

Evaluation of Coagulation Disturbances in Patients with Polycystic Ovary Syndrome

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Abstract

Background: Polycystic ovarian syndrome (PCOS) patients are prone to develop insulin resistance with compensatory hyperinsulinemia, dyslipidemia, hypertension, and obesity. There is evidence that plasma levels of several hemostatic factors are modulated by hyperglycemia, insulin resistance with compensatory hyperinsulinemia, proinflammatory agents, and dyslipidemia, all of which are typical in PCOS. Hence; we planned study to evaluate the coagulation disturbances in PCOS patients.

Materials & Methods: The present prospective study included assessment of 50 women with PCOS and 50 controls. Parameters like platelet count, bleeding & clotting time, prothrombin time, APTT, fibrinogen levels are tested. All the results will be analyzed by SPSS software 16.0.

Results: A total of 100 subjects were included in the present study; 50 with PCOS, and 50 healthy controls. Fibrinogen activity was found to be significantly higher in subjects of PCOS group.

Conclusion: Prothrombotic state might occur with greater frequency in PCOS women.

Keywords: Coagulation; Disturbances; Polycystic Ovary Syndrome.

Introduction

Polycystic ovarian syndrome (PCOS) is one of the most common endocrine problem in women of reproductive age group which is multifactorial in aetiology [1,2].

The studies have shown that women with PCOS having all the components of metabolic syndromes that increase the risk for type 2 diabetes and cardiovascular (CV) events are more prone to develop insulin resistance with compensatory hyperinsulinemia, dyslipidemia, hypertension, and obesity [3-5].

Coagulation and fibrinolysis disturbances may also contribute to CV disease (CVD). Several studies of women with PCOS have shown dysregulation of the hemostatic system. There is evidence that plasma levels of several hemostatic factors are modulated by hyperglycemia, insulin resistance with compensatory hyperinsulinemia, proinflammatory agents, and dyslipidemia, all of which are typical in PCOS [6-9]. Hence; we planned study to evaluate the coagulation disturbances in PCOS patients.

Materials & Methods

The present prospective study was conducted in in the department of OBG of RIMS, Raichur, during the period of 6 months in the year 2017. It included assessment of 50 women with PCOS and 50 controls.

Ethical approval was taken from institutional ethical committee and written consent was obtained after explaining in detail the entire research protocol.

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Inclusion criteria for the present study included

- Reproductive age group(18-40 years)
- Confirmed PCOS patients

Exclusion criteria for the present study included

- Patient’s younger age of less than 18 yrs & older patients of more than 40 yrs.
- Patients with HTN, DM, Cardiovascular diseases, Thyroid disorders, Bleeding disorders & dyslipidaemias

Haematological Analysis

Parameters like platelet count, bleeding & clotting time, prothrombin time, APTT, fibrinogen levels are tested. We measured the fibrinogen with a coagulation analyser.

Statistical Analysis

All the results will be analyzed by SPSS software 16.0. Chi-square test and multivariate regression curve will be used for the assessment of level of significance.

Results

A total of 100 subjects were included in the present study; 50 with PCOS, and 50 healthy controls. Mean age of the subjects of PCOS group and control group was 30.5 years and 32.1 years respectively. Mean weight of subjects of present study included 76.5 Kg and 69.2 Kg respectively. Fibrinogen activity was found to be significantly higher in subjects of PCOS group (p- value < 0.05). In the present study, we observed significant difference while comparing the bleeding time and platelet counts in patients with PCOS. (Table 1,2 & Graph 1).

