

ARTICLE

The clinical significance of monitoring serum levels of glutathione peroxidase and selenium in patients with polycystic ovary syndrome

Shaohui ZENG,¹ Juan XU,² Chaoping XIE,² and Weihong JIANG²

¹Department of Clinical Laboratory, Shenzhen Hospital of Guangzhou University of Chinese Medicine (Futian), Shenzhen 518034, China

²Department of Obstetrics and Gynecology, Shenzhen Hospital of Guangzhou University of Chinese Medicine (Futian), Shenzhen 518034, China

(Received 14 February 2024; revised 15 February 2024; accepted 25 February 2024; first published online 31 March 2024)

Abstract

Objective: This study aims to analyze the levels of the trace element selenium (Se), glutathione peroxidase (GSH-Px), and total antioxidant capacity (TAC) in the serum of women with polycystic ovary syndrome (PCOS) compared to women with normal menstrual cycles. By examining the relationship between Se levels, oxidative stress (OS), and PCOS, the study provides a theoretical basis for the supplementation of the potent antioxidant Se in women with PCOS, aiming to improve the prevention and management of PCOS and reduce its complications. **Methods:** Sixty-six females diagnosed with PCOS for the first time from June 2022 to June 2023 at the Shenzhen Hospital of Guangzhou University of Chinese Medicine (Futian) were selected as the observation group. Sixty-eight healthy volunteers with regular menstrual cycles were randomly selected as the control group. Serum levels of GSH-Px, TAC, and Se were measured and statistically analyzed for both groups. **Results:** Serum levels of Se, TAC, and GSH-Px were significantly lower in the observation group compared to the control group ($P < 0.05$), indicating a statistically significant difference. **Conclusion:** The deficiency of the trace element Se leads to a reduction in OS indicators, including levels of GSH-Px and TAC. It is inferred that Se deficiency may be associated with the pathogenesis of PCOS to a certain extent.

Keywords: Polycystic Ovary Syndrome (PCOS); Glutathione Peroxidase (GSH-Px); Selenium (Se); Oxidative Stress (OS); Total Antioxidant Capacity (TAC)

Polycystic ovary syndrome (PCOS) affects approximately 6% to 10% of women of reproductive age, with a trend of increasing prevalence. This condition significantly impacts the psychological, physiological, and reproductive health of women during their childbearing years.

Despite being recognized for over a century, the etiology and mechanisms underlying PCOS remain poorly understood. Hyperandrogenemia (HA) and insulin resistance (IR) are widely considered to be crucial pathophysiological changes associated with PCOS. Recent years have seen a growing interest in the study of trace elements and their relationship with gynecological diseases. However, research on the connection between the trace element selenium (Se) and PCOS is still lacking domestically. This study aims to measure and compare the serum Se levels in healthy women with normal menstrual cycles and patients with PCOS to explore the potential relationship between Se and PCOS.

1. **Materials and Methods**

1.1 **Study Participants**

Participants were selected from females who visited our hospital for the first time due to menstrual irregularities, infertility, hirsutism, and other related symptoms between June 2022 and June 2023, and were diagnosed with polycystic ovary syndrome (PCOS). Inclusion criteria for the study were as follows: women with regular menstrual cycles, not pregnant or breastfeeding, and with no abnormalities found in gynecological examinations. Both groups of women participating in the study were required to meet the following conditions:1.Age between 19 to 44 years.2.No history of hormonal medication use, including contraceptive pills, within the past 2 years.3.No exposure to copper, zinc, iron, manganese, lead, selenium, and similar elements in the past 3 years.4.No hair dyeing or perming in the past 3 months.5.No significant organ diseases such as heart, liver, or kidney diseases, and no acute or chronic infections.6.No history of coronary heart disease, chronic pancreatitis, cancer, Mediterranean anemia, sickle cell anemia, major osteoarticular diseases, Keshan disease, or multiple sclerosis, among others.7.No surgeries or burns in the past six months. The study was approved by our hospital’s ethics committee. The observation group consisted of 66 cases, while 68 healthy volunteers with regular menstrual cycles were randomly selected as the control group. There were no significant differences between the two groups in terms of age, educational background, and body mass index (BMI), ensuring their comparability ($P > 0.05$). Refer to Table 1 for a comparison of age, educational levels, and BMI between the two groups.

