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

Evaluation the Serum Levels of ADAMTS-13 among Iraqi Patients with Hypertension

Suhad Mohammad Hamed, Prof. Dr. Zafir Hassan Ghali
Department of Biology –College of Education for pure Sciences-University of Wasit –Iraq

Received: 2024, 15, Sep
Accepted: 2024, 21, Sep
Published: 2024, 07, Oct

Annotation: Hypertension is a major public health problem due to its high prevalence all around the globe. Adisentgrine and metallopeptedase with thrombospondin type1 motif13 (ADAMTS-13), which encodes a metalloproteinase responsible for cleaving von Willebrand factor (VWF), a key player in platelet adhesion and aggregation. The identification of specific ADAMTS-13 gene polymorphisms associated with hypertension could lead to the development of genetic biomarkers for risk stratification. The aim of this to evaluate serum levels of ADAMTS-13 in patients with hypertension in an Iraqi population. Forty five hypertensive patients (23 males and 22 females), their age 40-70 years and 35 healthy controls (18 males and 17 females), their age range between 40-70 years. were selected from Wasit Province using a convenient sampling method.Serum levels of ADAMTS-13 was performed using by enzyme-linked immunosorbent assay technique (ELISA) using Human- ADAMTS-13kit. In patients and controls. The results of serum levels of ADAMTS-13 reveal highly significant differences, the ADAMTS-13 levels in sera

from hypertensive patients were higher than that of controls (1553.69598+467.80990), controls (318.31783+9.39208), P=0.0227. It is noteworthy that the ADAMTS-13 levels in the current study were lower significantly among males and females patients withe hypertension compared with control group ,(1038.87133±231.08107) versus (337.86575± 15.83530) P=0.0001,(1855.16940±529.36715 versus (387.01973±64.50541) P=0.0002 respectively . ADAMTS-13 levels revealed non-significant difference when comparing male patients with female patients 1038.87133±231.08107 versus 1855.16940± 529.36715 with a non-significant difference P=0.1713. Based on the polymorphism of,serum (ADAMTS13) rs28503257 A/G levels of ADAMTS-13 showed that hypertensive patients with homozygous AA genotype appeared non-significant difference when compared with the healthy individuals with AAgenotype 2340.73550±421.37615 vs. 441.50058±111.61452,P= 0.0001.The patients carrying the heterozygous AG genotype revealed significant decline in ADAMTS-13 serum levels 1820.89450±180.06750 in comparison with controls carrying this genotype 340.87340±9.62072,P=0.0001. These results are in agreement with the results of association analysis which demonstrate that these genotypes represents the most ones predisposed to hypertension.In conclusion, Serum levels of ADAMTS-13 are significantly correlated with hypertension and may reflect the role of ADAMTS-13 in the pathogenesis of the diseases.

Introduction

Hypertension is a major risk factor for cardiovascular diseases, affecting millions of individuals worldwide. The pathogenesis of hypertension involves complex interactions between genetic and environmental factors. In recent years, research has focused on identifying genetic variants associated with hypertension susceptibility and severity. One gene that has gained attention in this context is *ADAMTS13*, which encodes a metalloproteinase responsible for cleaving von Willebrand factor (VWF), a key player in platelet adhesion and aggregation. One of the primary objectives is to elucidate the role of genetic variants in the *ADAMTS-13* gene in the development and progression of hypertension The current study aims to evaluate serum levels of ADAMTS-13 in patients with hypertension in an Iraqi population.

The objectives of current study

1. To measure the levels of ADAMTS-13 in sera from patients with hypertension by Enzyme-linked immunosorbent assay (ELISA)
2. To correlate the relationship between gene polymorphism of ADAMTS-13; allele frequency; genotype frequency and its levels in sera.

Materials and Methods

A total of 80 participants: 45 confirmed patients with hypertension and 35 healthy individuals as controls were selected by using a convenient sampling method.

1- Hypertensive patients group: 45 Patients with hypertension(25males and 20 females), and their age range was between 40–70 years (51.92 ± 51.50 years, median= 51 years).

2- Control group: the control group which comprised of 35 healthy individuals (19 males and 16 females) and their age range between 40-70 years (51.52 ± 47.18 years, median=48 years). All patients were diagnosed according to global criteria by the physician. The data recorded for all participants included: name, gender, age, other diseases, smoking, treatment, weight, height, body mass index, residence, profession, the patient's disease history, inheriting the disease in the family, and date of sample collection. All samples were collected from Al-Zahra'a Teaching Hospital, and blood bank in Kut, Iraq. The study criteria inclusion criteria were the ages of the controls match to the ages of the patients and that the patients had chronic hypertension. Exclusion criteria were the patients be free of other diseases or inflammatory diseases.

