EVALUATION OF HOMOCYSTEINE LEVELS AMONG WOMEN WITH POLYCYSTIC OVARY SYNDROME

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Abstract

Background: Polycystic ovary syndrome (PCOS) is a common hormonal disorder that affects women of reproductive age, which is characterized by hyperandrogenism, leading to ovarian dysfunction and hyperinsulinemia. Elevated homocysteine (Hcy) levels have been linked to PCOS**.**
Aims of the study: To determine Hcy levels among women with PCOS**.**
Subjects and Methods: This study is a case-control study conducted from January 2024 through April 2024 and involved 200 participants, 100 as patients with PCOS, and 100 women as the control group, who appeared healthy. Blood pressure (BP), body mass index (BMI), waist circumference (WC), plasma Hcy, testosterone, total cholesterol (TC), triglycerides (TG), high-density lipoprotein-cholesterol (HDL-C), and low-density lipoprotein-cholesterol (LDL-C) were measured in all participants**.**
Results: Pasma Hyc, testosterone, TC, TG, LDL-C were significantly higher among patients with PCOS than control women, P<0.001, while HDL-C was significantly lower among women with PCOS than among controls, P<0.001.
Conclusion: Women with PCOS have distinctly higher plasma Hcy concentrations. This may increase the risk of cardiovascular disease among patients with PCOS.
Keywords: Homocysteine, Polycystic Ovary Syndrome, Hyperhomocysteinemia

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Introduction

Polycystic ovary syndrome (PCOS) is a disorder that affects the ovaries of a large rate of women during reproductive age [1]. There are many clinical manifestations of PCOS including, insulin resistance, obesity, and androgen excess [٢]. However, PCOS women have been reported to suffer from Hyperhomocysteinemia (HHcy) [٣]. Homocysteine (Hcy) is an amino acid that contains sulfur and an intermediary in the metabolic process that converts methionine (Met) to cysteine and subsequently to glutathione [٤]. It is continuously re-cycled in a pathway called one-carbon metabolism (OCM), which involves re-methylating Homocystiene to methionine or trans-sulfurating it to cysteine [٥]. Hyperhomocysteinemia occurs in deficient activity of OCM enzymes including methionine synthase, cystathionine *β*-synthase, and betaine-homocysteine methyltransferase which results in Homocystien accumulation in blood [٦]. Therefore, HHcy promotes toxic activity resulting in several clinical implications such as cardiovascular disease (CVD) and thrombosis in the

maternal-fetal circulatory system [٧]. In PCOS patients, thrombosis disorders are more frequent than in non-PCOS women due to HHcy which affects blood composition and platelet functionality [٨,٩]. The aim of this study was to evaluate the level of which affects blood composition and platelet functionality .

Patients and methods

This is a case -control study extended from January, 2024 throughout April of 2024. The study included 200 participants, 100 patients with PCOS, and 100 women as a control group. The participants must be fasting at least for 8 hours as detail medical history gathered from participants including menstrual history, reproductive history, family history, and medications. PCOS was diagnosed using the 2003 Rotterdam criteria, which need the presence of two of the three following symptoms: oligo ovulation or anovulation, clinical and/or biochemical hyperandrogenism, and polycystic ovaries.

Blood pressure, BMI and WC were measured in all participants. Biochemical parameters were determined in fasting state. Hcy level determination by fully automated abbot system (chemiluminescent micro particle immunoassay), the ARCHITECT Hcy assay is a one-step immunoassay that uses CMIA technology to quantitatively determine the amount of total Hcy in the serum, with flexible assay protocols, referred to as s Chemiflex. Dithiothreitol (DTT) reduces bound or dimerized Hcy (oxidized form) to free Hcy, which is then transformed into S-adenosyl Hcy (SAH) by S-adenosyl Hcy hydrolase when sufficient adenosine is present.Subsequently, the SAH is in competition with particle-bound monoclonal antibodies with S-adenosyl cysteine tagged with acridinium. Relative light units (RLUs) are used to quantify the chemiluminescence that results when pre-trigger and trigger solutions are added to the reaction mixture following a wash step and magnetic separation is an indirect correlation between the RLUs identified by the ARCHITECT immunoassay System optics and the quantity of Hcy present in the sample.

Testosterone level was determined by VIDAS system (Enzyme Linked Fluorescent Assay). Lipid profile determined by full automated Dri-Chem Fujifilm system (colorimetric assay).

The study's data were analyzed using the Statistical Package for Social Science (SPSS) software, Version 26.0, which produced the mean ± standard deviation and percentage. The independent t-test and a chi-squared test were employed to compare the two different groups. A P-value of less than 0.05 was deemed statistically significant.\

Results

Characteristics and anthropometric measurements of PCOS women and control women are presented in Table 1. Age was not significantly different between patients with PCOS and control women, ($P>0.05$). Whereas BMI, WC and DBP ($P<0.001$), and SBP ($P<0.01$) were significantly higher among PCOS women in comparison to control women.

