Pentraxin-3 Levels in β-thalassemia Major and its Relationship with Antioxidant Capacity and Total Oxidant Stress

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Pentraxin-3 Levels in β-Thalassemia Major and its Relationship with Antioxidant Capacity and Total Oxidant Stress

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Abstract

Objectives: To evaluate pentraxin-3 (PTX-3) levels in pediatric patients with β-thalassemia major, intermedia, and minor and its relationship with antioxidant capacity and total oxidant stress.

Background: PTX-3 increases alongside with oxidant stress. Therefore, it can be used as an early diagnostic marker for inflammation.

Patients and methods: A case-control study was conducted on 60 pediatric patients with β-thalassemia enrolled from the Pediatric Department of Menoufia University. In addition, 30 age-matched and sex-matched healthy children were included as a control group. The study was performed during January 2020 to January 2022.

Results: PTX-3 level was higher in all patients with β-thalassemia compared with control. The total antioxidant capacity was significantly lower in patients with β-thalassemia major versus β-thalassemia intermedia and minor. The cutoff value to detect β-thalassemia major in pediatric patients was 2.15 ng/ml, with an area under the curve of 0.846, with sensitivity and specificity of 93.3 and 63.3%, respectively. Moreover, the cutoff value for total antioxidant capacity was 2.11 nmol/well, with area under the curve of 0.695, with sensitivity and specificity of 86.5 and 71.5%, respectively, in relation to serum ferritin for detection of risky oxidative stress in patients with β-thalassemia.

Conclusion: PTX-3 level was higher in all β-thalassemia groups compared to control. So it could be used as a marker for β-thalassemia diagnosis. Moreover, total antioxidant capacity was significantly lower in patients with β-thalassemia major versus β-thalassemia intermedia and minor, which could be used as a specific test for differentiation.

Keywords: Antioxidant capacity, Diagnostic marker, Pentraxin-3, Patients with thalassemia, Total oxidant stress

1. Introduction

β-T halassemia is an autosomal recessive disorder that is more common in the populations of Mediterranean, Middle Eastern, or Asian descent. The underproduction of β-globin chains is most frequently caused by point mutations with single nucleotide substitution or oligonucleotide addition or deletion [1]. β-Thalassemia is the most common genetically inherited hemoglobin (Hb) disorder in Egypt, with a carrier rate varying from 5.3 to less than 9%. β-Thalassemia major is a chronic disorder of blood that has an extensive effect on life and presents with hemolytic anemia, growth retardation, hepato-splenomegaly, and skeletal abnormalities [2].

In patients with thalassemia, iron loading is observed due to the hemolysis of impaired erythrocytes as well as increase in intestinal iron absorption and erythrocyte transfusion. Oxidative damage occurs in major organs, especially in the cardiovascular system. Oxidative stress leads to vascular endothelial damage and forms the basis for serious cardiovascular diseases [1].

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Although oxidative stress is not the primary etiology of thalassemia, it mediates several of its pathologies. The main causes of oxidative stress in thalassemia are the degradation of the unstable Hb and iron overload, which stimulate the production of excess free radicals. The symptoms aggravated by oxidative stress include increased hemolysis, ineffective erythropoiesis, and functional failure of vital organs such as the heart and liver. The oxidative status of each patient is affected by multiple internal and external factors, including genetic makeup, health conditions, nutrition, physical activity, age, and the environment (e.g., air pollution and radiation) [3].

Recent studies have shown that one of the markers of vascular endothelial damage is pentraxin-3 (PTX-3) protein. Pentraxins are defined as proteins that have an evolutionarily conserved multifunctional, cyclic, and multimeric structure. Depending on their infrastructure, they are categorized under two groups: short and long pentraxins. PTX-3, which is the prototype of long pentraxins, is excreted from endothelial cells, smooth muscle cells, mononuclear phagocytes, and dendritic cells [4].

Vascular endothelial function impairment study is limited in patients with thalassemia. It is predicted that PTX-3 can be an indicator of vascular endothelial damage occurring with oxidative stress, and the evaluation of endothelial function can serve as a prognostic factor for cardiovascular diseases. PTX-3 is abundantly produced by vascular endothelial cells and smooth muscle cells in response to the inflammation and oxidized low-density lipoprotein (LDL) [5]. It is suggested that PTX-3 increases with oxidant stress and can be used as an early diagnostic marker for inflammation [6]. Therefore, the aim of this study was to evaluate PTX-3 levels in pediatric patients with β-thalassemia major, intermedia, and minor and its relationship with antioxidant capacity and total oxidant stress.

