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SOLUBLE TRANSFERRIN RECEPTOR-FERRITIN INDEX IN THE DIAGNOSIS OF ANEMIA OF CHRONIC DISEASE IN PATIENTS WITH DIABETES

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ABSTRACT

The aim of the present research is to investigate the efficiency of sTfR, ferritin and the ratio sTfR/log ferritin (sTfR-ferritin index) in the diagnosis of anemia of chronic disease (ACD) in patients with diabetes mellitus and healthy controls. The patients' blood samples were taken from the University Hospital of the Medical University – Plovdiv. The serum levels of sTfR and ferritin were determined with commercially available ELISA kits. The measurements of sTfR and ferritin are reliable markers of iron deficiency anemia (IDA) and the calculation of the ratio sTfR/log ferritin can be used also to evaluate ACD. In diabetic patients sTfR is 0.866 (0.694 ÷ 1.201) and in healthy controls is 0.781 (0.585 ÷ 0.914), ($p = 0.017$) while ferritin is 125.76 (16.2 ÷ 358.85) and 31.21 (17.9 ÷ 54.2), ($p = 0.014$) respectively. The sTfR-ferritin index in diabetic patients is 0.423 (0.275 ÷ 0.638) and in the healthy controls it is 0.499 (0.378 ÷ 0.602), ($p = 0.222$). The same parameters are investigated separating the patients according to the CRP level. In the group with increased CRP (>8) the concentration of ferritin is significantly higher ($p = 0.03$). In this group the sTfR-ferritin index is with 27 % higher than the group with normal CRP (≤8). In contrast to rheumatoid arthritis occuring with acute inflammation where this index can be used for parameter confirming IDA, in diabetes we didn't find significant difference between the group with normal and increased CRP. Possible explanation of this fact is the low inflammation activity in diabetes where the determination of sTfR is more informative as a parameter for pure iron deficiency.

Key words: anemia of chronic disease, sTfR, ferritin, sTfR/log ferritin, diabetes, CRP

INTRODUCTION

Iron deficiency anemia can be caused both by decreased dietary intake or by iron malabsorption (1). Ferritin and sTfR are reliable and used markers for evaluation of iron deficiency. sTfR is a truncated form of the tissue receptor and exists as a transferrin – receptor complex (1, 2). Increased synthesis of TfR reflects iron requirement and iron depletion results in its induction. Insulin is known to cause a rapid iron uptake by fat cells, redistributing TfRs from the intracellular environment to the cell surface (1, 2). Insulin also stimulates the liver iron transport and accumulation that results in increased ferritin biosynthesis (3). The synthesis of ferritin and TfR is regulated reciprocally at posttranscriptional level according to the cellular iron status (4). The levels of sTfR are proportional to: the cellular iron status, the cellular expression of the membrane TfR and the concentration of sTfR is related to cellular iron demands – the higher ferritin level, the lower is the sTfR concentration (2, 4, 5). Iron plays a significant role in the development of diabetes and its complications (6).

The purpose of the present research is to evaluate the efficiency the efficiency of sTfR,

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ferritin and the ratio sTfR/log Ferritin (sTfR-Ferritin Index) in the diagnosis of ACD in patients with diabetes referred to control group.

METHODS

The study involved 81 patients with diabetes from the Clinic of Endocrinology, Medical University-Plovdiv and 41 healty controls. The mean age of the patients is 58.6 ± 14.7 years and the mean duration of diabetes was 12.8 ± 9.6 years.

The parameters of iron homeostasis s TfR and serum ferritin were determined with ELISA kits (Bio Vendor Research and Diagnostic Products, Czech Republic, Minias Globe Diagnostics Srl, Italy). Statistical analysis was performed using SPSS version 17. Data were presented as madian (25^{th} to 75^{th} percentile), because variables are not normally distributed. $p < 0.05$ was accepted as statistically significant level.

RESULTS

The medians of ferritin 125.8 (16.2 – 358.9) and of sTfR 0.866 (0.694 – 1.201)of the patients were significantly different from that of the control group , p=0.014 . p=0.017 **(Table 1).** There is no significant difference in sTfR–ferritin index between the two groups. In diabetic patients compared with the control group we found higher levels of ferritin and sTfR and lower sTfR–ferritin index. Mojiminiyi et al (6) report that similar results are associated with some of the complications of type 2 diabetes mellitus. Diabetic individuals showed tendency toward increased sTfR (0.866 vs 0.781, p=0.017) since sTfRs colocalize with insulin-responsive glucose transporters in cultured adipocytes, suggesting that regulation of iron uptake by insulin paralles its effects on glucose transport (2). Probably the increase of sTfR is due to lower insulin sensitivity.

Table 1. *Iron homeostasis parameters in patients with diabetes and healthy controls.*

Variable	Diabetes	Healthy controls	p
Ferritin	n = 80 125.8 (16.2 – 358.9)	n = 41 31.2 (17.9 – 54.2)	0.014
sTfR	n = 81 0.866 (0.694 – 1.201)	n = 41 0.781 (0.585 – 0.914)	0.017
sTfR/ log Ferritin	n = 79 0.423 (0.275 – 0.638)	n = 41 0.499 (0.378 – 0.602)	0.222

The same parameters are investigated separating the patients according to the CRP level. In the group with increased CRP the concentration of serum ferritin is significantly higher (p = 0.03) . There is no significant difference of sTfR and sTfR/log Ferritin index **(Table 2)**.

