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Study of Fatty Acid Binding Protein 4 (FABP4) levels in Patients with Beta-thalassemia and its Related Complications

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Abstract:

Introduction: Duo to iron overload, patients with beta-thalassemia may experience complications. Several adipokines have been proposed as potential contributors to the development of beta-thalassemia complications. One of the adipokines, fatty acid-binding protein 4 (FABP4), connects various elements of the inflammatory and metabolic pathways.

Aim of the study: This study assessed B-thalassemia patients' serum (FABP4) levels and linked them to complications related to thalassemia.

Subjects and Methods: There were fifty adult participants in this cross-sectional study. A thorough clinical examination and medical history were completed. Every participant had their serum levels of fatty acid binding protein four measured.

Results: According to our findings, 24% of patients had HCV +ve, 36% had gall bladder stones, and 44% had elevated liver enzymes. Patients with serum ferritin levels greater than 2500 ng/ml and FABP4 level did not significantly correlate (p value < 0.05).

Conclusions: Patients with beta thalassemia had elevated liver enzymes, GB stones, and a high prevalence of HCV +ve. There was no discernible relationship between patients with serum ferritin levels higher than 2500 ng/ml and FABP4 level.

Keywords: FABP4; beta-thalassemia; complications.

1. Introduction

An inherited hematological disorder is thalassemia [1]. Beta-thalassemia is caused by one or more mutations in the beta-globin gene [1, 2]. Ineffective erythropoiesis

brought on by a decrease in or absence of beta-globin chains is the cause of anemia [2].

Transfusion-dependent and non-transfusion-dependent beta-thalassemia diseases are the two types that exist today. Based on the clinical severity of the patients, which establishes whether or not they require regular blood transfusions to survive the two types of thalassemia are distinguished [3].

Heart disease (heart failure and arrhythmias), endocrine problems (hypogonadism, hypothyroidism, diabetes, hypoparathyroidism), chronic hepatitis (which can lead to cirrhosis and, in rare cases, hepatocellular carcinoma), stunted growth, osteoporosis, and thrombophilia are among the still-common complications of beta-thalassemia. The prevalence of issues is decreasing in younger patient cohorts who have received blood that has been screened for viruses thanks to the development of novel imaging techniques and oral iron chelators [4].

The family of 14–15 kDa proteins known as the intracellular lipid chaperones, or free fatty acid binding proteins, or FABPs, regulates lipid trafficking and cell responses [5]. FABPs can reversibly bind to hydrophobic ligands such as eicosanoids, other lipids, and saturated and unsaturated long-chain fatty acids (FAs) with high affinity and broad selectivity. All species have FABPs, demonstrating strong evolutionary conservation [6]. Different FABP family isoforms are expressed by tissues engaged in active lipid metabolism [7]. Broadly speaking, there is a correlation between the amounts of FABP in cells and the rates of FA metabolism [5]. The family consists of the following isoforms: adipocyte (A-FABP /FABP4 /aP2), brain (B-FABP/FABP7), ileal (IlFABP/FABP6), intestinal (I-FABP /FABP2), heart (HFABP /FABP3), liver (L-FABP/FABP1), brain (E-FABP/FABP5), myelin (M-FABP /FABP8), and testis (TFABP /FABP9) [6].

Iron is one of the minerals required for cellular activity; however, too much iron can harm cells, as seen in beta-thalassemia patients [8]. In addition to potentially causing free radical reactions, iron may have an impact on how cells metabolize lipids, proteins, carbs, and nucleic acids. Beta-thalassemia major patients suffered from a chronic inflammatory condition [9].

The main cells that express serum FABP4 are macrophages and adipocytes. It has been associated with several disorders involving the inflammatory and metabolic pathways, such as metabolic syndrome and

cardiovascular disease [10]. Increased circulating FABP4 levels have been linked to insulin resistance and obesity, according to reports, heart failure, atherosclerosis, hypertension, and type 2 diabetes [10]. There have also been reports of associations between FABP4 levels and the development of diastolic and systolic cardiac dysfunction, as well as left ventricular hypertrophy [11]. Additionally, it has been documented that the carotid intima-media thickness, a measure of atherosclerosis, and the serum FABP4 level are related [12].

2. Subjects and Methods

2.1.Subjects

This study was carried out at Fayoum University Hospital and was a cross-sectional observational study**.**

Inclusion criteria

Every B-thalassemia patient who is older than 18 years.

Exclusion criteria

infection at the moment.