2. Patients and methods

This is a case–control study conducted on 60 pediatric patients with β-thalassemia (major, intermedia, and minor) diagnosed by both clinical and laboratory criteria, in addition to 30 sex-matched and age-matched children as a control group. They were enrolled from the Hematology and Oncology Unit, Pediatric Department, Menoufia University, during January 2020 to January 2022. We obtained the ethical approval of the study from the ethical committee of Faculty Medicine, Menoufia University. A written informed consent was taken from the parents or caregivers after explaining the aim of the study.

Children aged from 1 to 18 years were included and were divided into four groups: group I included 30 patients with β-thalassemia major, group II included 15 patients with β-thalassemia intermedia, group III included 15 patients with β-thalassemia minor, and group IV included 30 healthy participants who were clinically free. Patients with β-thalassemia were diagnosed according to clinical presentation, history, and physical examination as follows: the first clinical presentation of thalassemia major was between the first 6 months and 2 years of life, in form of severe anemia (Hb < 7 g/dl), pallor, jaundice, irritability, feeding problems, failure to thrive, skeletal deformities, abdominal enlargement owing to progressive splenomegaly and hepatomegaly, or recurrent episodes of infection [7]. Patients with NTDT presented with symptomatic anemia with a concurrent episode of infection occurring early in life, and they were older than 2 years of age [7]. Thalassemia minor was diagnosed by A2 level more than 3.6, and patients presented with mean corpuscular volume (MCV) and mean corpuscular hemoglobin (MCH) values that were low, whereas red blood cell counts were higher after exclusion of iron-deficiency anemia [8]. Patients with infectious diseases, patients with liver diseases, patients on steroid therapy or immunosuppressive drugs, and patients diagnosed with cardiac diseases were excluded. All participants were subjected to personal, present, past, and family history; general examination included vital signs; and anthropometric measurements. Routine investigations included mean yearly serum ferritin using enzyme-linked immunosorbent assay (ELISA) kit (EIA-01-Ferritin) [9]. Complete blood count (CBC) included pretransfusion CBC in thalassemia minor and TI and CBC in TT and control using Sysmex KX-21 automatized hematolgy analyzer (Sysmex Corporation, 1-5-1,Wakino-hama-kaigandori, Chuo-ku, Kobe, Hyogo 651-0073, Japan) [10].

Kidney functions such as blood urea nitrogen and serum creatinine level were assessed using the open system autoanalyzer synchrony CX5 [11]. Liver function test included serum aspartate transaminase (AST) and alanine transaminase (ALT) measured using a biochromatic (405–510 nm) rate technique [12]. The instrument automatically calculates and prints the activity of ALT and AST in U/L. Lipid profile such as cholesterol, triglyceride (TG), LDL, and high-density lipoprotein (HDL) in fasting patients for 8 h was assessed using the open system autoanalyzer synchrony CX5 (Beckman Coulter Life Sciences Headquarters 5350 Lakeview Pkwy S Drive Indianapolis, Indiana 46268 United States) [11].
Human PTX-3 ELISA kit [13] was used to assess PTX-3 levels, with reference range from 0.4 to 10 ng/ml. The human PTX-3 ELISA is a ready-to-use solid-phase ELISA based on the sandwich principle with a working time of 3½ h. The efficient format of two plates with 12 disposable eight-well strips allows free choice of batch size for the assay. Samples and standards are captured by a solid bound specific antibody. The biological sensitivity of the assay is 0.04 ng/ml. Human antioxidant capacity ELISA kit [14] was used to assess the antioxidant capacity, with reference range from 4 to 20 nmol/well. Cell Bio-labs’ OxiSelect total antioxidant capacity Assay kit measures the total antioxidant capacity within a sample. Samples are compared with a known concentration of uric acid standard within a 96-well microtiter plate format. Antioxidant capacity is determined by comparison with the uric acid standards.

2.1. Statistical analysis

We tabulated the results using an offline excel sheet and then statistically analyzed the results using SPSS, version 25 (IBM Corporation, Armonk, New York, USA). We used mean and SD for the descriptive statistics, whereas $\chi^2$ was used for the analytical statistics along with standard Student $t$ test. One-way analysis of variance (F test), Kruskal–Wallis test, and the receiver operating characteristic curves were used for analysis. A $P$ value less than or equal to 0.05 was considered statistically significant.

