Sumer Journal for Pure Science (ISSN: 2790-7031)
SJPS 2026 (June), Vol. 5, No. 1, p.p.: 632-638

Evaluation of Serum CYP2C19 Levels in Hypertensive Patients vs. Healthy Controls

Ahmed Ibrahim Abdulridha [1]*, Zafir Hassan Ghali[2]
[1]*Department of Biology, College of pure Sciences Education, University of Wasit, Wasit, Iraq*
[2]*Department of Biology, College of pure Sciences, University of Wasit, Wasit, Iraq*
* Email address of the Corresponding Author: ahm20013g@gmail.com
Phone number: 07702055761

Abstract

Hypertension is a complex condition arising from the interaction of genetic and environmental factors and represents a major global health challenge due to is contribution to cardiovascular morbidity and mortality. The case-control study was performed in Wasit Province, Iraq, between October 2025 and March 2026 to assess the levels of circulating CYP2C19 in patients with hypertension. A total of 80 participants were recruited; 45 patients with clinically confirmed hypertension and 35 healthy controls. ELISA-based analysis demonstrated significantly elevated serum CYP2C19 levels in hypertensive patients (6.29 ± 0.71 ng/mL) compared with healthy controls (4.17 ± 0.22 ng/mL), with a highly significant difference ($p = 0.0001$). Gender-based analysis showed no significant differences within controls ($p = 0.458$) or patients ($p = 0.100$), yet serum levels were significantly higher in patients than controls for both males ($p = 0.01$) and females ($p = 0.001$).In conclusion ,there is a potential association between increased CYP2C19 expression and pathophysiology of hypertension. Serum CPY2C19 is elevated in hypertensive patients regardless of gender, indicating its potential involvement in disease

Keywords: CYP2C19, Hypertension, ELISA ,Serum Level .

تقييم مستويات CYP2C19 في مصل الدم لدى مرضى ارتفاع ضغط الدم مقابل الافراد الاصحاء

احمد إبراهيم عبدالرضا[1]* , ا.د ظافر حسن غالي[2]
[1]قسم علوم الحياة , كلية التربية للعلوم الصرفة , جامعة واسط , محافظة واسط , العراق
[2]قسم علوم الحياة , كلية التربية للعلوم الصرفة , جامعة واسط , محافظة واسط , العراق

الخلاصة

ارتفاع ضغط الدم هو حالة معقدة تنشأ من تفاعل العوامل الجينية والبيئية ويمثل تحديا صحيا عالميا كبيرا بسبب مساهمته في أمراض القلب والأوعية الدموية والوفيات. أجريت دراسة الحالة والشاهد في محافظة واسط بالعراق بين أكتوبر 2024 ومارس 2026 لتقييم مستويات CYP2C19 المنتشرة لدى مرضى ارتفاع ضغط الدم. تم تجنيد ما مجموعه 80 مشاركا؛ 45 مريضا لديهم ارتفاع ضغط دم مؤكد سريريا و35 ضابطا صحيا. أظهرت التحليلات المبنية على ELISA مستويات CYP2C19 مصل مرتفعة بشكل ملحوظ لدى مرضى ارتفاع ضغط الدم (6.29 ± 0.71 نانوغرام/مل) مقارنة بالضابطين الأصحاء (4.17 ± 0.22 نانوغرام/مل)، مع فرق ذو دلالة كبيرة ($p = 0.0001$). أظهر التحليل القائم على النوع الاجتماعي عدم وجود فروق ذات دلالة إحصائية بين الضوابط ($p = 0.458$) أو المرضى ($p = 0.100$)، ومع ذلك كانت مستويات المصل أعلى بشكل ملحوظ لدى المرضى مقارنة بالمجموعة الضابطة لكل من الذكور ($p = 0.01$) والإناث ($p = 0.001$). في الختام، هناك ارتباط محتمل بين زيادة التعبير CYP2C19 والفيزيولوجيا المرضية لارتفاع ضغط الدم. يرتفع CPY2C19 المصل لدى مرضى ارتفاع ضغط الدم بغض النظر عن الجنس، مما يشير إلى احتمال تورطه في المرض.

1. Introduction

Hypertension (raised blood pressure) is a leading modifiable risk factor for cardiovascular disease, stroke, kidney failure and premature death worldwide. It is frequently asymptomatic, which contributes to delayed diagnosis and suboptimal control; globally, many people with hypertension remain unaware of their condition or do not have adequate blood-pressure control [1].Determinants of the rising burden include population ageing, urbanization, dietary transition (increased salt and processed-food intake), rising prevalence of overweight/obesity, and reduced physical activity [2][3].

