactive protein concentrations independently predicts those at risk for coronary heart disease and type 2 diabetes.[12] Women with polycystic ovary syndrome are insulin resistant and have increased risk for CHD and type II diabetes.[13]

In the present study MDA levels were found to be significantly increased in cases compared to controls ($p<0.0001$) , this is in agreement with previous research findings which have reported increased oxidative stress in PCOS women irrespective of their BMI.[14-16] Oxidative stress was previously linked to obesity commonly seen in these PCOS women.[17,18] Oxidative stress has been implicated in a number of diseases such as cardiovascular disease, neurological disease, malignancies, renal disease, diabetes, inflammatory problems, skin diseases, aging, respiratory diseases, liver diseases and different types of viral infections. Recent studies have documented increased oxidative stress in patients with PCOS which may increase the risk of cardiovascular disease in such patients.

In addition to insulin resistance, oxidative stress has also been implicated as a causal factor for hyperandrogenism in these women.[19] However, recent experimental studies suggest that androgen excess in PCOS women increases leucocytic ROS generation, p47phox gene expression, and plasma TBARS to promote oxidative stress in the presence of hyperglycemia. Thus in PCOS, hyperandrogenism may be the progenitor of diet-induced oxidative stress independent of obesity or excess abdominal adiposity.[20] This could explain the presence of oxidative stress even in the absence of obesity in our PCOS women. Our findings are in accordance with study done by Sabuncu T et al and Fenkci V et al.[21,22]

CONCLUSION

In the present study, statistically significant increase in the serum MDA level was found in PCOS cases, which indicates an increased formation of reactive oxygen species and lipid peroxidation which leads to increased oxidative stress and this may increase cardiovascular risk in PCOS. hs-CRP, an inflammatory marker and an acute phase protein was increased in cases of PCOS as compared to healthy controls and was not statistically significant. Hence these cardiovascular risk predictors along with other documented traditional risk factors for CVD in PCOS, if studied in a larger population of PCOS women with different BMI, will help in early diagnosis, early management and reduce mortality, morbidity due to CVD in PCOS women.

Limitations of present study

Small sample size

Funding: No funding sources
Conflict of interest: None declared
Ethical approval: The study was approved by the Institutional Ethics Committee

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