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STUDY ON THE VARIATION OF FERRITIN CONCENTRATION IN PATIENTS TESTED FOR HEALTH ASSESSMENT

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Key words: *ferritin, transferrin, hemosiderin, TIBC (total iron binding capacity), sideremia, reticuloendothelial system, hemochromatosis, iron deficiency anemia*

INTRODUCTION

Intracellular iron is stored in the form of ferritin and hemosiderin. Apoferitin (iron free ferritin) has weight of 440 kD, the shape of hollow sphere with a central cavity of 6 nm, where iron is stored. This cavity communicates with the outside through six channels (through these channels the iron enters and leaves). Iron enters the molecule in the form of Fe^{2+} and is oxidized under the catalytic action of apoferritin. It is stored in the form of trivalent ferric phosphate hydroxide polymer. The protein coat protects the cell from the toxic effects of iron ions. Apoferritin synthesis is stimulated by iron exposure.

Ferritin is found in the blood (it is glycosylated, suggesting secretion by phagocytes) in small amounts and its concentration correlates with iron stores. Ferritin is a complex globular protein containing 24 protein subunits, forming a nanocage with multiple metal-protein interactions. It is the main storage depot of iron in both eukaryotes and prokaryotes, keeps Fe in soluble and non-toxic form, releases it in a controlled manner. Protein is produced by almost all living organisms, including bacteria, algae, higher plants and animals. In humans, it acts as a buffer against iron deficiency or overload. It is found in most tissues as the ctosolic protein, but small amounts are secreted into the serum, where it functions as an Fe transporter.

Plasma ferritin is also an indirect marker of the total amount of Fe in the body and its determination is used as a test for iron deficiency anemia. It serves to store Fe in non-toxic forms, store it in safe forms and transport it to areas where it is needed. Function and structure vary in different cell types. These are controlled by the amount and stability of messenger RNA. The presence of Fe is a major trigger of ferritin production. Free Fe is toxic to cells, acts as a catalyst and forms free radicals from reactive oxygen species via the Fenton reaction pathway. Vertebrates develop an elaborate set of protective mechanisms by sequestering Fe in different tissue compartments. Intracellular Fe is stored in complex proteins such as ferritin and hemosiderin. As ferritin accumulates inside the cell, protein aggregates in the reticuloendothelial system form hemosiderin.

The concentration of ferritin increases spectacularly in infections or cancer. Endotoxins are a regulator of the gene that codes for ferritin, producing excess ferritin. Fe is retained by the infecting agent which prevents its metabolism.

Ferritin level correlates with Fe stored in the body. However, the level may be artificially elevated in cases of anemia, in chronic diseases, where ferritin is elevated by the capacity of the acute phase reactant protein and not as a marker for iron loading.

MATERIAL AND METHODS

The study was carried out on a number of 128 patients, who requested analyzes in a specialized outpatient clinic at the recommendation of the family doctor. The following determinations were made for these subjects: biochemistry, HLG, ESR, coagulation times, immunology (ferritin, thyroid hormones, FR, CRP, ASLO, serology: VDRL, HBV, HCV, HIV, etc.).

The principle of the determination methods was: spectrophotometry for biochemical determinations, hemogram on the automatic analyzer, coagulometry, agglutination, immunochromatography and chemiluminescence for the determination of ferritin, hormones. The obtained data were analyzed and correlated with the diagnosis.

RESULTS AND DISCUSSION

The study was conducted over a period of two months and 128 subjects were investigated: 85 women (66%) and 43 men (34%), aged between 11 and 90 years. (Fig. 1).

As can be seen, the number of investigated female patients is almost double that of male patients. The breakdown by age group of the investigated patients was as follows (fig. 2).

Analyzing the figure, the age group with the largest number of investigated patients was the 51-60 years group, followed by 81-90. Following the determinations, the average values were calculated for: ferritin, sideremia, hemoglobin, average

erythrocyte volume (MCV), average erythrocyte hemoglobin (MCH), platelets (PLT).

Analyzing the data in the table and in the last figure, it is observed that for each age group, the average values for the determined analytes were within the reference range. For platelets, the highest average values were recorded in the age group 11-20 years, and the lowest values in the age group 81-90 years, in this group the average value of hemoglobin was the lowest, a confirmed fact and the data from the specialized literature according to which, with advancing age, the risk of the appearance of certain pathologies increases.