Table 1: Comparison of demographic and metabolic details of the patients

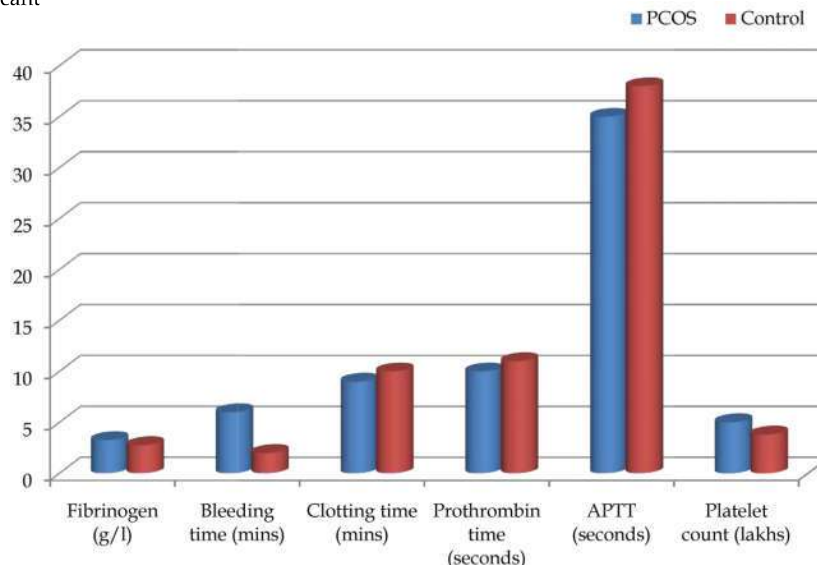
Parameter	PCOS	Control	P- value
Mean age (years)	30.5	32.1	0.22
Mean weight (Kg)	76.5	69.2	0.67

*: Significant

Table 2: Comparison of haemostatic and coagulation variables of patients

Parameter	PCOS	Control	P- value
Fibrinogen (g/l)	3.25	2.76	0.01*
Bleeding time (mins)	6	2	0.02*
Clotting time (mins)	9	10	0.81
Prothrombin time (seconds)	10	11	0.45
APTT (seconds)	35	38	0.82
Platelet count (lakhs)	5	3.8	0.01*

*: Significant



Graph 1: Description of haemostatic variables of patients

Discussion

In the present study, we observed that fibrinogen was significantly higher in PCOS patients in comparison to the controls. Oral et al selected forty-eight women with polycystic ovary syndrome (PCOS) and evaluated the thrombin-activatable fibrinolysis inhibitor (TAFI) level in plasma to evaluate its proportionality to different parameters of metabolic, hormonal and hemostatic entities. 43 women were selected as controlled after matching for age and BMI. The period of study was for 20 months. All the subjects underwent laboratory tests for evaluation of plasma lipid and lipoprotein level, reproductive hormonal level, insulin, TAFI antigen concentration, plasminogen activator inhibitor-1 (PAI-1) activity, fibrinogen concentration, thrombomodulin, thrombin-antithrombin (TAT) complexes, D-dimer, Protein C Antigen, Protein S Antigen, Antithrombin III (AT III) and activated protein C (APC) resistance. They observed that women with PCOS had significantly increased levels plasma TAFI, plasma levels of D-dimer, AT III, PAI-1 and thrombomodulin as compared to control subjects. Significant comparable levels of hemostatic parameters consisting TAT complexes; Protein C; APC; and Protein S between both the groups were observed. It was concluded that women with PCOS had significantly elevated plasma levels of TAFI, PAI-1, D-dimer, AT III and thrombomodulin as compared to control subjects [9]. Stener-Victorin et al conducted study on women with PCOS to evaluate effects of physical exercise and low frequency electroacupuncture on insulin sensitivity, coagulation and fibrinolysis. The subjects were randomly grouped for low frequency EA, physical exercise and no activity. The parameters recorded at baseline, after 16 weeks of activity and after 16 weeks of follow up were anthropometrics, circulating coagulation and fibrinolytic markers, insulin sensitivity (euglycemic hyperinsulinemic clamp), hemodynamics, and adipose tissue morphology/function. They observed that subjects in low-frequency EA group had 21.8% decrease in the circulating plasminogen activator inhibitor 1 activity after 16 weeks of activity and 31.1% decrease at the 16-week follow-up. The levels were significantly different from the subjects in physical exercise and no activity groups. Also, the subjects in EA group had significantly decreased level of circulating fibrinogen and tissue plasminogen activator, sagittal diameter, and diastolic blood pressure after treatment. At the 16-week follow-up period, it was observed that the level of fibrinogen was decreased as compared to baseline levels. Subjects in the physical exercise group had increased level of lipoprotein lipase