The LDL-C, TC, TG, Hcy, and total testosterone levels were significantly greater in PCOS women than in controls ($P<0.001$). In contrast to control women, HDL-C was significantly lower in PCOS women ($P<0.001$), Table 2.

Discussion

Polycystic ovary syndrome is a complex condition occur in women during reproductive age and considered, the most common endocrinological disturbance in this age [10].

Several studies reported that Hcy level elevated in PCOS women ; however, the results of the association between HHcy and obesity have not yet been clarified [11]. Therefore, the present study aimed to clarify the correlation between HHcy in PCOS women and some anthropometric features and biochemical markers.

According to this study findings, in PCOS women the BMI and WC are elevated more than the control group, these could be due to increased androgen levels [12]. These outcomes in agreement with several previous studies for instance one previous study conducted in Duhok city, Iraq by Sulaiman et al. [13], that found significantly higher BMI compared to the BMI of controls. While another study conducted in Turky by Kaya et al [١4] , which found no significant difference between PCOS women and control group. In addition; there is a relationship between Hcy concentrations in PCOS and obesity that could be due to higher concentration of Hcy induces alterations in Lipid profile and accumulation of lipids in tissues, contributing to obesity. Additionally, Hcy disrupts the biosynthetic pathways of cholesterol and triglycerides due to endoplasmic reticulum stress, resulting in irregular lipid metabolism [١5].

The current study found significantly elevated in Hcy level in PCOS women in comparison to the control group; these outcomes in agreement with several studies for instance one previous study conducted in India by Maleedhu et al [16], (2014) which found Hcy significantly increased in women with PCOS when comparison to the control group. In addition, another study conducted in India by Bhushan et al [17], (2022) also found that Hcy significantly increased in women with PCOS when comparison to the control group.

Furthermore, this study found significantly elevated testosterone levels among women with PCOS in comparison to the control group; This could be due to is due to oxidative stress conditions that may stimulate androgen production by increasing the expression of enzymes associated to testosterone synthesis. which is considered an essential factor in elevated testosterone in PCOS patients [18]. In addition, Obesity increases ovarian androgen production, magnifies this could be revised to functional ovarian activity and makes theca cells more sensitive to luteinizing hormone (LH) exposure. [19]. These findings agreement with several previous studies for instance one previous study conducted by Panidis et al [19], (2013) which found highly significant testosterone levels of 74.2 ng/dL among PCOS women compared to control group with levels of 37.3 ng/dL. While Elias [20], (2024) found that women with PCOS exhibited significantly higher testoterorone levels (39.52 ±1.89 ng/dL) compared to controls (16.51 ±1.18 ng/dL).

Regarding lipid profile, this study showed that the PCOS patients' total cholesterol TC, TG, and LDL-C were significantly higher among PCOS women than among controls, while HDL-C was significantly lower among patients with PCOS than among women in the control group. The dyslipidemia in PCOS women can be related to hyperinsulin and hyperandrogen. This facilitated adipocytes to have enhanced lipolysis due to catecholamine, releasing free fatty acids into the bloodstream. Elevated liver FFAs stimulate VLDL production, resulting in hypertriglyceridemia. This

subsequently results through the reverse cholesterol transfer pathway, resulting in elevated LDL-C and decreased HDL-C. Early-life enhanced androgenic priming of adipocytes predisposes people to dyslipidemia linked to PCOS. [٢1].

In conclusion, PCOS women have significantly higher plasma Hcy levels

Therefore, the risk of CVD in PCOS may be adversely augmented in the presence of an increased Hcy level.

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Table 1. clinical and anthropometric measurements among the study groups

Characteristic	PCOS group N=100	Control group N=100	P-value
Age (years)	28.21±7.6	28.46 ± 6.7	0.80
BMI (kg/m^2)	٢8.34 ±5.2	22.25±2.3	0.001
WC (cm)	91.3±12.08	77.27± 6.03	0.001
SBP (mmHg)	120.49 ± 9.7	116.9 ± 6.9	0.01
DBP (mmHg)	79.2 ± 7.89	75.6 ± 6.35	0.001

Data are presented as mean ± SD

Table 2. Biochemical parameters among patients with PCOS and controls

Biochemical markers Parameters (mean ± SD)	PCOS group N=100	control Group N=100	P-value
Hcy (µmol/L)	13.85 ± 2.68	5.58 ± 1.52	0.001
Testosterone (ng/Ml)	1.006 ± 0.34	0.47 ± 0.15	0.001
T. Cholesterol (mg/ dL)	181.83 ±15.5	167.37 ± 16.37	0.001
Triglycerides (mg/dL)	124.7 ± 25.25	88.8 ±20.2	0.001
HDL-C (mg/ dL)	48.06 ± 6.5	54.06 ± 5.3	0.001
LDL-C (mg/ dL)	109.1± 19.86	95.58 ± 16.3	0.001

Data are presented as mean ± SD