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SOME BIOCHEMICAL PARAMETERS VALUES ON THALASSEMIA INDIVIDUALS

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Key words: Cooley's anemia, beta thalassemia, beta thalassemia major, splenomegaly, blood disorder, hemoglobin disorder, blood disease.

Abstract: In our study resulted that Cooley's anemia is more frequent with female subjects and most of them are 30-35 years old. Anemia is severe, with very low hemoglobin values and a decrease in the number of erythrocytes.

INTRODUCTION

The severe anemia occurred early in individual's life, associated with the splenomegaly and bone changes, was described by Cooley and Lee in 1925. Whipple and Bradford in 1932 named that form of anemia thalassemia because early patients were all of Mediterranean background. It was only in the period after 1940 that the true genetic character of this disorder was fully appreciated. It became clear that the disease described by Cooley was the homozygous state for an autosomal gene, while the heterozygous state was associated with much milder hematologic changes. The severely affected homozygous condition became known as thalassemia major, while the heterozygous state, according to their severity, were designated thalassemia minor or minima. Since 1950 it has been established that thalassemia is not a single disease but a group of disorders which result from an inherited abnormality of globin production and are therefore classifiable as hemoglobinopathies. It is now clear that inherited hemoglobinopathies are of two types. First, there are those, like sickle-cell anemia, which result from an inherited structural abnormality in one of the constituent globin chains. Disorders in the second major group of inherited abnormalities of hemoglobin synthesis, the thalassemias, result from inherited defects in the rate of synthesis of one of the globin chains.

THE PURPOSE OF THE INVESTIGATIONS

In this paper we proposed the evaluation of some biochemical and hematological parameters values on individuals with Cooley's anemia from Neamţ County.

MATERIAL AND METHODS

Our research took place at the Clinical Laboratory of Neamţ County Hospital from Piatra Neamţ. We studied 11 individuals with Cooley's anemia (5 men and 6 women). The subjects were part of two groups of age: 30-35 years old and 35-40 years old.

To establish the diagnosis we took blood samples and performed laboratory investigations (erythrocytes, thrombocytes and leucocytes counting, leucocytes formula, the peripheral blood swab examination, the haemoglobin dosage in blood) (Drabkin method), the immunoglobulin determination using the Mancini, Carbonara, Heremans method and the dosage of fibrinogen using the Weichselbaum method.

RESULTS AND DISCUSSIONS

Examination of the blood reveals severe anemia with hypochromic and microcytic erythrocytes. The reticulocyte count is only moderately elevated. The stained blood film reveals extreme variations in size and shape of cells, with many teardrop, oval, target, stippled and bizzare forms. The cells are very poorly and irregularly filled with hemoglobin so that only a thin rim of hemoglobin may be seen. The predominant picture is hypochromicity in bizzarely shaped microcytes. The leukocyte count is frequently slightly elevated; the platelet count is within normal limits.

The peripheral blood smear was typical, suggesting the diagnosis from the first investigations. The hypochromatism was high and accompanied by a high level of anisopoikilocytosis. The smears we analyzed particularly contained numerous target cells, frequent red cells in drops and ovalocytes, together with a large number of shapeless red cells and schizocytes in different shapes and sizes. The target cells with folded borders have a "Mexican hat" appearance and sometimes are macromegalocytic (12-15¼□. When hemoglobin is very low, some red cells seem content-free and have the appearance of "erythrocytic shadows". Red cells with Cabot's ring, Jolly's bodies and basophilic points are frequent. The erythrooblast presence is constant (5-20/100 leucocytes), their number being several times bigger than the number of leucocytes in case of splenectomy (300-500/100 leucocytes). The high polychromatophilia on the smear reflects a high reticulocytosis (5-15%) and is in accordance with the specialized literature data (Berceanu, 1977).

The studied subjects manifested anisocytosis, with frequent microcytes, hypochromia (ovulocytes, target cells), external poikilocytosis (numerous red cells in drops, schizocytes, elliptocytes). The patients manifested fatigability, tegument paleness, sore left and right hypochondrium.

Hemoglobin values of female patients with Cooley's anemia (fig. 1) ranged between 6.68%-6.73 g %. With male patients the values were between 6.75-6.97 g % (fig. 2). With both sexes, hemoglobin is very low. Specialized literature claims that hemoglobin values are between 5 and 7 g/dl blood (sometimes lower, even 2 g/dl), with an adequate reduction of the erythrocyte number and the hematocrit. The HEM and CHEM erythrocyte constants are below normal, in accordance with the hemoglobin deficit of the erythrocytes. However, VEM is variable, in accordance with the folic acid deficiency and secondary macrocytosis.

