Zagazig University Medical Journal
www.zumj.journals.ekb.eg
https://doi.org/10.21608/zumj.2022.161721.2639 Volume 30, Issue 1.4, JUNE 2024, Supplement Issue
Manuscript ID ZUMJ-2209-2639
DOI 10.21608/ZUMJ.2022.161721.2639
ORIGINAL ARTICLE

Plasma Level of Matrix Metalloproteinase 9 In Beta Thalassemia

Samah Abdelrasheed Elbiheery Youssif[1*], Mohamed Ahmed Badr[2], Tamer Hasan Hassan[2], Nermin Raafat Abd El Fattah[3]
[1] Department of Pediatrics, Mit Ghamr General Hospital, Dakahlia, Egypt.
[2] Department of Pediatrics, Faculty of Medicine, Zagazig University, Zagazig, Egypt.
[3] Department of Medical Biochemistry, Faculty of Medicine, Zagazig University, Zagazig, Egypt.

Corresponding author:
Samah Abdelrasheed Elbiheery Youssif

E-mail:
smsmaelbiheery12@yahoo.com

Submit Date 2022-09-19
Accept Date 2022-11-10

ABSTRACT

Background: Beta-thalassemia major (β-TM) is a genetic hemoglobinopathy that necessitates frequent blood transfusions and is brought on by defective β-globin chain synthesis. The matrix metalloproteinases (MMPs) family of zinc-dependent endopeptidases is in responsible of both physiological and pathological tissue restructuring. This study aims at assessing plasma levels of matrix metalloproteinase 9 in patients with beta thalassemia.

Methods: This case-control study was done in the pediatric hematology out-patient clinic of Zagazig University Hospitals from March 2019 till October 2019. We included 50 patients more than 10 years of both sexes and with beta thalassemia during their regular follow up visits. 50 age- and sex-matched healthy children were also included as a control group. All participants were subjected to full medical history and precise clinical examination. Routine laboratory investigations for beta thalassemia were done. Biochemical study of plasma matrix metalloproteinase 9 was also conducted by ELISA.

Results: MMP-9 was significantly higher in patients than controls (112.5 versus 18.5 pg/ml), respectively. Regarding the relation between serum level of MMP-9 and demographic characteristics of patients, though patients >15 years and females had higher levels of MMP-9 yet, the difference didn't reach a statistically significant level. MMP-9 levels were significantly higher in patients with complications than those without complications.

Conclusion: Thalassemia major patients had considerably increased plasma MMP-9 levels. MMP-9 seems to be a valuable marker in those patients.

Keywords: β-thalassemia, Matrix, Metalloproteinase, Children.

INTRODUCTION

Beta-thalassemia major (β-TM) is a genetic hemoglobinopathy that necessitates frequent blood transfusions and is brought on by defective β-globin chain synthesis. The matrix metalloproteinases (MMPs) family of zinc-dependent endopeptidases is in responsible of both physiological and pathological tissue restructuring. All structural components of the extracellular matrix (ECM) are broken down by MMPs, along with several non-ECM substrates. To maintain cardiac integrity and function during cardiovascular illness, the collagen network is broken down during tissue remodeling of the heart muscle. The MMPs MMP-1, -2, -8, -9, and -14 may break collagen [1].

According to several reports, MMP-9 also contributes significantly to neovascularization via the proteolytic destruction of blood vessel basal lamina proteins and the release of vascular endothelial growth factor in its physiologically active form. MMP-9 is crucial for immune cell

activity. During an allergen challenge, MMP-9 deletion encourages the migration of Th2 and eosinophil cells to both lungs. MMP-9 is increased in pathophysiological circumstances such as development, wound healing, and inflammatory diseases such as cancer, diabetes, and arthritis [2].

The immune system is stimulated in these pathophysiological situations by MMP-9 proteolytic characteristics, which help to start pathogenesis and speed up disease development. Several cardiovascular disorders, such as hypertension, atherosclerosis, and myocardial infarction, are accompanied with a significant rise in MMP-9 (MI). The abundance of MMP-9 papers demonstrates the enzyme's significance among potential and significant biomarkers, which might be utilized in conjunction with other biomarkers to speed up drug discovery or enhance diagnosis [3].

This study aims at assessing assess plasma levels of matrix metalloproteinase 9 in patients with beta thalassemia.

METHODS

This case-control study was done in the pediatric hematology out-patient clinic of Zagazig university hospitals from March 2019 till October 2019. The study included 50 patients more than 10 years of both sexes and with beta thalassemia during their regular follow up visits. 50 age- and sex-matched healthy children were also included as a control group. Exclusion criteria involved children out the mentioned age group or with chronic hemolytic anemia, other than beta thalassemia, other systemic disorders, any cardiac disease other than beta thalassemia or who refused to share in the study.