Epidemiological estimates have documented a large and growing absolute burden of raised blood pressure. The WHO's most recent fact sheet reports that an estimated 1.4 billion adults aged 30–79 years had hypertension in 2024 (approximately 33% of people in that age range), with about two-thirds living in low- and middle-income countries (WHO, 2025). Historical pooled analyses show a long-term rise in the absolute number of adults with raised blood pressure (from hundreds of millions in 1975 to over a billion by 2015), driven principally by demographic change and by rising burdens in lower-resource regions [3]. Comprehensive narrative and systematic reviews further note persistent global gaps in awareness, treatment initiation and adequate control, particularly in resource-limited settings [2]

Available nationally representative data indicate that hypertension is highly prevalent in Iraq and that control rates are low. The Iraq STEPS household survey (national survey of behavioral and biomedical NCD risk factors) documented the national prevalence of raised blood pressure among adults in the 2015 survey and provides a publicly accessible fact sheet and dataset[4]. A clinic-based study in Baghdad reported that roughly one quarter of adults attending primary health-care centers had hypertension[5] . Analysis of Iraqi survey data and facility-based audits indicates overall population prevalence estimates in many reports clustered in the mid-20s to mid-30s percent range depending on case definition, age distribution and whether previously diagnosed individuals were included[5][4]. Moreover, facility-based studies in Baghdad and other Iraqi centers have repeatedly shown suboptimal control among those identified as hypertensive[6]. Together, these findings point to substantial national burden and important gaps in detection, treatment and long-term control.

In the Eastern Mediterranean and wider Middle East region, systematic reviews and pooled analyses report prevalence estimates similar to or exceeding global averages in many countries, with particularly high prevalence among older age groups. Age-specific prevalence increases sharply, and regional determinants (urbanisation, changes in diet, high level of obesity) are similar to those in the global population [7][8]. Barriers in health system support (screening, access to preventive care and affordability of medication) compound poor control rates in multiple countries throughout the region [2].

High prevalence, often unrecognized, with poor control creates a substantial burden of preventable heart and kidney disease. In Iraq, the national STEP results and other studies suggest an action plan should address population prevention (salt intake, diet and physical activity promotion), population screening (particularly for the elderly and other risk groups), primary-care management (guidelines and follow-up) and policies to combat out-of-pocket costs for long-term antihypertensive drugs. At the regional and global level, the evidence indicates a regional and global public-health response to enhance awareness, treatment

initiation, adherence and treatment targets in the context of equity and capacity in resource-poor settings[8][2].

The CYP2C19 enzyme, a member of the cytochrome P450 family,plays a critical role in the metabolism of several cardiovascular drugs,including clopidogrel and certain antihypertensive agents[9][10]. A common single nucleotide polymorphism, rs4244285 (CYP2C19), produces a loss of function allele that diminishes enzymatic activity.

Pharmacogenomic profiling of *CYP2C19* variants provides an opportunity for personalized medicine, allowing treatment to be according to a patient's genetic makeup. Evidence suggests that CYP2C19 polymorphism not only influences clopidogrel response but it may contribute to the pathophysiology of hypertension through its effects on endogenous vasoactive compounds[9].Examining the relationship between genotype and serum enzyme levels can therefore guide clinical decision-making, optimize therapy, and reduce adverse outcomes.

Genetic variability in CYP2C19 may influence both susceptibility to hypertension and interindividual response to cardiovascular medications, highlighting its potential value as a biomarker for precision medicine[9][10].

The current study aims to assess CYP2C19 levels ,and evaluate their association with hypertension risk and drug response in hypertensive patients and compare it with healthy people in Wasit Governorate.

2.Materials and methods

- **Study Design**

A total of 80 participants were included in this study using a convenience sampling approach. The study population included 45 clinically confirmed patients and 35 apparently healthy individuals who served as the control group.

The patient group consisted of 45 individuals diagnosed with hypertension, aged between 35-63 years, patients mean age ± SD 53.33±9.51,Median :55.All patients were residents of Wasit Province, Iraq, and included 20 males and 25 females.

The control group comprised 35 healthy subjects (17males and 18 females) with an age range 40-60 years,(mean age±SD:, 46.73 ± 7.39 Median :45.These individuals were selected from the local community of Wasit Province, Iraq, and had no known history of hypertension or related chronic conditions.

All patients were diagnosed by a physician based on internationally accepted diagnostic criteria.