From the total of 128 analyzed subjects, 61 presented values, for certain analytes, outside the reference range (fig. 4).

Low values for ferritin were presented by 34 patients aged between 11 and 87 years (Table 2).

Fig. 1. Distribution of investigated patients by gender

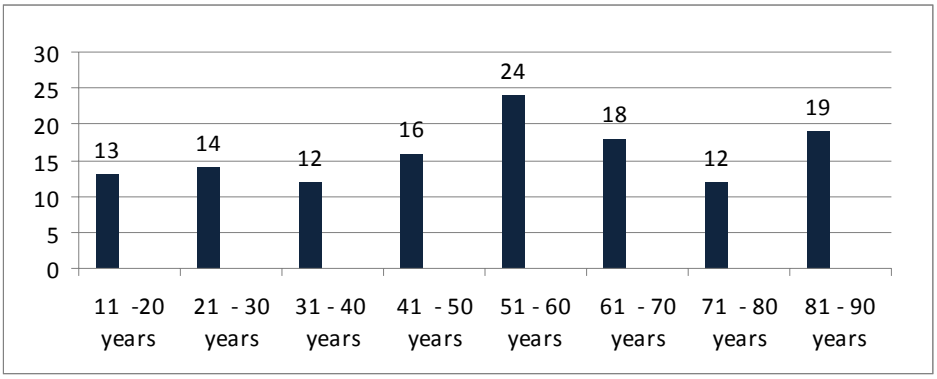

Fig. 2. Distribution of investigated patients by age group

Table 1. Mean values for iron (Fe), ferritin (Feri), hemoglobin (Hgb), mean erythrocyte volume (MCM), mean erythrocyte hemoglobin (MCH), platelets (PLT)

Age (ani)	**Fe** (37-145fg/dl)	**Feri** (F: 15-232; B: 125-350 ng/mL)	**Hgb** (B: 12,6-17,4; F: 11,7-16 g/dl)	**MCV** (81-101 fl)	**MCH** (27-35)	**PLT** (150-350 x 10^3)
11-20	77.53	60.05	13.83	83.72	28.96	316.12
21-30	76.97	52.58	13.82	86.20	30.10	205.36
31-40	89.69	56.13	13.98	86.65	30.65	235.84
41-50	79.99	73.60	14.07	86.22	29.86	247.37
51-60	78.56	100.48	13.45	87.72	30.44	242.19
61-70	76.20	126.9	13.42	88.33	27.92	229.20
71-80	61.63	95.78	12.81	83.54	28.57	198.22
81-90	57.79	159.44	12.42	86.72	29.25	186.31

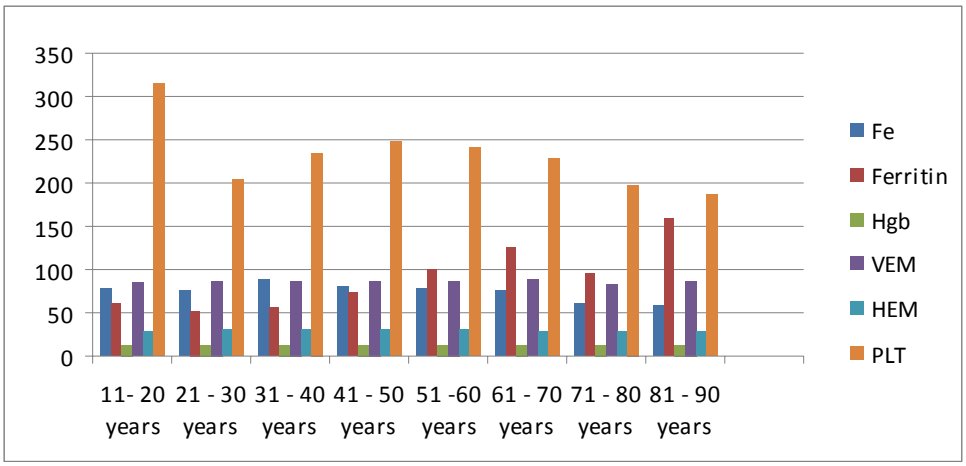

Fig. 3. Average values of investigated analytes of patients distributed by age groups