All participants were subjected to full medical history and precise clinical examination with stress on detecting the complications of the disease. Either transfusion or chelation details of patients were analyzed. Routine tests for beta thalassemia included a CBC (complete blood count), hemoglobin level, hematocrit value, WBC count (total and differential), platelet count, and Hb electrophoresis. Biochemical study of plasma matrix metalloproteinase 9 was also conducted by ELISA.

After a thorough description of the project, all participants provided written informed permission, and the study was authorized by the research ethics committee of Zagazig University's Faculty of Medicine (Institutional Research Board "IRB"). The work was done in conformity with the World Medical Association's Code of Ethics (Declaration of Helsinki) for human studies.

Statistical analysis:

The data was coded and analyzed using the SPSS version 24 program (Armonk, NY, IBM Corp). Numbers and percentages were used to convey categorical data. Categorical variables were analyzed using the Chi square test (X2). The mean, standard deviation, median, and range were used to express quantitative data. The "t" test was developed to compare normally distributed variables between two independent groups. To compare two sets of non-parametric data, the Mann Whitney test was utilized. In this study, the acceptable threshold of significance was 0.05 (P 0.05 was considered significant).

RESULTS

Table (1) shows the demographic characteristics of the studied participants. This table shows that patients and controls were age- and sex-matched. Table (2) demonstrates the disease complications for all patients with Beta thalassemia. The most prevalent illness consequences in our patients were hepatomegaly, growth retardation, and hypogonadism. We also analyzed the plasma MMP-9 levels in all subjects as shown in Table (3). MMP-9 was elevated in patients than controls significantly (112.5 versus 18.5 pg/ml), respectively.

Regarding the relation between serum level of MMP-9 and demographic characteristics of patients, Table (4) reveals that though patients >15 years and females had higher levels of MMP-9 yet, the difference did not reach a statistically significant level. Table (5) shows a significant relation between MMP-9 and disease complications. MMP-9 levels were substantially greater in patients who had issues than in those who did not.

Table 1: Demographic data and type of Beta thalassemia patients.

	Patients N=50	Controls N=50	Test	P
Age (years) Mean±SD (range)	15.3±3.5 (10-24)	15.0±3.2 (10-24)	t = 0.4	0.66
Sex **Males** **Females**	 26 24	 25 25	 X^2 = 0.04	 0.8
Diagnosis (n, %) **BTM** **BTI**	 35 70% 15 30%			

Data are presented as mean ± SD, median (Range), or number (%). Student "t" test and Chi square test (X2) were used.

Table 2: Disease complications for all patients with Beta thalassemia.

Complications	N	%
Hepatosplenomegaly	41	82.0%
HCV	20	40.0%
Cardiac complications	14	28.0%
Growth retardation	35	70.0%
Hypogonadism	29	58.0%
Hypothyrodism	6	12.0%
Hypoparathyrodism	8	16.0%
Diabetes Mellitus	4	8.0%

Qualitative data is represented as number and percentage.

Table 3: Plasma MMP-9 levels in patients and controls.

	Patients N=50	Controls N=50	t test	P Value
MMP-9 (pg/ml) **Mean±SD** **Range** **Median**	 112.5±101.4 18.5-321 78.5	 18.5±14.0 18.3 - 60.8 23.3	 6.5	 < 0.001

Data are presented as mean ± SD, median (Range), or number (%). Student "t" test was used.

Table 4: Relationship between serum level of MMP-9 and demographic characteristics of patients.

	n	MMP-9 Mean±SD (Range)	MW	P
Age (years) **≤15** **>15**	 30 20	 93.9 (18.8 – 321) 137.3 (18.5-294)	0.05	0.81
Gender **Males** **Females**	 26 24	 68.9 (18.5 – 294.3) 111.1 (18.5 – 321.0)	0.09	0.76

MW: Mann Whitney test.

Table 5: Relationship between serum level of MMP-9 and disease complications in patients.

	MMP-9 median (Range)	MW	P
Hepatosplenomegaly No Yes	 43.3 (18.8-68.9) 93.9 (18.5-321)	7.6	0.005*
Cardiac Complications -Ve +Ve	 43.8 (18.5 – 95.8) 243.8 (68.9 – 321)	23.4	<0.001**
Growth retardation -Ve +Ve	 56.3 (18.5 – 95.8) 293.9 (118.9 – 321)	29.8	<0.001**
Hypogonadism -Ve +Ve	 19.9 (18.8 – 68.9) 94.0 (18.5- 321)	21.3	<0.001**
Hypothyrodism -Ve +Ve	 19.9 (18.5-94.0) 95.0 (42.8-321)	22.6	<0.001**
Hypoparathyrodism -Ve +Ve	 68.9 (18.5-321) 268.8 (68.9 – 294)	6.7	0.009*
Diabetes mellitus -Ve +Ve	 68.9 (18.5 – 321) 293.9 (293.9 – 294)	7.4	0.006*

MW: Mann Whitney test , * : significant , ** : highly significant.