- **Sample Collection and Processing**

From each participant, 5 mL of blood was collected via venipuncture. The sample was placed in a tube without anticoagulant. Serum was separated by centrifugation at 2000 × g for 10 minutes, aliquoted into Eppendorf tubes, and stored in a deep freezer until analysis of serum CYP2C19 levels by ELISA.

- **CYP2C19 Measurement**

Serum concentrations of CYP2C19 in hypertension patients and healthy controls were measured using a Human CYP2C19 ELISA Kit (Bioassay Technology Laboratory) following the manufacturer's instructions. The kit is a sandwich ELISA, designed for the quantitative measurement of human CYP2C19 protein in plasma, serum, cell culture supernatants, and urine.

- **Statistical Analysis**

The data were analyzed using SPSS version 21.0 (SPSS Inc., Chicago, IL, USA). Serum of CYP2C19 levels were expressed as mean ± SE and compared using Student's t-test or ANOVA as appropriate. The level of significance was categorized as Sig. for significant difference ($P < 0.05$), HS for highly significant difference ($P < 0.01$), and NS for non-significant difference ($P > 0.05$).

3.Results

Table 1: Demographic variables of hypertension patients and healthy controls

variable	patients (n=45)	Healthy controls (n=35)
Age (years)(±SD)	53.27 ± 9.43	47.00±7.42
Sex (male/ female)	20/25	17/18

A total of 45 hypertension patients and 35 healthy controls were enrolled in this case control study. Among them, 20 (44.44%) were males, and 25 (55.56%) were females in the patient group, whereas 17 (48.57%) were males and 18 (51.43%) were females in the control group.

Table 2: Serum CYP2C19 concentrations in patients with hypertension and healthy controls (Mean ± SE, P-value)

Groups/Parameters	**ng/ml** **Mean ± SE**
Control	4.17 ± 0.22
Patients	6.29 ± 0.71
P-value	0.0001
Significant level	*** Sig.

The mean serum levels of the CYP2C19 were significantly higher in patients compared to healthy controls .

Table 3 : Serum CYP2C19 concentrations among male and female patients and healthy controls (Mean ± SE, P-value)

Groups/Parameters	ng/ml Mean ±SE			
	Male	**Female**	**P-value**	**Significant**
Control	4.34 ± 0.33	4.01 ± 0.31	0.458	NS.
Patients	6.07 ± 0.54	6.47 ± 1.22	0.100	NS.
P-value	0.01	0.001		
Significant level	**Sig.	***Sig.		

No significant difference between genders (P = 0.458) when compared between males and females within each group and between patients and controls However, when comparing between groups, serum levels were significantly higher in patients than in controls for both males (P = 0.01) and females (P = 0.001), indicating a clear elevation of the protein in patients regardless of gender.

4. Discussion

In terms of baseline characteristics, patients with hypertension revealed a higher mean age compared to healthy subjects. This is in agreement with the widely recognized role of aging as a key risk factor for hypertension [11]. No significant difference in sex distribution was observed between the two groups, suggesting that gender has no apparent effect on disease prevalence in the current study.

Analysis of serum CYP2C19 levels revealed higher levels in hypertensive patients compared to controls with significant difference . Although studies evaluating circulating CYP2C19 remain limited, this increase in concentration of serum CYP2C19 may inductee altered metabolic activity or compensatory mechanisms associated with hypertensive pathology. The role of genetic variability in influencing enzyme activity and drug metabolism highlighted [12].

Our findings of elevated serum CYP2C19 levels in hypertensive patients are consistent with evidence that cytochrome P450 enzymes contribute to vascular homeostasis through the metabolism of endogenous vasoactive compounds [8]. Zanger and Schwab emphasized that variability in CYP expression and activity can alter the balance of vasodilators and vasoconstrictors, thereby influencing blood pressure regulation [8]The observed increase in circulating CYP2C19 may therefore represent a compensatory mechanism in hypertensive pathology, reflecting altered metabolic activity rather than genetic variation alone. This highlights the potential utility of serum CYP2C19 measurement as a biomarker for hypertension risk and therapeutic monitoring, independent of genotypic profiling.

Serum CYP2C19 levels were not observed with differences in expression within each gender suggesting that gender has limited influence on expression. However, the significantly elevated levels in hypertensive patients compared to healthy controls in both males and females suggest that CYP2C19 levels may be associated with disease.

5.Conclusions

According to the results of the current study there is a potential association between increased CYP2C19 expression and pathophysiology of hypertension. Serum CPY2C19 is elevated in hypertensive patients regardless of gender, indicating its potential involvement in disease

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