2.2.Research methodology

Every participant endured the following:

- Gathering medical history.
- A comprehensive physical assessment in general.
- Laboratory tests (HBs-Ag, HCV-Ab, HIV, serum ferritin, hepatic enzymes, and complete blood counts)-
- Fatty acid binding protein four measurement using enzyme linked immunosorbent (E2036Hu, China) bioassay.

2.3.Statistical Approaches

The computer was fed data, and IBM SPSS software package version 20.0 was used for analysis. (IBM Corp, Armonk, NY). Numerical and percentage representations were used for categorical data. The Shapiro-Wilk test was used to check for normalcy in continuous data. The mean and standard deviation were used to express quantitative data. Two groups were compared using the student t-test. The results were deemed significant at the 5% level.

3. Results

This study displays the frequency of the most typical complications in patients with thalassemia. This table displayed the frequency of the most common complications among the 50 patients with thalassemia. Twenty-two (44%) of the patients had increased liver enzymes; twelve (24%) had HCV infection; eighteen (36%) had gall bladder stones; and twelve (24%) had episodes of acute hemolytic anemia (**Table 1**). Mean Ferritin was (4.69 ± 4.26) in thalassemia patients with Ferritin (≤2500) while was (3.67 ± 1.20) in thalassemia patients with Ferritin (>2500) (P value = 0.451) (**Table 2**).

Table 1: The most common complications among the studied beta-thalassemia patients' group.

Variables	Frequency
Acute Hemolytic crisis	12 (24%)
HCV +ve	12(24%)
GB stones	18(36%)
Elevated liver enzymes	22(44%)

Table 2: Comparison between FABP4 levels in patients with high (>2500) and low (<2500) S. Ferritin levels.

FABP4 (ng/ml)	Ferritin (≤2500) (n= 40) (ng/ml)	Ferritin (>2500) (n= 10) (ng/ml)	*P*
Mean ± SD.	4.69 ± 4.26	3.67 ± 1.20	0.451

4. Discussion

The consequences of iron excess in patients with thalassemia major have continued to draw more attention because of the elevated morbidity and mortality in this population. The accumulation of iron may cause an increase in the production of unstable iron, which may affect the production of reactive oxygen species and consequently prolong the damage to organs [13]. Previous studies have shown that individuals with thalassemia, particularly those who go on to develop cardiovascular diseases, have a favorable inflammatory profile [14] Furthermore, the metabolization

of iron may be impacted by an accumulation of iron in tissues. In patients with beta-thalassemia, FABP4, a biomarker for low-grade chronic inflammation driven by metabolism, may provide insight into the mechanisms underlying these events [12]. Cardiovascular dysfunctions are the most severe problems that patients with beta-thalassemia major encounter [14]. Among these are fatal cardiac arrhythmias and congestive heart failure [14]. Additionally, a growing body of evidence indicates that FABP4 may play a role in the inflammatory and metabolic pathways that result in cardiovascular dysfunction [12].

We discovered that 12 (24%) of the patients had an HCV virus infection, and 22 (44%) of the patients had elevated liver enzymes. Our results were in line with those of Paparo et al., who showed that in laboratory testing on thalassemia patients, two aminotransferases, alanine transaminase (ALT) and aspartate transaminase (AST), may show modest increases (2–3 times higher than the upper limit of normal [15].

Between thalassemia patients with ferritin ≤2500 and thalassemia patients with ferritin >2500, there was no significant correlation between FABP4 and ferritin; mean FABP4 was 4.69 ± 4.26 in patients with ferritin ≤2500, and mean FABP4 was 3.67 ± 1.20 in patients with ferritin >2500 (P value = 0.451). Our research supported the findings of Pandji et al., who discovered that serum ferritin and serum FABP4 levels in thalassemia major patients have an inverse relationship. This could be related to the negative effects of high iron levels in adipocytes, which can prevent them from secreting or producing FABP4 [16].

On the other hand, Recardo et al. (2019) discovered a connection between high blood levels of FABP4 and the presence of inflammatory indicators, such as S. ferritin [17].

Conclusion

Patients with beta thalassemia had elevated liver enzymes, GB stones, and a high prevalence of HCV +ve. There was no discernible relationship between patients with serum ferritin levels higher than 2500 ng/ml and FABP4 level. Since this study was conducted at a single center with a small number of patients, more research involving many centers and participants is necessary.

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Ethical Approval Statement: The study was approved by the Institutional Ethics Committee of Fayoum Faculty of Medicine, Fayoum, Egypt. Informed Consent Statement: Written informed consents were obtained from all patients.

Conflicts of Interest: All authors declare no conflict of interest.

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