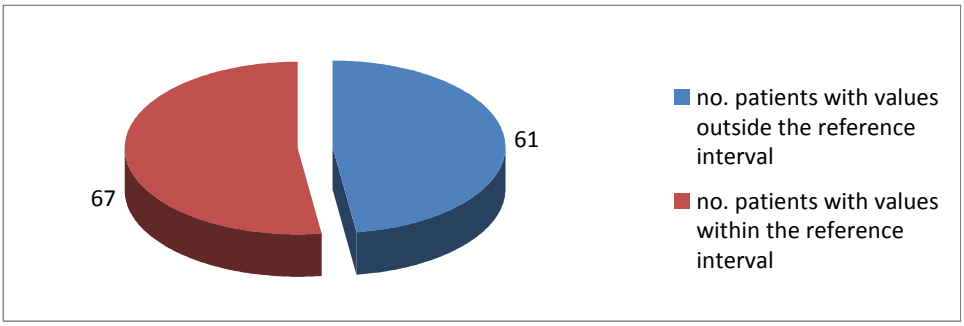

Fig. 4. Distribution of patients according to analyte values

Table 2. Patients with low values for ferritin

No	Sex	Age	**Ferit**	**Fe**	**Hgb**	**MCV**	**MCH**	**PLT**	Obs.
1.	F	79	15.93	51.32	12.9	77.6	26.7	214	AcU↑, Crea↑, Col↑.
2.	F	17	4.59	20.0	10.4	76.4	26.1	312	VSH 60; Fibr 768↑; fT4 8.092↓; TSH 5.847↑.
3.	F	53	20.68	40.38	12.4	84.4	29.6	246	Crea↑,ATPO↑, Fibr si proteine↓
4.	F	39	4.52	37.8	11.5	77.6	25.6	202	VSH 25;ATPO 830↑
5.	B	54	18.2	33.02	12.7	80.7	26.3	256	RDW-CV 16.4↑
6.	F	26	15.11	42.36	13.1	89.1	31.3	247	
7.	F	17	16.48	38.95	12.7	84.5	31.7	255	ATPO168↑
8.	F	16	10.54	40.23	12.5	81.1	28.6	244	Limf↑;Monoc↑;TSH9.49↑
9.	F	11	6.49	31.8	11.9	67.2	21.2	674	Leuc↑; Limf↑; VSH↑; AST↑; ATPO↑; C3↑
10.	F	35	15.56	36.20	12.1	81.2	27.1	318	Leuc↑; VSH↑;Fibr↑; AcU↑; GGT↑
11.	F	87	20.24	18.96	9.1	76.6	25.2	239	Mg↓; Proteine↓Uree↑; fT4↓(8.85); TSH ↑(12.74)
12.	F	46	8.94	21.54	10.2	68.7	20.9	193	Leuc↓; Neutr↓; Limf↓; Fibr↓; Timp protr↑; Col↑
13.	F	34	8.44	37.21	10.4	88.4	27.6	207	VSH↑; TSH↑ (11.28)
14.	F	80	5.59	37.23	10.1	78.2	26.6	229	
15.	B	76	23.88	40.08	10.7	83.6	26.4	117	TSH 22.97↑
16.	B	82	11.05	26.93	11.1	71.7	22.4	319	VSH 48; Fibr 953; ATPO 390; DBil 0.68
	13F; 3B.		12.89	34.63	11.49	79.19	26.46	251.75	

According to data from the specialized literature, the low level of ferritin indicates a severe protein deficiency, iron deficiency anemia, hemodialysis, malnutrition. Sideremia is low in iron-deficient anemias, in normochromic anemias from infections and chronic diseases, in nephrotic syndrome (due to urinary loss of iron-binding protein).

From the analysis of the obtained data, a greater number of female patients with low ferritin values (15-232 ng/mL) is found compared to male patients (25-350 ng/mL). By correlating the values obtained for ferritin with sideremia and hemogram,

we deduce that from the total of 61 subjects with certain values of the investigated analytes outside the reference range, 16 of the investigated subjects have iron deficiency anemia (fig 6)

Regarding the Hemoleucogram and Erythrocyte Indices (table 2): the low level of hemoglobin and hematocrit confirms anemia, as does the average erythrocyte hemoglobin, and the average erythrocyte volume falls below 80 fl in erythrocyte anemia, iron deficiency anemia, anemia of chronic diseases. More precisely, MCV □ 80 fl indicates iron deficiency anemia, having as causes: inadequate intake, reduced absorption, increased iron needs, anemia from chronic diseases.