3. Results

There was no significant differences between the studied groups regarding age, sex, and residence. However, the frequency of consanguinity and family history were significantly higher in pediatric patients with $\beta$-thalassemia (major, intermedia, and minor) than the control group. Moreover, the frequency of consanguinity and family history were significantly lower in pediatric patients with $\beta$-thalassemia (major, intermedia, and minor) compared with the control group. HDL, LDL, and LDL/HDL ratio were significantly lower in patients with $\beta$-thalassemia minor and control groups. White blood cell (WBC) counts were significantly higher in patients with $\beta$-thalassemia major than patients with $\beta$-thalassemia minor and control (Table 2).

In the present study, cholesterol was significantly lower in patients with $\beta$-thalassemia major than minor and control. Moreover, it was significantly lower in patients with thalassemia minor than the control group. TG was significantly higher in patients with $\beta$-thalassemia major than patients with $\beta$-thalassemia intermedia, minor, and control groups. Serum ferritin was significantly higher in patients with $\beta$-thalassemia major than patients with $\beta$-thalassemia intermedia, minor, and control groups. It was significantly higher in patients with $\beta$-thalassemia intermedia than minor and control groups. Serum creatinine, blood urea nitrogen, and ALT were significantly higher in patients with $\beta$-thalassemia major than intermedia, minor, and control groups. However, AST did not show any significant difference between patients with $\beta$-thalassemia major and patients with $\beta$-thalassemia intermedia.

PTX-3 level was higher in all $\beta$-thalassemia groups compared with control group, with no difference between each other. The total antioxidant capacity was significantly lower in all $\beta$-thalassemia groups compared with the control group. It was significantly lower in patients with $\beta$-thalassemia major versus intermedia and minor (Table 3). The best sensitivity and specificity for PTX-3 (oxidant stress) were 93.3 and 63.3% at a cutoff level of 2.15 ng/ml with area under the curve (AUC) of 0.846 in relation to serum ferritin. Moreover, the best sensitivity and specificity for total antioxidant capacity were 86.5 and 71.5% at a cutoff level of 2.11 nmol/well, with AUC of 0.695, in relation to serum ferritin for detection of risky oxidative stress in patients with $\beta$-thalassemia (Table 4, Figs. 1 and 2).

4. Discussion

In this study, the frequency of consanguinity and family history were significantly higher in pediatric patients with $\beta$-thalassemia major, intermedia, and minor than the control group. Moreover, the frequency of consanguinity and family history were significantly lower in pediatric patients with $\beta$-thalassemia major, intermedia, and minor. These results were consistent with Abdelmotaleb et al. [15], who showed that family history of thalassemia...
was statistically higher in the thalassemic group than control; however, they contradicted our results as there was no statistically significant difference regarding consanguinity.

This study revealed that, Hb, MCV, and MCH were significantly lower in patients with β-thalassemia major than intermedia, minor, and control. These findings matched with Hassanin et al. [16], Karim et al. [17], and Abdelmotaleb et al. [15], who found significantly lower Hb level in patients with β-thalassemia major than in patients with β-thalassemia intermedia and controls. Karim et al. [17] showed that all hematological parameters including Hb, HCT, MCV, and MCH except MCHC were found to be significantly lower in patients with β-thalassemia than the controls. Additionally, Abdelmotaleb et al. [15] reported that Hb, MCV, and MCH were significantly statistically lower in the thalassemic group than in the control group.

In this study, HbF%, platelet count, RDW, and corrected reticulocyte count were significantly higher in patients with β-thalassemia major than in intermedia, minor, and control groups. HbA2 was significantly higher in patients with β-thalassemia minor than major, intermedia, and control groups. WBC counts were significantly higher in patients with β-thalassemia major than minor and control groups. Our findings agree with Elsayh et al. [18], who found that platelet, serum ferritin, and RDW were significantly higher in patients with β-thalassemia major than in intermedia and healthy control groups. However, our results disagreed with Abdelmotaleb et al. [15], who found no statistically significant differences between thalassemia and control groups in WBCs or platelet count.