Table 1. Comparison of Age, Educational Level, and Body Mass Index (BMI) Between the Two Groups (mean ± SD)

(Group)	Age(Y)	Educational Background (weighted mean)	BMI
Observation group(n=66)	27.27±5.434	4.652±0.969	23.90±1.986
Control group(n=68)	28.95±5.227	4.927±0.779	23.43±1.436
F	0.007	3.097	3.123
P	0.935	0.081	0.080

1.2 Diagnostic Criteria

The diagnosis of Polycystic Ovary Syndrome (PCOS) was based on the criteria revised at the ESHRE/ASRM-sponsored PCOS consensus workshop in October 2003[4]: (1) Oligo-ovulation or anovulation. (2) Clinical and/or biochemical signs of hyperandrogenism. (3) Polycystic ovaries: the presence of 12 or more follicles in each ovary measuring 2–9mm in diameter, and/or increased ovarian volume (>10 ml). (4) At least two of the above criteria are met, excluding other etiologies such as congenital adrenal hyperplasia, hyperprolactinemia, androgen-secreting tumors, and Cushing's syndrome.

1.3 Research Methods

1.3.1 Instruments and Reagents

Trace element selenium (Se) levels were measured using the ICPMS7800 trace element analyzer. Total antioxidant capacity (TAC) was assessed using colorimetry, and glutathione peroxidase (GSH-Px) activity was measured using UV spectrophotometry on the Beckman AU5800 automatic biochemistry analyzer. Corresponding Se, GSH-Px, and TAC reagent kits and standards, all within their valid usage period, were strictly used according to the operational procedures.

1.3.2 Measurement of Se, GSH-Px, and TAC

Blood samples were collected from fasting participants between 8:00 and 12:00, using lithium heparin as an anticoagulant for Se, and clot activator tubes for GSH-Px and TAC. After thorough mixing, the samples for Se were processed within one week. For GSH-Px and TAC, after resting for 30 minutes and centrifuging at 3000 rpm for 15 minutes, the supernatant serum was stored at -80°C and tested within 90 days.

1.4 Statistical Analysis

Data were statistically analyzed using SPSS software version 25.0. Quantitative data were presented as mean $\pm$ standard deviation (SD). The t-test was used for comparison, with $P < 0.05$ considered statistically significant.

2. Results

The analysis of the data and statistical results indicated that the serum levels of selenium (Se), glutathione peroxidase (GSH-Px), and total antioxidant capacity (TAC) in the observation group (women diagnosed with PCOS) were significantly lower than those in the control group (healthy women with regular menstrual cycles), with $P < 0.05$, denoting a statistically significant difference. For detailed data, refer to Table 2.

3. Discussion

The clinical manifestations of Polycystic Ovary Syndrome (PCOS) are primarily characterized by hyperandrogenism, insulin resistance, and ovulatory dysfunction[5]. Insulin resistance (IR) and hyperandrogenemia (HA) are acknowledged as significant pathophysiological alterations in PCOS. Current studies indicate that the level of oxidative stress (OS) in

Table 2. Comparison of Selenium (Se), Total Antioxidant Capacity (TAC), and Glutathione Peroxidase (GSH-Px) Levels Between the Two Groups (mean $\pm$ SD)

(Group)	Se (ug/L)	GSH-Px (U/L)	TAC (mmol/L)
Observation group(n=66)	118.932 $\pm$ 22.320	42.33 $\pm$ 10.39	1.446 $\pm$ 0.010
Control group(n=68)	133.393 $\pm$ 28.253	48.81 $\pm$ 13.55	1.507 $\pm$ 0.131
F	4.334	8.235	6.871
P	0.039	0.005	0.010

patients with PCOS is significantly higher than in healthy individuals[6], with OS levels closely associated with central obesity, IR, and HA[7-9], suggesting that OS might be a potential factor in the pathogenesis of PCOS[10].

The body has two types of antioxidant systems: enzymatic antioxidants, including glutathione peroxidase (GSH-Px), superoxide dismutase (SOD), catalase (CAT); and non-enzymatic antioxidants, such as trace elements (copper, zinc, selenium), glutathione, melatonin, α -lipoic acid, ergothioneine, vitamins C, E, and carotenoids[7]. Research has confirmed that certain gynecological conditions (e.g., infertility, habitual miscarriage) are associated with abnormal distributions and metabolism of trace elements[11]. Various studies both domestically and internationally[12-13] have indicated that deficiencies in trace elements may significantly impact the fertility functions of patients with PCOS. Supplementing trace elements like Cu, Zn, Fe can not only improve the ovulatory response in infertile patients with PCOS but also their pregnancy outcomes. To date, no studies have been found regarding the relationship between selenium (Se) and PCOS within the domestic literature.