Elevated values for ferritin (over 232 ng/mL) were obtained for 17 patients.

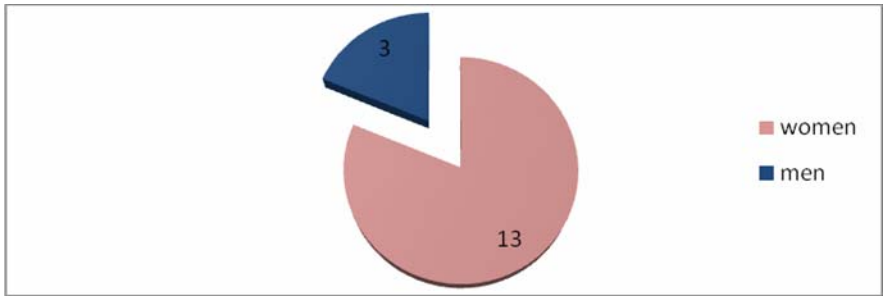

Fig. 5. Distribution of patients with low ferritin values by gender

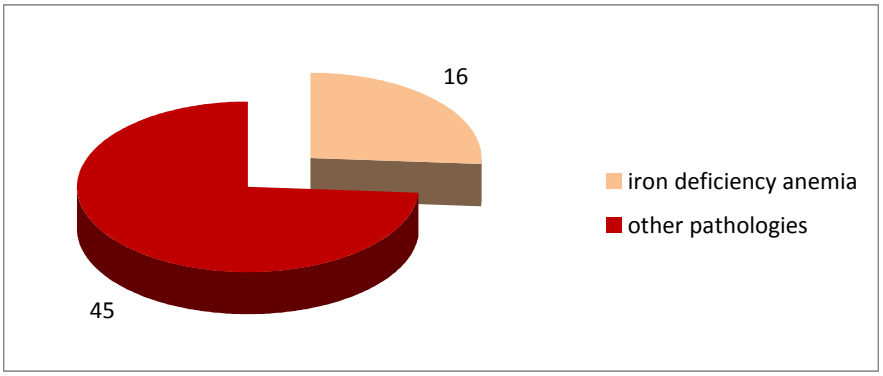

Fig. 6. Incidence of patients with iron deficiency anemia

Table 3. Patients with elevated values for ferritin

No	Sex	Age	**Ferit**	**Fe**	**Hgb**	**MCV**	**MCH**	**PLT**	Obs.
1.	B	63	431.4	166	17.8	89.4	31.6	183	TBil1.36↑; ATPO328↑; fPSA0.65; PSA5.2↑
2.	B	82	351.6	96.7	14.1	83.9	29.7	164	RDW-CV16.1↑; ALP180.7↑; Alb.46.6↓; γ 24.6; Fibr 640↑.
3.	B	78	242.2	50.5	15.0	81.9	29.4	153	Fibr. 712; ALP 134↑
4.	B	83	279.9	103	15.1	89.2	31.5	171	
5.	B	18	387.7	99.9	14.6	86.7	29.6	208	Monoc. 8.5↑
6.	F	81	318	98	12.4	93.3	30.7	181	AcU 7.2; Crea 1.16; Uree 67.9
7.	B	43	287.8	67.2	15.7	87.1	30.5	250	ALT71;CRP12;Ferit/ALT=4.05
8.	B	60	**1423**	60.5	10.2	92.8	31.9	157	RDW-CV 18.1↑; RDW-SD 66.7↑;
9.	F	89	315.4	42.4	13.8	86.1	28.1	192	Fbrinog 682↑;
10.	B	64	335.8	25.3	9.7	86.1	28.7	226	VSH 52; Timp protr. 25.18↑;α2 14.9↑;
11.	B	33	260.2	116	15.0	88.1	34.1	182	ALT 52; Ferit/ALT=5
12.	B	66	410.9	64.1	14.3	85.5	28.7	212	Fibrinog 698↑;
13.	F	82	259.3	53	13.0	92.5	30.4	209	
14.	F	78	268.5	52.5	14.2	88.5	29.3	176	VSH 49; Fibrinog 1000.5; α2 14.9↑;
15.	F	68	439.7	69.7	12.7	87.3	29.6	201	GLU 168; γ 22.7↑;
16.	B	45	399.9	71.5	15.6	84.4	28.7	210	
17.	F	68	447.5	78	13.1	85.7	28.1	197	GLU 152; γ 24.3↑.
		VM	403.5	74.3	13.9	87.6	30.0	193	