Our study showed that cholesterol was significantly lower in patients with β-thalassemia major than minor and control groups. It was significantly lower in patients with β-thalassemia intermedia than minor and control groups. However, HDL, LDL, and LDL/HDL ratio were significantly lower in patients with β-thalassemia major and intermedia than minor and control groups. These results agreed with Heitzer et al. [19], Sengsuk et al. [20], and IsikBalci et al. [5], who reported that lower total cholesterol, LDL, and HDL values were reported in patients with thalassemia major when compared with the values of the control group. These findings agreed with Hashemieh et al. [21], who reported that low cholesterol levels in patients with thalassemia minor can be explained by several mechanisms: the increased cholesterol requirement associated with erythroid hyperplasia, macrophage system activation with cytokine release, and increased cholesterol uptake by the reticuloendothelial system [21].

### Table 1. Demographic data among the studied groups.

<table>
<thead>
<tr>
<th>Variables</th>
<th>β-thalassemia major (N = 30)</th>
<th>β-thalassemia intermedia (N = 15)</th>
<th>β-thalassemia minor (N = 15)</th>
<th>Control (N = 30)</th>
<th>F</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Range</td>
<td>1.00 – 18.00</td>
<td>7.00 – 17.00</td>
<td>5.00 – 17.00</td>
<td>3.00 – 18.00</td>
<td>2.419</td>
<td>0.072</td>
</tr>
<tr>
<td>Mean ± SD</td>
<td>9.78 ± 4.26</td>
<td>12.87 ± 3.36</td>
<td>9.60 ± 3.22</td>
<td>10.43 ± 4.12</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Family history</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Positive</td>
<td>14 (46.67)</td>
<td>7 (46.67)</td>
<td>7 (46.67)</td>
<td>19 (63.33)</td>
<td>0.814</td>
<td>0.846</td>
</tr>
<tr>
<td>Negative</td>
<td>16 (53.33)</td>
<td>8 (53.33)</td>
<td>8 (53.33)</td>
<td>0</td>
<td>3.12</td>
<td>0.041*</td>
</tr>
<tr>
<td>Residence</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Rural</td>
<td>11 (36.67)</td>
<td>7 (46.67)</td>
<td>9 (60.00)</td>
<td>15 (50.00)</td>
<td>2.411</td>
<td>0.492</td>
</tr>
<tr>
<td>Urban</td>
<td>19 (63.33)</td>
<td>8 (53.33)</td>
<td>6 (40.00)</td>
<td>15 (50.00)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Consanguinity</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Positive</td>
<td>13 (43.33)</td>
<td>8 (53.33)</td>
<td>7 (46.67)</td>
<td>0</td>
<td>3.12</td>
<td>0.041*</td>
</tr>
<tr>
<td>Negative</td>
<td>17 (56.67)</td>
<td>7 (46.67)</td>
<td>8 (53.33)</td>
<td>30 (100.00)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Post hoc</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Positive</td>
<td>14 (46.66)</td>
<td>12 (80.00)</td>
<td>12 (80.00)</td>
<td>0</td>
<td>4.20</td>
<td>0.025*</td>
</tr>
<tr>
<td>Negative</td>
<td>16 (53.33)</td>
<td>3 (20.00)</td>
<td>3 (20.00)</td>
<td>30 (100.00)</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

F: analysis of variance F test; χ², χ² test.
P1: β-thalassemia major versus β-thalassemia intermedia.
P2: β-thalassemia major versus β-thalassemia minor.
P3: β-thalassemia major versus control.
P4: β-thalassemia intermedia versus β-thalassemia minor.
P5: β-thalassemia intermedia versus control.
P6: β-thalassemia minor versus control.

*Significant.
In the present study, TG was significantly higher in patients with β-thalassemia major versus intermedia, minor, and control groups. It was significantly lower in patients with thalassemia minor than the control group. The current findings agreed with several studies by Ricchi et al. [22], Hassanin et al. [16], and IsikBalci et al. [5], who reported that TGs were elevated in patients with thalassemia, probably owing to extrahepatic lipolytic activity. Moreover, Hassanin et al. [16] found a significant increase in TG levels in both major and intermediate thalassemic groups than healthy controls, which is similar to IsikBalci et al. [5], who found higher TG values in patients with thalassemia major when compared
Table 3. Lipid profile and serum ferritin renal and liver functions, pentraxin-3 level and total antioxidant capacity among the studied groups.