Selenium is a vital component of GSH-Px and selenoprotein P in the body, playing a crucial role in balancing redox reactions. In GSH-Px, selenocysteine is at the active site of the enzyme, catalyzing the redox reaction between glutathione (GSH) and peroxides, acting as an antioxidant and a potent free radical scavenger, with antioxidant power up to 500 times that of vitamin E. The activity of this enzyme positively correlates with Se levels, making GSH-Px activity a marker for assessing Se deficiency or the effectiveness of Se supplementation.

Studies such as Coskun et al.[14] on Turkish patients with PCOS found reduced serum Se concentrations, negatively correlated with serum luteinizing hormone and total testosterone levels, suggesting Se's potential involvement in the pathophysiological process of hyperandrogenemia in PCOS. However, research by P. Zagrodzki et al.[15] found no significant difference in Se parameters, including selenoprotein P, between PCOS patients and the non-PCOS group, not supporting Se's involvement in PCOS pathophysiology. A systematic review by Fatemeh et al.[16] on studies published before December 2018 on the impact of Se on polycystic conditions confirmed an inverse relationship between serum Se levels and certain androgens in PCOS patients, with Se reducing insulin resistance and dyslipidemia. Yet, current data are insufficient to support Se's protective role in PCOS. Mehri et al.[17] found that supplementing Se in women with PCOS for 8 weeks had beneficial effects on insulin metabolic parameters, triglycerides, and VLDL-C levels; however, it did not affect FPG and other lipid profiles. Rezvanfar et al.[18] showed that a selenium-based herbal

medicine, treated with electromagnetic therapy for hyperandrogenism-induced PCOS, could prevent ovarian histopathological, endocrine, and biochemical changes caused by hyperandrogenemia.

Köse et al.[19] explored the effect of Se on oxidative stress and Ca^{2+} levels in the TRPV1 channels of neutrophils in patients with PCOS, highlighting the significance of Ca^{2+} influx through TRPV1 channels in neutrophils during PCOS. Selenium appears to protect against cellular oxidative stress and Ca^{2+} entry by regulating the TRPV1 calcium channel in neutrophils. Studies by An-Su, Tu et al.[20] suggest that antioxidants could improve the prognosis for patients with PCOS. Serum TAC levels are a good indicator of the overall oxidative stress level in the body, reflecting the total value of antioxidants in bodily fluids. Zuo et al.[21] demonstrated that serum TAC levels are lower in the PCOS group compared to the control group.

Our study findings show that serum TAC, GSH-PX, and Se levels are significantly lower in the PCOS group than in the control group, indicating that Se deficiency may lead to a greater reduction in GSH-PX and TAC levels, corroborating the hypothesis that OS might be a potential factor in the pathogenesis of PCOS, aligning with the results of most literature.

The results suggest a potential link between selenium deficiency and the development of PCOS. However, due to the limited duration and sample size of this study, along with the lack of further investigation into the effects of selenium supplementation on OS levels and other relevant indicators in PCOS, future studies should consider expanding the sample size and conducting more in-depth research. It is recommended that routine testing for trace element Se in PCOS patients be conducted, and if a deficiency is found, selenium supplementation could be considered to potentially enhance therapeutic outcomes.

REFERENCES

- [1]Bozdag G, Mumusoglu S, Zengin D, et al. The prevalence and phenotypic features of polycystic ovary syndrome: a systematic review and Meta-analysis[J]. Hum Reprod, 2016, 31(12):2841.
- [2]Bremer AA,Miller WL.The serine phosphorylation hypothesis of polycystic ovary syndrome: a unifying mechanism for hyperandrogenemia and insulin resistance.[J].Fertility and Sterility: Official Journal of the American Fertility Society, Pacific Coast Fertility Society, and the Canadian Fertility and Andrology Society,2008,89(5):1039-1048.
- [3]Zhihao,Zhang,Yanli,Hong,Minmin,Chen,Ninghua,Tan,Shijia,Liu,Xiaowei,Nie,Wei,Zhou. Serum metabolomics reveals metabolic profiling for women with hyperandrogenism and insulin resistance in polycystic ovary syndrome.[J]. Metabolomics: Official journal of the Metabolomic Society,2020,16(2):20.
- [4]The Rotterdam ESHRE/ASRM-Sponsored PCOS consensus workshop group.Revised 2003 consensus on diagnostic criteria and long-term health risks relate to polycystic ovary syndrome[J].Hum Reprod,2004,19(1):41.
- [5]Dumesic DA, Oberfield SE, Stenervictorin E, et al. Scientific statement on the diagnostic criteria, epidemiology, pathophysiology, and molecular genetics of polycystic ovary syndrome[J]. Endocr Rev, 2015, 36(5):487-525..