Determination of serum level of Metallopeptedase with aThrombospondin type 1 Motif13 (ADAMTS-13)

This kit is an Enzyme-Linked Immunosorbent Assay (ELISA). The plate has been pre-coated with Human ADAMTS13 antibody. ADAMTS13 present in the sample is added and binds to antibodies coated on the wells. And then biotinylated Human ADAMTS13 Antibody is added and binds to ADAMTS13 in the sample. Then Streptavidin-HRP is added and binds to the Biotinylated ADAMTS13 antibody. After incubation unbound Streptavidin-HRP is washed away during a washing step. Substrate solution is then added and color develops in proportion to the amount of Human ADAMTS13. The reaction is terminated by addition of acidic stop solution and absorbance is measured at 450 nm.

Results

Serum levels of Adisentegrin and metallopeptedase with a thrombospondin type1 motif 13(ADAMTS-13) in patients with hypertension and controls

Determination of Adisentegrin and metallopeptedase with a thrombospondin type1 motif 13(ADAMTS-13) in sera of patients with hypertensive and controls was done by using an Enzyme-linked immunosorbent assay (ELISA). The results are shown in Tables (1). The results reveal highly significant differences, the ADAMTS-13 levels in sera from hypertensive patients were higher than

that of controls (1553.69598+467.80990), controls (318.31783+9.39208), *P*=0.0227.

Table 1: Mean levels of ADMATS-13 in hypertensive patients and controls groups

Parameters Groups	ng/ml Mean+SE
Control	318.31783±9.39208*
Patients	1553.6959846±7.80990
***P*-value**	0.0227
Significance level	Sig.[1]

Sig.[1]: *P* value (P<0.01)

ng: nanogram

*: Data was shown as meanS±E

Serum ADAMTS-13 levels among males and females of studied groups

The ADAMTS-13 levels were elevated among male and female patients with hypertension compared to the control group, (1038.87133±231.08107versus 337.86575±15.83530), *P* =, 0.0001

1855.16940±529.36715 versus 387.01973±64.50541, *P*=0.0002 respectively. It is noteworthy that the ADAMTS-13 levels were higher in females than in males when comparing male patients with female patients 1855.16940±529.36715versus

1038.87133±231.08107 with a non-significant difference *P*=0.1713.

Table 2: Mean comparison of ADAMTS-13 in male versus female in the study group

Parameters Groups	ng/ml Mean+SE			
	Male	**Female**	***P*-value**	**Significe level**
Control	337.865751±5.83530*	387.01973±64.50541	0.4530	Ns.
Hypertensive Patients	1038.871332±31.08107	1855.169405±29.36715	0.1713	Ns.
***P*-value**	0.0001	0.0002		
Significance	Sig.[1]	Sig.[1]		

Sig[1] *P*<0.001

ng: nanogram

*: Data was shown as mean± SE

Serum levels of ADAMTS-13 in relation to *A disintegrin and metallopeptedase with a thrombospondin type 1 motif13(ADAMTS-13)* gene rs28503257 genotypes

Serum levels of ADAMTS-13 according to *ADAMTS-13* gene rs28503257genotypes are shown in Table (3). The results showed that hypertensive patients with the AA genotype had higher levels of ADAMTS-13 (2340.73550±421.37615) compared with controls (441.50058±111.61452)*P*=0.0001. Similarly, the AG genotype showed an increase in ADAMTS-13 levels in patients (1820.89450±180.06750) compared with controls (340.87340±9.62072) *P*=0.0001, indicating significant differences. These results indicate that hypertensive patients have increased levels of ADAMTS-13 regardless of the type of genotype. Referring to the previous resultsin the table 3.2, these results suggest that there is an association of the genotypes with the predisposition to disease in patients carrying the genotype AA.

Table 3: Concentrations of ADMATS-13 in each genotype

Parameters Groups	ng/mL Mean+SE		
	AA	**AG**	**GG**
Control	441.50058±111.61452	340.873409±.62072	
Patients	2340.735504±21.37615	1820.894501±80.06750	
***P*-value**	0.0001	0.0001	
Significant	Sig.	Sig.	

Significant at P value (P<0.01).

Discussion

The of adisentgrine and metallopeptedase with a thrombospondin type1 motife13(ADAMTS-13) enzyme is involved in controlling the size and activity of von Willebrand factor, which affects platelet aggregation and thrombus formation. Serum levels of Adisentegrin and metallopeptedase with a thrombospondin type1 motif 13(ADAMTS-13) in patients with hypertension and controlsIn patients with hypertension, ADAMTS-13 levels can be of particular interest due to the potential relationship between hypertension and endothelial dysfunction. Low levels of ADAMTS13 are associated with various thrombotic disorders, including Thrombotic Thrombocytopenic Purpura (TTP).