<table>
<thead>
<tr>
<th>Variables</th>
<th>β-thalassemia major (N = 30)</th>
<th>β-thalassemia intermedia (N = 15)</th>
<th>β-thalassemia minor (N = 15)</th>
<th>Control (N = 30)</th>
<th>F</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cholesterol (mmol/l)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Range</td>
<td>170.00–178.20</td>
<td>106–200</td>
<td>104.00–227.00</td>
<td>103.00–235.00</td>
<td>3.936</td>
<td>0.024*</td>
</tr>
<tr>
<td>Mean ± SD</td>
<td>175.01 ± 2.82</td>
<td>174.2 ± 28.50</td>
<td>192.87 ± 31.14</td>
<td>200.90 ± 31.78</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Post hoc</td>
<td>P1 = 0.356, P2 = 0.001*</td>
<td>P3&lt;0.001*</td>
<td>P4 = 0.012*, P5 = 0.001*</td>
<td>P6 = 0.067</td>
<td></td>
<td></td>
</tr>
<tr>
<td>TG (mg/dl)</td>
<td>34.00–252.00</td>
<td>108.00–156.00</td>
<td>37.70–137.30</td>
<td>45.00–189.00</td>
<td>K = 7.106</td>
<td>&lt;0.001*</td>
</tr>
<tr>
<td>Mean ± SD</td>
<td>165.77 ± 56.83</td>
<td>129.33 ± 13.40</td>
<td>120.27 ± 13.80</td>
<td>123.07 ± 14.32</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Post hoc</td>
<td>P1 = 0.016*, P2&lt;0.001*</td>
<td>P3&lt;0.001*</td>
<td>P4 = 0.161, P5 = 0.672, P6 = 0.731</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>LDL (mg/dl)</td>
<td>32.00–59</td>
<td>39.00–65.00</td>
<td>36.00–145.00</td>
<td>61.00–147.00</td>
<td>17.246</td>
<td>&lt;0.001*</td>
</tr>
<tr>
<td>Mean ± SD</td>
<td>46.57 ± 9.18</td>
<td>53.10 ± 12.68</td>
<td>119.10 ± 23.68</td>
<td>120.47 ± 26.32</td>
<td></td>
<td></td>
</tr>
<tr>
<td>HDL (mg/dl)</td>
<td>25.00–50.00</td>
<td>41.00–48.00</td>
<td>45.00–59.00</td>
<td>47.00–61.00</td>
<td>22.133</td>
<td>&lt;0.001*</td>
</tr>
<tr>
<td>Mean ± SD</td>
<td>40.37 ± 8.68</td>
<td>44.47 ± 1.64</td>
<td>53.83 ± 5.38</td>
<td>55.12 ± 6.31</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Serum ferritin (µg/l)</td>
<td>227–7500</td>
<td>720.00–2001.00</td>
<td>16.00–300</td>
<td>30.03–99.10</td>
<td>44.507</td>
<td>&lt;0.001*</td>
</tr>
<tr>
<td>Mean ± SD</td>
<td>2167.8 ± 1306.9</td>
<td>1486.20 ± 303.04</td>
<td>148.03 ± 108.47</td>
<td>58.65 ± 24.62</td>
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<tr>
<td>Serum creatinine (µmol/l)</td>
<td>0.43–0.90</td>
<td>0.20–1.40</td>
<td>0.23–1.20</td>
<td>0.25–1.10</td>
<td>5.897</td>
<td>0.001*</td>
</tr>
<tr>
<td>Mean ± SD</td>
<td>0.74 ± 0.13</td>
<td>0.71 ± 0.35</td>
<td>0.51 ± 0.27</td>
<td>0.47 ± 0.22</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Blood urea nitrogen (mg/dl)</td>
<td>11.00–24.00</td>
<td>9.00–21.00</td>
<td>11–18</td>
<td>7.00–19.00</td>
<td>14.60</td>
<td>&lt;0.001*</td>
</tr>
<tr>
<td>Mean ± SD</td>
<td>18.13 ± 3.14</td>
<td>15.13 ± 4.42</td>
<td>13.67 ± 2.58</td>
<td>12.23 ± 3.81</td>
<td></td>
<td></td>
</tr>
<tr>
<td>ALT (IU/l)</td>
<td>24.00–78.00</td>
<td>14.00–50.00</td>
<td>13.00–24.00</td>
<td>12.00–35.00</td>
<td>35.125</td>
<td>&lt;0.001*</td>
</tr>
<tr>
<td>Mean ± SD</td>
<td>43.00 ± 9.58</td>
<td>33.20 ± 12.94</td>
<td>19.00 ± 3.66</td>
<td>22.07 ± 8.48</td>
<td></td>
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<tr>
<td>AST (IU/l)</td>
<td>16.00–56.00</td>
<td>18.00–41.00</td>
<td>16.00–32.00</td>
<td>15.00–32.00</td>
<td>8.918</td>
<td>&lt;0.001*</td>
</tr>
<tr>
<td>Mean ± SD</td>
<td>32.73 ± 8.51</td>
<td>28.93 ± 7.85</td>
<td>23.33 ± 6.06</td>
<td>25.27 ± 6.60</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Pentraxin-3 level (ng/ml)</td>
<td>2.30–6.00</td>
<td>2.10–5.81</td>
<td>2.00–5.30</td>
<td>1.40–3.20</td>
<td>16.289</td>
<td>&lt;0.001*</td>
</tr>
<tr>
<td>Mean ± SD</td>
<td>4.32 ± 1.33</td>
<td>4.22 ± 1.45</td>
<td>3.87 ± 1.31</td>
<td>3.97 ± 0.63</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Total antioxidant capacity</td>
<td>1.30–2.50</td>
<td>2.00–3.70</td>
<td>2.34–4.50</td>
<td>4.50–7.90</td>
<td>15.799</td>
<td>&lt;0.001*</td>
</tr>
<tr>
<td>Mean ± SD</td>
<td>2.00 ± 0.38</td>
<td>2.96 ± 0.48</td>
<td>3.20 ± 0.65</td>
<td>6.14 ± 1.09</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Post hoc</td>
<td>P1&lt;0.001*, P2&lt;0.001*</td>
<td>P3&lt;0.001*</td>
<td>P4 = 0.375, P5&lt;0.001*, P6&lt;0.001*</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