activity and decreased diastolic blood pressure. They observed that diastolic and systolic blood pressure was significantly lower at follow-up in these patents. Other variables had no change due to this activity. The decrease in plasminogen activator inhibitor 1 activity in low-frequency EA counteracted a possible prothrombotic state in women with PCOS. They did not notice any intra group differences in the anthropometric, metabolic, or hemodynamic variables after 16 weeks of EA or physical exercise at the dose/intensity studied [10].

Mean insulin levels was found to be significantly higher in patients with PCOS in comparison to controls. Mannerås-Holm et al conducted study on women with PCOS to evaluate change in circulating levels of fibrinolysis/coagulation markers in women with PCOS and their correlation to hemodynamics, metabolic variables, sex steroids, SHBG, lipids, and inflammatory variables. The measurement of anthropometric variables, hemodynamics, circulating hemostatic and inflammatory markers, and serum lipid profile was done in 74 women with untreated PCOS and 31 control subjects.

They observed that women with PCOS had elevated circulating plasminogen activator inhibitor 1 (PAI-1) activity and fibrinogen levels. Comparable values were observed in both the groups with respect to lipid profile, blood pressure, and levels of D-dimer, von Willebrand factor, factor VIII, tissue plasminogen activator, and inflammatory markers. The statistical analysis was conducted using multiple linear regression models. The analysis implied that in women with PCOS high fibrinogen is projected by elevated high sensitivity C-reactive protein and soluble E-selectin in combination with heart rate and high PA I-1 activity projected by low SHBG and high insulin.. Differences in PAI-1 activity were not significant after adjustments for age, BMI, SHBG, and insulin. PCOS is characterized by a prothrombotic state, as reflected by increased PAI-1 activity and fibrinogen, without signs of dyslipidemia or a proinflammatory state. Low SHBG and high insulin may partly explain the BMI-independent difference in PAI-1 activity between women with PCOS and controls. High-sensitivity C-reactive protein and E-selectin may be involved in regulating fibrinogen in PCOS [11]. PCOS women might have obesity-independent elevation fibrinogen, which could cause hypercoagulability. Factor VIII and vWF are involved in platelet adhesion and clot formation. Erdođan et al. assessed circulating thrombin activatable fibrinolysis inhibitor (TAFI) levels and carotid intima-media thickness (CIMT) in PCOS patients and control subjects. In this study we aimed to

evaluate the relation between the levels of TAFI and homocysteine, high sensitive CRP (hsCRP), fibrinogen and CIMT in PCOS patients carrying a potential risk for developing CVD and diabetes and compared with age- and body mass index-matched controls. They studied 68 PCOS patients and 26 healthy controls. They conducted an observational study examining noninvasive markers of early CV disease in women with PCOS including structural CIMT. Noninvasive markers of early CVD, CIMT were measured in PCOS patients and control subjects. Metabolic parameters included fasting insulin and glucose levels, lipid and androgen levels, TAFI levels, hsCRP. Fasting glucose levels, prolactin, TSH, Total-cholesterol, LDL-cholesterol, triglyceride, estradiol, DHEA-S and age were similar in the two groups, whereas serum insulin, fibrinogen, hs-CRP, 17-OHP, free-testosterone, total testosterone, HOMA-IR, HDL were significantly elevated in PCOS patients in comparison to control subjects ($p < 0.05$). Plasma TAFI levels were similarly in PCOS patients compared with healthy controls. No difference was observed in the combined IMT among the studied groups. In their study, no significant difference in lipid parameters was determined between patients with PCOS and healthy controls. In their study, they did not observed any difference in CIMT measurements and TAFI levels between patients with PCOS and healthy controls that can be explained by their low ages and short duration of PCOS [12].

Conclusion

From the above results, the authors concluded that prothrombotic state might occur with greater frequency in PCOS women. However; further studies are recommended in the future.

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