The present study evaluated the relationships between serum levels of ADAMTS-13 in patients with hypertension. The results reveal highly significant differences, the ADAMTS-13 levels in sera from hypertensive patients were higher than that of controls. The ADAMTS-13 levels were elevated among male and female patients with hypertension compared to the control group. It is noteworthy that the ADAMTS-13 levels were higher in females than in males when comparing male patients with female patients. These results are in agreement with (Ma *et al*.,2014) .They found increased levels of ADAMTS-13 in patients with essential hypertension. However, the results of this study are inconsistent with Bongers. W*et al*.,2009 who found that levels of ADAMTS-13 are lower and levels of VWF are higher in young patients with cardiovascular disease compared to healthy individuals. The authors found no difference in ADAMTS13 between pulmonary arterial hypertension(PAH) patients and healthy controls,(newnham *et al*.,2019) inconsistent with the results of the current study.(ahmed *et al*.,2021) revealed significant differences in ADAMTS-13 between pulmonary arterial hypertension(PAH) patients and healthy controls. The discrepancy in results with regard to ADAMTS-13, could thus be ascribed to the different sampling time and could also be attributed to a putative effect of treatment response.

Enooku *et al*.,2013 found that serum ADAMTS-13 concentrations were lower in men than in women and in older age. The serum ADAMTS-13 concentration was significantly and inversely correlated with the systolic blood pressure, pulse pressure, and serum C reactive protein concentration in both men and women and with the serum γ-glutamyltransferase concentration in men only. In 88 subjects, who underwent a carotid artery evaluation, serum ADAMTS-13 concentrations were significantly lower in the subjects with a thicker carotid intima–media. ADAMTS-13 may play a role in not only TTP, but also inflammation, oxidative stress, and atherosclerosis. (Enooku *et al*.,2013).

Prolonged high blood pressure can lead to structural and functional changes in the endothelium. This can potentially affect ADAMTS-13 secretion or activity. Chronic inflammation and oxidative stress associated with hypertension may also interfere with ADAMTS-13 function.In cases of acute hypertensive crises, there may be transient changes in ADAMTS-13 levels due to rapid shifts in endothelial cell function and vWF release. Lower levels of ADAMTS-13 activity have been observed in patients with hypertension, although this is not universally consistent. The reduced enzyme activity may contribute to an increased risk of thrombosis by allowing larger vWF

multimers to persist, which can enhance platelet aggregation. Hypertension is often associated with other conditions like diabetes and chronic kidney disease, which can also impact ADAMTS-13 levels. For example, diabetic nephropathy can influence both ADAMTS-13 and vWF levels. Hypertension, a progressing in chronic inflammation and cardiovascular syndrome with various causes, results in functional and structural changes of heart and arterial vessels.(Ma *et al*.,2014) evaluated the relationships between left atrial (LA)size and plasma levels of on Willebrand factor (vWF), ADAMTS-13 in essential hypertension. They revealed that vWF/ADAMTS13 were positively correlated with left atrial diameter (LAD), left atrial volume (LAV), left atrial volume index (LAVi) ($P < 0.01$). Increased vWF and vWF/ADAMTS-13 is associated with LAD, LAV and LAVi in essential hypertension.

Serum levels of ADAMTS-13 according to *ADAMTS-13* gene rs28503257genotypes showed that hypertensive patients with the AA genotype had higher levels of ADAMTS-13 .Similarly, the AG genotype showed a significant increase in ADAMTS-13 levels in patients compared with controls.

These results indicate that hypertensive patients have increased levels of ADAMTS-13 regardless of the type of genotype. Referring to the previous results in the table3.2, these results suggest that there is an association of the genotypes with the predisposition to disease in patients carrying the genotype AA.

In summary, ADAMTS-13 plays a critical role in thrombotic regulation, and its levels can be influenced by the state of endothelial health, which is affected by hypertension. While there is evidence suggesting a relationship between hypertension and ADAMTS-13 levels.

Conclusions

1. Serum levels of ADAMTS-13 are significantly correlated with hypertension and may reflect the role of ADAMTS-13 in the pathogenesis of the diseases.
2. The hypertensive patients have increased levels of ADAMTS-13 regardless of the type of genotype of ADAMTS-13 rs28503257 variant A/G.

References

1. Ahmed, A., Ahmed, S. and Rådegran, G., 2021. Plasma ADAMTS13 and von Willebrand factor in diagnosis and prediction of prognosis in pulmonary arterial hypertension. Pulmonary Circulation, 11(4), p.20458940211041500.
2. Enooku, Kenichiro, Reiko Kato, Hitoshi Ikeda, Makoto Kurano, Yukio Kume, Haruhiko Yoshida, Tomoko Ono et al. "Inverse correlations between serum ADAMTS13 levels and systolic blood pressure, pulse pressure, and serum C-reactive protein levels observed at a general health examination in a Japanese population: a cross-sectional study." Clinica chimica acta 421 (2013): 147-151.
3. Ma, W.H., Sheng, L., Gong, H.P., Guo, L.L. and Lu, Q.H., 2014. The application of vWF/ADAMTS13 in essential hypertension. International Journal of Clinical and Experimental Medicine, 7(12), p.5636.
4. Newnham, M., South, K., Bleda, M., Auger, W.R., Barberà, J.A., Bogaard, H., Bunclark, K., Cannon, J.E., Delcroix, M., Hadinnapola, C. and Howard, L.S., 2019. The ADAMTS13–VWF axis is dysregulated in chronic thromboembolic pulmonary hypertension. European Respiratory Journal, 53(3).