- [6]Murri M, Luque-Ramírez M, Insenser M, et al. Circulating markers of oxidative stress and polycystic ovary syndrome (PCOS): a systematic review and Meta-analysis[J]. *Hum Reprod Update*, 2013, 19(3):268.
- [7]Nasiri N, Moini A, Eftekhari-Yazdi P, et al. Abdominal obesity can induce both systemic and follicular fluid oxidative stress independent from polycystic ovary syndrome[J]. *Eur J Obstet Gynecol Reprod Biol*, 2015, 184:112-116.
- [8]Savicradojevic A, Bozic AI, Coric V, et al. Effect of hyperglycemia and hyperinsulinemia on glutathione peroxidase activity in non-obese women with polycystic ovary syndrome[J]. *Hormones*, 2015, 14(1):101-108.
- [9]González F, Nair KS, Daniels JK, et al. Hyperandrogenism sensitizes mononuclear cells to promote glucose-induced inflammation in lean reproductive-age women[J]. *Am J Physiol Endocrinol Metab*, 2012, 302(3):297-306.
- [10]Ashok,Agarwal,Anamar,Aponte-Mellado,Beena J,Premkumar,Amani,Shaman,Sajal, Gupta.The effects of oxidative stress on female reproduction: a review.[J].*Reproductive biology and endocrinology* : RB&E,2012,10:49.
- [11]Riddhi,Thaker,Hina,Oza,Ildrish,Shaikh,Sunil,Kumar.Correlation of Copper and Zinc in Spontaneous Abortion.[J].*International journal of fertility & sterility*,2019,13(2):97-101.
- [12]Spritzer, Poli Mara,Lecke, Sheila Bunecker,Fabris, et al.Blood Trace Element Concentrations in Polycystic Ovary Syndrome: Systematic Review and Meta-analysis[J].*Biological trace element research*,2017,175(2):254-262.
- [13]Guanchao Zheng,Lijun Wang,Zhizhun Guo,Lingbin Sun.Association of Serum Heavy Metals and Trace Element Concentrations with Reproductive Hormone Levels and Polycystic Ovary Syndrome in a Chinese Population[J]. *Biological trace element research*,2015,167(1):1-10.
- [14]Coskun A.Plasma selenium levels in Turkish women with polycystic ovary syndrome[J]. *Eur J Obstet Gynecol Reprod Biol*,(2013), 168:183-186.
- [15]Zagrodzki, P.,Krzyczkowska-Sendrakowska, M.,Nicol, F.,Wietecha-Posfuszny, R.,Milewicz, T.,Kryczyk-Kozioł, J.,Chaykivska, Z.,Jach, R..Selenium status parameters in patients with polycystic ovary syndrome[J].*Journal of trace elements in medicine and biology: Organ of the Society for Minerals and Trace Elements (GMS)*,2017,44:241-246.
- [16]Hajizadeh-Sharafabad F et al.Selenium and Polycystic Ovary Syndrome; Current Knowledge and Future Directions: A Systematic Review[J].*Horm Metab Res* ,2019; 51: 279-287.
- [17]M Jamilian;M Razavi;Z Fakhrie Kashan,et al.Metabolic response to selenium supplementation in women with polycystic ovary syndrome: a randomized, double-blind, placebo-controlled trial[J]. *Volume82, Issue6,June 2015*.
- [18]Rezvanfar MA , Rezvanfar MA , Ahmadi A ,et al.Molecular mechanisms of a novel selenium-based complementary medicine which confers protection against hyperandrogenism-induced polycystic ovary[J].*Theriogenology*, 2012,78 (2012):620-631.
- [19]Köse SA,Nazıroğlu M.Selenium reduces oxidative stress and calcium entry through TRPV1 channels in the neutrophils of patients with polycystic ovary syndrome[J].*Biol Trace Elem Res*.2014 May;158(2):136-42
- [20]An-Su,Tu,Ying,Zhong,Xi-Guang,Mao.Changes of serum TOS and TAS levels and

their association with apolipoprotein(a) in patients with polycystic ovary syndrome and infertility.[J].Nan fang yi ke da xue xue bao = Journal of Southern Medical University,2016,36(3):405-9.

[21]Tao Zuo, Minghui Zhu, Wenming Xu.Roles of Oxidative Stress in Polycystic Ovary Syndrome and Cancers[J].Oxidative Medicine and Cellular Longevity, vol. 2016, Article ID 8589318, 14 pages, 2016. <https://doi.org/10.1155/2016/8589318>.