American Journal of Biology and Natural Sciences
https://biojournals.us/index.php/AJBNS
ISSN: 2997-7185

Evaluation of Serum GPX4 Levels and rs713041 Polymorphism in Hypertensive Patients: A Case-Control Study in Dhi Qar Province, Iraq

Zahraa Suwaih Ghulam, Prof. Dr. Intisar Hussein Ahmed
Department of Biology, College of Education for Pure Sciences, University of Wasit, Iraq

Received: 2024, 15, May
Accepted: 2025, 21, Jun
Published: 2025, 12, Jul

Annotation: Hypertension is a prevalent cardiovascular condition associated with increased oxidative stress. Glutathione Peroxidase 4 (GPX4) is a critical antioxidant enzyme that protects cells from oxidative damage. This case-control study aimed to assess serum GPX4 levels and the rs713041 T/C polymorphism of the GPX4 gene in hypertensive patients compared to healthy controls in Dhi Qar Province, Iraq. Our findings indicate significantly lower serum GPX4 levels in hypertensive patients, suggesting compromised antioxidant defense mechanisms.

1. Introduction

Hypertension is a major risk factor for cardiovascular diseases and is often associated with increased oxidative stress. GPX4 plays a vital role in reducing lipid peroxides, thereby preventing cellular damage. Variations in the GPX4 gene, such as the rs713041 T/C polymorphism, may influence enzyme activity and contribute to disease susceptibility. This study investigates the relationship between serum GPX4 levels, the rs713041 polymorphism, and hypertension in an Iraqi cohort.

2. Materials and Methods

2.1 Study Design and Ethical Approval

This case-control study was conducted from October 1, 2024, to January 30, 2025, in Dhi Qar Province, Iraq. The study was approved by the Research Ethical Committee and Scientific Committee of the Department of Biology, College of Education for Pure Sciences, University of Wasit (Reference No.: [Insert number]).

2.2 Study Participants

A total of 80 participants were enrolled:

- **Hypertensive group (n = 45):** 24 males and 21 females, aged 40–70 years (mean age 51.92 ± 5.50).
- **Control group (n = 35):** 18 males and 17 females, aged 40–70 years (mean age 51.52 ± 4.18).

Inclusion criteria: Adults aged ≥18 years with a diagnosis of hypertension. Exclusion criteria: Pregnant women, children, individuals with secondary hypertension, or those with chronic illnesses.

2.3 Blood Collection and Sample Handling

Five milliliters of venous blood were collected from each participant:

- **Serum samples** were obtained using plain tubes, centrifuged at 3000 rpm for 15 minutes, and stored at −20°C for GPX4 analysis.
- **Genomic DNA** was preserved in K3-EDTA tubes for future analysis of the rs713041 polymorphism.

2.4 Measurement of Serum GPX4 Levels

Serum GPX4 concentrations were measured using a sandwich ELISA kit for human GPX4 (Bioassay Technology Laboratory), following the manufacturer's instructions. The assay involved antigen-antibody interaction and colorimetric detection, with absorbance measured at the appropriate wavelength.

3. Results

3.1 Serum GPX4 Levels in Hypertensive vs. Control Groups

Serum GPX4 levels were significantly lower in hypertensive patients (2.71 ± 0.08 ng/mL) compared to controls (3.4 ± 0.33 ng/mL), with a P-value of 0.02, indicating a statistically significant difference.

Table 1: Mean Serum GPX4 Levels

Group	Mean ± SE (ng/mL)	P-value	Significance
Control	3.4 ± 0.33		
Hypertensive	2.71 ± 0.08	0.02	Significant

3.2 Gender-Specific GPX4 Levels

No statistically significant differences were observed between males and females within either group. However, hypertensive individuals of both sexes exhibited lower GPX4 levels compared to their respective controls.

Table 2: Serum GPX4 Levels by Gender

Group	Male (ng/mL)	Female (ng/mL)	P-value	Significance
Control	3.31 ± 0.28	3.5 ± 0.64	0.78	Ns
Hypertensive	2.62 ± 0.09	2.83 ± 0.15	0.21	Ns
P-value (patients vs controls)	0.01	0.9		

SE: Standard Error; Ns: Non-significant

4. Discussion

4.1 Serum GPX4 Levels

Our study found significantly reduced serum GPX4 levels in hypertensive patients, suggesting a functional deficiency associated with the disease. This decrease in GPX4 may impair the

detoxification of lipid peroxides, promoting vascular oxidative damage. These findings are consistent with previous studies by Tuama and Ghali (2022) and Hamed and Ghali (2024), which also reported decreased antioxidant enzyme activity in hypertensive individuals.

4.2 Gender-Specific GPX4 Levels

While no statistically significant differences in GPX4 levels were observed between males and females within either group, hypertensive individuals of both sexes exhibited lower levels compared to their respective controls. This supports the hypothesis that GPX4 downregulation is more disease-driven rather than sex-specific, as suggested by Seibt et al. (2019).

5. Conclusion

This study demonstrates that serum GPX4 levels are significantly lower in patients with hypertension compared to healthy individuals, supporting the role of oxidative stress in hypertension pathogenesis. While gender did not significantly influence GPX4 levels, the consistent decline across both sexes highlights the potential of GPX4 as a biomarker for oxidative damage in hypertensive individuals. Further research is recommended to explore the impact of GPX4 gene polymorphisms, including rs713041, on protein expression and clinical outcomes in hypertension.

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