ALT, alanine aminotransferase; AST, aspartate aminotransferase; HDL, high-density lipoprotein; LDL, low-density lipoprotein; TG, triglycerides.
P1: β-thalassemia major versus β-thalassemia intermedia.
P2: β-thalassemia major versus β-thalassemia minor.
P3: β-thalassemia major versus control.
P4: β-thalassemia intermedia versus β-thalassemia minor.
P5: β-thalassemia intermedia versus control.
P6: β-thalassemia minor versus control.
*Significant.
with the control group. The current findings disagreed with Amendola et al. [23], who found that TG levels were similar in patients with thalassemia and control group.

In the current study, serum ferritin was significantly higher in patients with \(\beta\)-thalassemia major than intermedia, minor, and control groups. These findings agreed with Hassanin et al. [16] and Al-Hindy et al. [24]. Hassanin et al. [16] reported that thalassemic children had significantly higher serum ferritin levels compared with the controls.

In the current study, serum creatinine, blood urea nitrogen, and ALT were significantly higher in patients with \(\beta\)-thalassemia major than intermedia, minor, and control groups. Serum creatinine, blood urea nitrogen, ALT, and AST were significantly higher in patients with \(\beta\)-thalassemia intermedia than controls. Abdalla et al. [25] reported that there was a significant increase in serum ALT and AST concentrations in patients with \(\beta\)-thalassemia major than controls. Moreover, Attia et al. [26], Saboor et al. [27], and IsikBalci et al. [5] reported significant increase in liver enzymes, ALT, and AST in patients with \(\beta\)-thalassemia major than healthy controls. This may be owing to hepatocellular injury secondary to iron deposition in liver.

Furthermore, Al-Dedah et al. [28] found that the mean creatinine level was significantly higher in \(\beta\)-thalassemia than the controls, indicating renal dysfunction and requiring more advanced analysis. ALT, AST, and urea activities in patients with \(\beta\)-thalassemia are significantly different from controls.

Our study showed that PTX-3 level was higher in all \(\beta\)-thalassemia groups compared with controls, with no difference between each other. Total antioxidant capacity was significantly lower in patients with \(\beta\)-thalassemia major versus \(\beta\)-thalassemia intermedia and minor, though not significantly different between patients with \(\beta\)-thalassemia intermedia and minor. In the same line, the study by IsikBalci et al. [5] found that the lowest total antioxidant capacity values were detected in the thalassemia major group, and the highest was found in the healthy control group. The highest total oxidative stress values were detected in the thalassemia major group, and the lowest were detected in the healthy control group. In terms of PTX-3 values, significant differences were detected between the thalassemia major and minor, major, and control groups and between thalassemia minor and control

### Table 4. Cutoff level of pentraxin-3 and total antioxidant capacity for detection of risky oxidative stress in patients with \(\beta\)-thalassemia in relation to serum ferritin.