Table 2. *Iron homeostasis parameters in patients with diabetes grouped according to the CRP level.*

Variable	CRP ≤ 8 μg/ml	CRP > 8 μg/ml	p
Ferritin	n = 49 83.9 (9.4 – 355.1)	n = 13 350.1 (157.4 – 390.1)	0.030
sTfR	n = 49 0.775 (0.623 – 1.158)	n = 13 1.080 (0.881 – 1.322)	0.087
sTfR/log Ferritin	n = 49 0.353 (0.252-0.692)	n = 13 0.482 (0.350-0.839)	0.373

CONCLUSIONS Our results showed that in the low inflammation activity in diabetes the determination of sTfR is more informative as a parameter for pure iron deficiency.

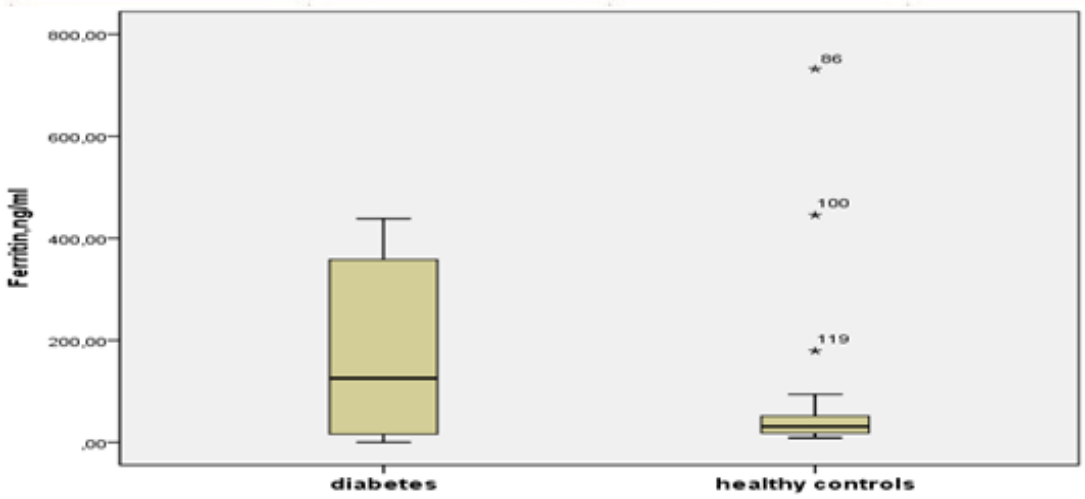

Figure 1. Serum ferritin concentration in patients with diabetes and healthy controls.

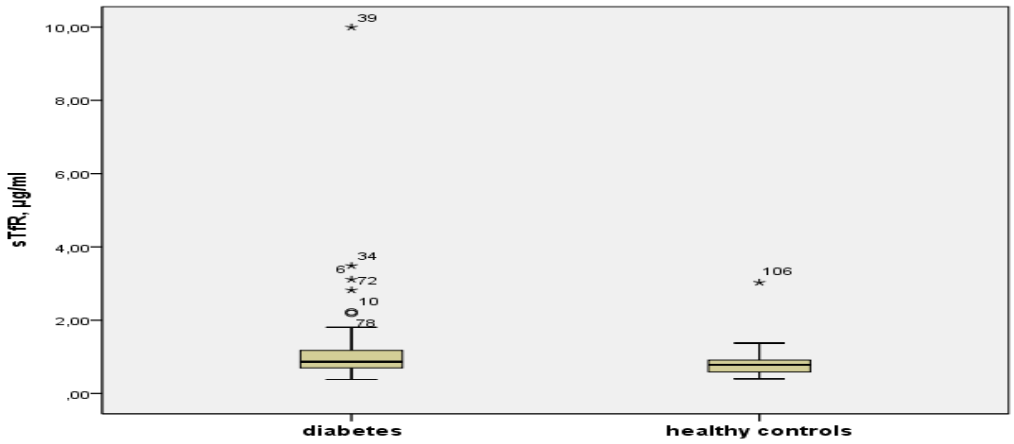

Figure 2. s TfR concentration in patients with diabetes and healthy controls.

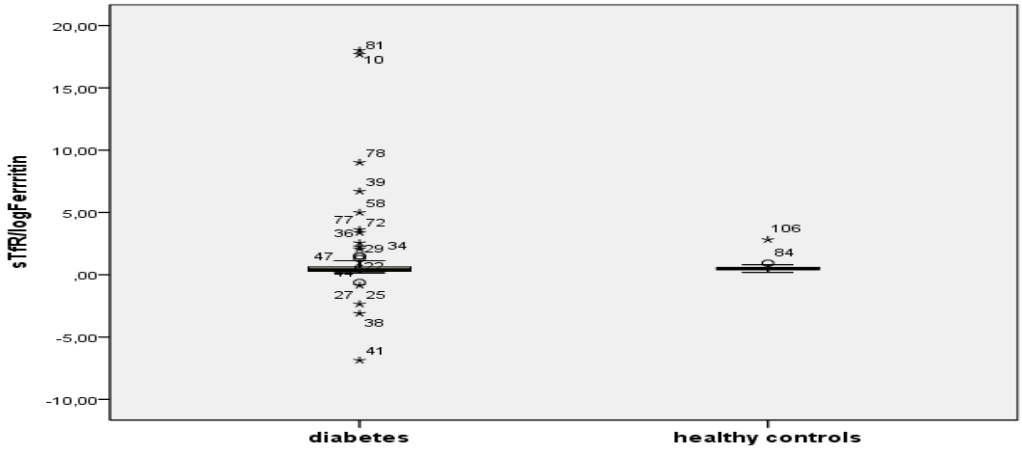

Figure 3. The sTfR/log ferritin ratio (sTfR-ferritin index) in patients with diabetes and healthy controls.

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