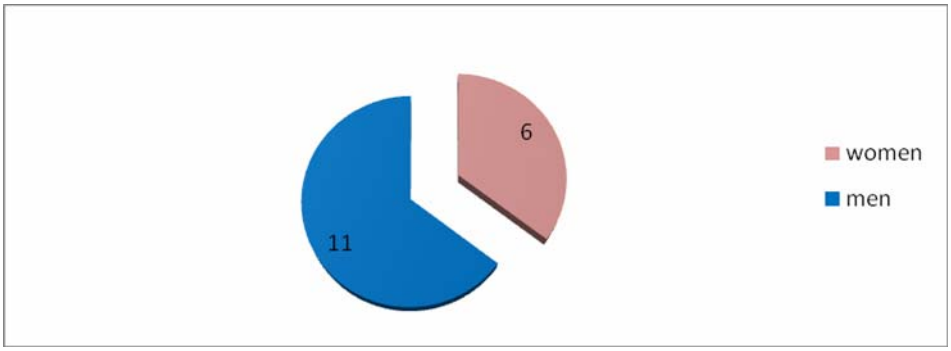

Fig. 7. Distribution of patients with elevated ferritin values by gender

Analyzing the figure above, it can be seen that the proportion of patients with elevated ferritin values was in male patients. From the analysis of the values of the other investigated analytes in patients with elevated ferritin values (table 3), corroboration with other medical investigations is necessary to support the presumptive diagnosis.

According to data from the specialized literature, ferritin is an acute phase reactant, being increased in many patients with various acute and chronic liver diseases, alcoholism, neoplasia, infections and inflammations, hyperthyroidism, myocardial infarction, Gaucher disease. When iron deficiency coexists with one of these conditions, ferritin may not be low. Iron overload (hemosiderosis, idiopathic hemochromatosis) can significantly increase ferritin. In this situation, transferrin saturation is more sensitive for early detection of iron overload.

The ratio of serum ferritin (ng/mL) to ALT (U/L) is ≥ 10 in patients with thalassemia and Fe overload, but the mean is ≥ 2 in those with viral hepatitis. The ratio decreases with successful iron chelator therapy.

Chronic inflammations, such as inflammatory bowel disease, collagenoses, but also iron deficiency anemia can lead to an increase in the number of platelets.

MCV (mean erythrocyte volume) showed values within the reference range for all subjects who had an elevated ferritin concentration.

CONCLUSIONS

Serum ferritin is a useful analyte in the diagnosis of iron deficiency or excess and correlates with total body Fe stores. It is the main iron storage protein in the body.

Determination of ferritin is required in the following situations: prediction and monitoring of iron deficiency; determining response to Fe therapy or compliance to treatment; differentiation of iron deficiency anemia from anemia of chronic diseases; discovery of iron overload.

It is an acute phase reactant, and the various acute or chronic conditions, infections and inflammations are confirmed, in the case of this work, by the increased values for other analytes such as: VSH, fibrinogen, PCR, etc.

ABSTRACT

The serum level of ferritin, the protein synthesized in the spleen, bone marrow, liver, correlates with the body's iron deposits and total iron binding capacity (TIBC). Moreover, the blood concentration of ferritin is more sensitive and specific than sideremia and TIBC.

Ferritin is an acute phase reagent, being increased in patients with acute or chronic liver disease, kidney disease, alcoholism, neoplasm, hyperthyroidism, infections and inflammation.

The determination and correlation of the values obtained for ferritin with HLG, ESR, sideremia and other acute phase reactants (fibrinogen, C-Reactive Protein), allow the correct establishment of the diagnosis and an adequate treatment.

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