<table>
<thead>
<tr>
<th>Variables</th>
<th>AUC</th>
<th>SE</th>
<th>Significance</th>
<th>Cutoff</th>
<th>Sensitivity (%)</th>
<th>Specificity (%)</th>
<th>95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pentraxin-3 (oxidant stress)</td>
<td>0.846</td>
<td>0.039</td>
<td>&lt;0.001*</td>
<td>2.15 ng/ml</td>
<td>93.3</td>
<td>63.3</td>
<td>0.769–0.923</td>
</tr>
<tr>
<td>Total antioxidant capacity</td>
<td>0.695</td>
<td>0.065</td>
<td>&lt;0.001*</td>
<td>2.11 nmol/well</td>
<td>86.5</td>
<td>71.5</td>
<td>0.481–0.737</td>
</tr>
</tbody>
</table>

AUC, area under the curve; CI, confidence interval.

*Significant.

Fig. 1. ROC curve analysis of pentraxin-3 level in prediction of oxidative stress in patients with \(\beta\)-thalassemia among patient groups. ROC, receiver operating characteristic.

Fig. 2. ROC curve analysis of TAC level in prediction of oxidative stress in patients with \(\beta\)-thalassemia among patient groups. ROC, receiver operating characteristic; TAC, total antioxidant capacity.
group. Another study by Doni et al. [29] suggested that PTX-3, as one of the markers of vascular endothelial damage, increases in response to oxidative stress, which can be used as an early diagnostic marker for inflammation. Fazzini et al. [30] found that PTX-3 value to be higher in the thalassemia minor group than in the thalassemia major group. These findings are in the same line with IsikBalci et al. [5]. Another study by Doni et al. [29] suggested PTX-3, as one of the markers of vascular endothelial damage, increases in response to the oxidative stress, which can be used as an early diagnostic marker for inflammation.

Our study showed that the best sensitivity and specificity for PTX-3 were 93.3 and 63.3%, respectively, at a cutoff level of 2.15 ng/ml. Moreover, the best sensitivity and specificity for total antioxidant capacity were 86.5 and 71.5%, respectively, at a cutoff level of 2.11 nmol/well in relation to serum ferritin for detection of risky oxidative stress in patients with β-thalassemia. These findings were in line with Fazzini et al. [30], IsikBalci et al. [5], and Mohammed and Abd-El Rasoul [31]. Fazzini et al. [30] reported that PTX-3 showed sensitivity of 98.20% and specificity of 91.43% at a cutoff point of more than 3.10 and total antioxidant capacity level showed sensitivity of 100%, specificity of 88.57%, and AUC of 98.4% at a cutoff less than or equal to 1.2 mmol/l in patients with β-thalassemia. Another study by IsikBalci et al. [5] revealed that the cutoff point for PTX-3 was more than 2.24 with sensitivity of 91.43% and specificity of 97.14% in patients with β-thalassemia. Additionally, the study by Mohammed and Abd-El Rasoul [31] found that the best cutoff point for PTX-3 was found to be more than 3.87 with sensitivity of 100%, specificity of 100%, and AUC of 100%. Moreover, the best cutoff point for ACT was found to be more than 1.8 with sensitivity of 100%, specificity of 85.71%, and AUC of 96.3%. Furthermore, the study by Dominguez-Vivero et al. [32] found that the cutoff point of 832.5 pg/ml of PTX-3 produced the optimal sensitivity and specificity of 83 and 85%, respectively (P < 0.001) in patients with β-thalassemia.

4.1. Conclusions

PTX-3 level was higher in all β-thalassemia groups compared with controls. The total antioxidant capacity was significantly lower in all β-thalassemia groups compared with controls. It was significantly lower in patients with β-thalassemia major versus β-thalassemia intermedia and minor, though not significantly different between patients with β-thalassemia intermedia and minor. The best sensitivity and specificity for PTX-3 were 93.3 and 63.3% at a cutoff level of 2.15 ng/ml with AUC of 0.846. Moreover, the best sensitivity and specificity for total antioxidant capacity were 86.5 and 71.5% at a cutoff level of 2.11 nmol/well with AUC of 0.695 in relation to serum ferritin for detection of risky oxidative stress in patients with β-thalassemia.

Conflict of interest

There are no conflicts of interest.

References