DISCUSSION

In many pathophysiological disorders, MMP-9 proteolytic properties contribute to the immune response that begins pathogenesis and exacerbates disease progression. MMP-9 levels skyrocket in several cardiovascular diseases, including hypertension, atherosclerosis, and myocardial infarction (MI). The abundance of studies on MMP-9 highlights the enzyme's importance as a prospective and critical biomarker that might be used in conjunction with other biomarkers to improve diagnosis or accelerate drug discovery [2].

This study aimed to assess plasma levels of matrix metalloproteinase 9 in patients with beta thalassemia in Zagazig University Hospitals. This case-control study was done on 50 patients with beta thalassemia who were followed in Pediatric Hematology clinic at Zagazig University Hospital and fifty healthy control subjects, sex and age matched to the cases, in the period from June 2018 to February 2019.

The most prevalent illness consequences in our patients were hepatomegaly, growth retardation, and hypogonadism (82%, 70% and 58% respectively) followed by hepatitis C, cardiac complications hypoparathyroidism, hypothyroidism, and diabetes mellitus (40%, 28%, 16%, 12% and 8% respectively). This is consistent with the findings of Grow and colleagues, who discovered cardiac problems in 23.3 percent of thalassemic cases [4].

According to Hassan and colleagues, the most prevalent endocrinal complications are growth retardation and hypogonadism (68.5% and 49.3%, respectively). Hepatomegaly was seen in 41 individuals (56.2%) [5].

Cardiac disorders are characterized by inflammation and abnormal tissue remodeling caused by ECM reconfiguration and MMP-9 activation. MMPs are an enzyme family that mediates a variety of activities in tissue damage and immunological responses in autoimmune disorders. MMPs have been found to play a key role in both acute cardiac injury and chronic heart remodeling [6,7].

In our study, MMP-9 was significantly elevated in patients with beta thalassemia than controls (112.5 versus 28.5 pg/ml respectively). Even through a substantial body of research clarifying the MMP-9's function in cardiovascular disorders as

atherosclerosis, hypertension, heart failure, and acute myocardial infarction, scarce studies examined the relationship among thalassemia major and gingival inflammation by assessing MMP-9 levels in all body fluids. Gumus and colleagues discovered that salivary MMP-9 levels were considerably greater in thalassemic cases compared to healthy controls in this research (P< 0.001) [8].

CONCLUSION

We concluded that thalassemia major patients had considerably increased plasma MMP-9 levels. In these cases, MMP-9 appears to be a valuable marker. MMP-9 plasma levels should be given more attention as a helpful measure in beta thalassemia patients. More large-scale multicenter investigations are needed to back up our findings.

REFERENCES

1 **Jabłonska AG, Matejczyk MA and Rosochacki ST.** Matrix metalloproteinases (MMPs), the main extracellular matrix (ECM) enzymes in collagen degradation, as a target for anticancer drugs. J Enzyme Inhib Med Chem. 2016;31(sup1):177-83.

2 **Halade GV, Jin YF and Lindsey ML.** Matrix metalloproteinase (MMP)-9: a proximal biomarker for cardiac remodeling and a distal biomarker for inflammation. Pharm Ther. 2013;139(1):32-40.

3 **Jones CB, Sane DC and Herrington DM.** Matrix metalloproteinases: a review of their structure and role in acute coronary syndrome. Cardiovasc Res. 2003;59(4):812-23.

4 **Grow KI, Abrol PA, Vashist MI, Yadav RI and Sharma SH.** Associated complication in beta thalassemia patients. IOSR J Pharm. 2013;3(1):22-5.

5 **Hassan TA, Zakaria MA, Fathy MA, Arafa MO, El Gebaly SH, et al.** Association between genotype and disease complications in Egyptian patients with beta thalassemia: A Cross-sectional study. Sci Rep. 2018;8(1):1-9.

6 **Spinale FG, Coker ML, Heung LJ, Bond BR, Gunasinghe HR, Etoh TA, et al.** A matrix metalloproteinase induction/activation system exists in the human left ventricular myocardium and is upregulated in heart failure. Circulation. 2000;102(16):1944-9.

7 **Matsumura SI, Iwanaga SH, Mochizuki SA, Okamoto HI, Ogawa SA, Okada YA.** Targeted deletion or pharmacological inhibition of MMP-2 prevents cardiac rupture after myocardial infarction in mice. J Clin invest. 2005;115(3):599-609.

8 **Gumus PI, Kahraman CE, Akcali AL, Sorsa TI, Tervahartiala TA, Buduneli NU, et al.** Association of thalassemia major and gingival inflammation: a pilot study. Arch Oral Bio. 2016 Apr 1.

To Cite:

Elbiheery, S., Badr, M., Hassan, T., Abd El Fattah, N. Plasma Level of Matrix Metalloproteinase 9 In Beta Thalassemia. *Zagazig University Medical Journal*, 2024; (328-332): -. doi: 10.21608/zumj.2022.161721.2639