



ESTIMATION OF SERUM HOMOCYSTEINE LEVEL IN WOMEN WITH POLYCYSTIC OVARIAN SYNDROME (PCOS) - A CASE CONTROL STUDY.

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ABSTRACT

Polycystic ovarian syndrome (PCOS) is one of the common endocrine conditions roughly affecting about 6-10% women of reproductive age. It is characterized by ovarian dysfunction, hirsutism, hyperandrogenism, insulin resistance and obesity. Homocysteine is a sulphur containing amino acid formed during the metabolism of methionine. It has cytotoxic effects on vascular endothelium. Hyperhomocystinemia contribute to the development of cardiovascular disease as evidenced by many studies. Women with PCOS are likely to develop components of metabolic syndrome, such as disturbance of carbohydrate metabolism, obesity, hypertension and dyslipidemia, which in turn are risk factors for cardiovascular disease (CVD), since there is a strong association between serum homocysteine levels and insulin resistance. With this background, this study focuses the level of homocysteine in PCOS patients and to compare the same in normal healthy women. This study is a Case Control Study conducted in Sree Balaji Medical College and Hospital. Fifty women of reproductive age were included in this study, comprising of 25 PCOS women and 25 women without PCOS. The serum homocysteine level was measured using GenX homocysteine enzymatic method (Proton) in fully automated analyzer. Mean level of homocysteine in PCOS was 10 μ mol/l and non-PCOS was 4 μ mol/l. The *p*-value of 0.01 was taken statistically significant. Homocysteine level was found to be elevated in women with PCOS when compared to the women without PCOS.

KEY WORDS: PCOS, HOMOCYSTEINE, ATHEROSCLEROSIS

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INTRODUCTION

Polycystic ovary syndrome (PCOS) which affects approximately 6 – 10% of women of reproductive age, is characterized by ovarian dysfunction, hirsutism, hyperandrogenism, insulin resistance and obesity. Patients with PCOS have dyslipidemia, hypertension, hyperinsulinaemia, and are prone to get cardiovascular diseases.¹ Hyperinsulinaemic insulin resistance is a key feature of PCOS which increases circulating ovarian androgen concentration and impedes ovulation. Homocysteine is a sulphur containing amino acid formed during the metabolism of methionine.² It has cytotoxic effects on vascular endothelium⁽³⁾. Hyperhomocystinemia contributes to the development of cardiovascular disease as evidenced by many studies⁽⁴⁾. *Badawy et al* in 2007⁽⁵⁾ suggested that there was a strong association between serum homocysteine levels and insulin resistance. Obesity and hyperinsulinaemia are frequently encountered in PCOS. Insulin resistance plays a major role in the pathogenesis of PCOS. Insulin resistance is defined as the reduced reaction to normal circulating level of insulin that may be one of the risk factors for cardiovascular disease in women with PCOS^(6, 7). PCOS has been associated with elevated plasma homocysteine, insulin resistance, reproductive failure⁽⁸⁾ and late vascular complications⁽⁹⁾. Complications like NIDDM, dyslipidaemia, atherosclerosis, hypertension and vascular disease occur in later stages of PCOS as evidenced by other investigators^(10, 11, and 12). Based on the above knowledge this study was designed to estimate the level of homocysteine in PCOS women and comparing the same in non-PCOS women.

MATERIALS AND METHODS

This study is a case control study conducted in Sree Balaji Medical College and Hospital. Fifty women of reproductive age were included in this study and divided into two groups A & B.

Group-A (CASES) - women with PCOS (n=25) was diagnosed according to Rotterdam 2003 criteria.

Group-B (CONTROLS) - women without PCOS (n=25) with same age and BMI were included in this group.

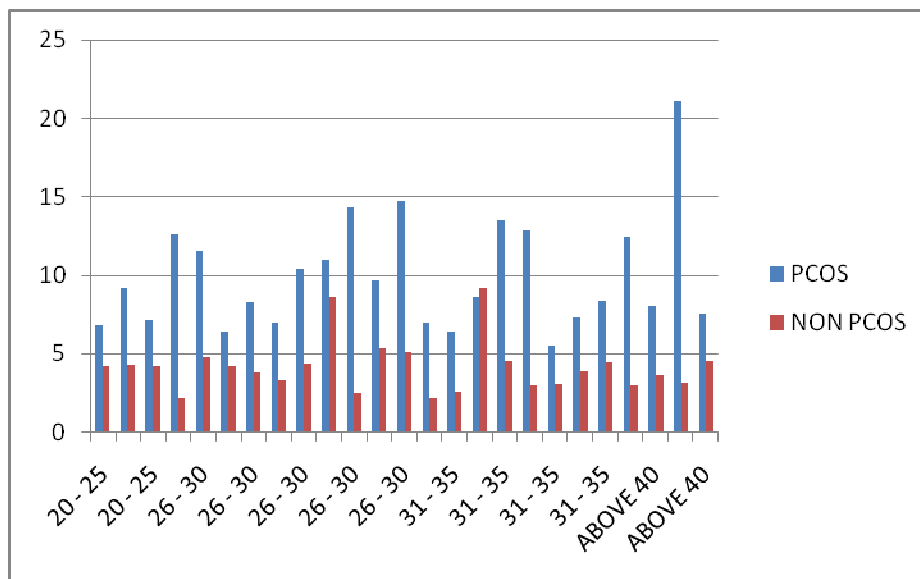
Rotterdam criteria: To confirm at least two of the three following criteria:

1. Polycystic ovaries were identified by transvaginal or transabdominal ultrasound examination.
2. Clinical features of hirsutism by Ferriman Gallway Score.
3. Biochemical signs of hyperandrogenism by elevated testosterone (>2.0 nmol/l).

Exclusion criteria: Patients with impaired fasting glucose, diabetes mellitus, hypopituitarism, prolactinoma and active thyroid disease were excluded from this study. Institutional ethical committee clearance was obtained and informed consent obtained from all the participants. Blood samples were taken after an overnight fast and centrifuged immediately. The serum was separated and frozen at -70°C until assayed. The serum homocysteine level was measured using GenX Homocysteine enzymatic method (Proton) in fully automated analyzer.

RESULTS

Statistical calculations were performed using the SPSS. Differences between the study groups were analyzed using an unpaired student's *t*-test. Correlations were determined by *pearson's* simple linear regression analysis (only significant correlation coefficients are reported). Mean age of Group -A was 32.4 years and Group-B was 31.2 years. Mean level of homocysteine in PCOS was $10\mu\text{mol/l}$ and in non-PCOS was $4\mu\text{mol/l}$. The *p*-value of 0.01 was taken statistically significant.



DISCUSSION

In the present study, elevated serum levels of homocysteine were found in our PCOS patients, which are similar to reports by some other investigators⁽⁷⁾. Elevated level of homocysteine suggests that an alteration in homocysteine metabolism might play a role in the increased cardiovascular risk associated with PCOS. Hyperhomocysteinaemia seems to be directly related to atherogenesis; hence, high homocysteine levels may be useful in identifying the sub group of PCOS women who are at risk for the subsequent development of atherosclerosis. *Badawy et al* in 2007⁽⁵⁾ reported that insulin resistance and hyperhomocysteinaemia contributed to the long term complications of PCOS and found a significantly higher homocysteine level among PCOS women with insulin resistance when compared to those without insulin resistance^(13,5). In our study among twenty five non-PCOS women, two of them had marginal elevation of homocysteine values which may be attributed to vitamin B-complex deficiency as evidenced by other studies^(14, 15). Methionine an amino acid is converted into homocysteine which in turn is converted to cystathionine by cystathionine β synthase. This enzyme requires vitamin B₆ as co-enzyme for its action. So vitamin B₆ deficiency leads to the elevation of homocysteine level in those individuals. Classic homocysteinaemia is associated with the

accumulation of homocysteine due to defect in the enzymatic pathways⁽¹⁶⁾. Insulin levels are also a modulating factor of homocysteine which inhibits hepatic cystathionine β synthase activity^(17, 18). Increased levels of homocysteine have been positively associated with insulin levels in many clinical situations. The possible determinants for elevation of homocysteine concentration is still in debate among researchers who found significant correlation between homocysteine and insulin resistance⁽⁹⁾ as well as those who didn't find such correlations⁽¹³⁾. Homocysteine levels are influenced by a number of variables like smoking, renal function, vitamin B status and enzyme dysfunction states which are not examined in this study. Elevated homocysteine level aggravate the level of plasminogen activator inhibitor-1 (PAI-1) ultimately affecting the blood flow resulting in the vascular aspect of PCOS as shown in previous studies⁽¹⁹⁾. The results from this study suggest that these findings need to be confirmed in larger group of PCOS subjects and requires a long term follow-up.

CONCLUSION

In our study homocysteine levels of women with PCOS was significantly higher when compared to non-PCOS women. Studies confirm that men are at high risk for cardiovascular disease when compared to women of the same age group. In

women with PCOS, when their homocysteine levels are elevated the risk becomes on par with men with similar age group. Since hyperhomocysteinaemia is prone to cardiovascular disease, homocysteine can also be added as an investigation along with other

investigations to identify the earlier chances of getting coronary artery disease so that preventive measures can be considered at the earliest.

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