If we analyze the distribution of people suffering from major target-cell anemia on age groups, we notice that their number is between 2 and 3 in the case of male patients, and 3 in that of female patients.

Erythrocyte values range between 3266666-3633333/mm3 in the case of female patients (fig. 3) and between 4150000-4200000 (fig. 4) in that of male patients. Thus,

there can be noticed a reduction in the number of erythrocytes in the case of all patients suffering from Cooley's anemia.

The number of thrombocytes ranges between 260000-280000/mm3 in the case of female patients (fig. 5) and between 240000-285000 (fig. 6) in the case of male patients we analyzed. With both sexes the values are within normal limits.

Specialized literature claims that moderate leucocytosis is constant in major target-cell anemia (10000-20000/mm3) frequently accompanied by the deviation of the leucocytes formula. Leucocytes count points out pseudo-leukemic values (30000-35000/mm3). In fact, these figures also include, beside the number of leucocytes, the large number of erythroblasts. Erythroblasts from peripheral blood always have as their origin extramedullar erythropoiesis foci. Most of the patients also have slightly larger number of thrombocytes. Easy cases usually have a normal number of leucocytes and thrombocytes, or a number situated at the upper limit of normality.

When analyzing the leucocytes formula of female patients suffering from Cooley's anemia, one can notice that leucocytes range between 15000-20000/mm3 (fig. 7). Non-segmented neutrophils (2%) and eosinophils (1%) have lower values than normal (3% and 2.7% respectively). The percentage of segmented neutrophils (53%) and monocytes (3%) undergo changes, being below normal (57% and 5% respectively). The lymphocyte percentage of 41% (fig. 8) exceeds normal values.

In the case of male patients with Cooley's anemia, the leucocytes formula is the following: leucocytes range between 13333-18000/mm3 (fig. 9). Non-segmented neutrophils (2%), eosinophils (1%), segmented neutrophils (50%) as well as monocytes (3%) are present in lower percentages than normal values. Lymphocytes (43%) exceed the normal percentage (33%) (fig. 10). The quantity of fibrinogen is low with female patients (0.17-0.20g%) (fig. 11) as well as with male patients (0.1-0.2g%) (fig. 12).

Immunoglobulin in the blood of female and male patients with Cooley's anemia has the following values: 1000-1600 mg% (female patients) and 1100-1400 mg% (male patients) of IgG. In both cases the values are normal (800-1600 mg%).

In both cases, the quantity of IgA is at the lower normal limit (100-360mg%), being of 106-112 mg% with women and 110-115mg% with men.

IgM values exceed, in both cases, the upper normal limit (84-170mg%), ranging between 384-680mg% with female patients and 362-780mg% with male patients.

Hetterozygote β target-cell anemia leads to an increase of the percentage of A2 and/or F hemoglobin. Most cases of heterozygote target-cell anemia (about 90%) have high levels of A2 hemoglobin, normally ranging between 4-6%. About 50% of heterozygote β target-cell anemia with high A2 hemoglobin cases also have slightly higher values of F hemoglobin, determined with an alkali tolerance test.

Cases of heterozygote β target-cell anemia presenting only higher levels of HbF are more unusual (about 10% of heterozygotes in our population), the HbF level being between 2-30%, while normal values are between 5-15%. In these cases, HbA2 is normal or low, the rest of hemoglobin being represented by HbA. These cases must be distinguished from physiological and pathological cases when also present high HbF values.

CONCLUSIONS

Cooley's anemia or major beta thalassemia is characterized by the total blocking of the beta globin chains.

In our study resulted that Cooley's anemia is more frequent with female subjects.

Most of the subjects are 30-35 years old.

Peripheral blood swab is typical and suggests a diagnosis from the first investigations.

Anemia is severe, with very low hemoglobin values and a decrease in the number of erythrocytes.

The number of thrombocytes is normal but the leucocytes count shows pseudoleukemic values.

Fibrinogen values are low. G and A immunoglobins are within normal values, with the exception of IgM which has very high values.

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Table 1

Hemoglobin concentration in female patients blood with Cooley's anemia

Biochemical parameter	Normal (g%)	Statistical values			
		Pathological(g%)			
		30 - 35 years old		35 – 40 years old	
		x± Es	CV%	x ± Es	CV %
Hemoglobin	**12-16**	**6,73 ± 0,321**	**4,76**	**6,68 ± 0,160**	**2,39**

Table 2

Hemoglobin concentration in male patients blood with Cooley's anemia

Biochemical parameter	Normal (g%)	Statistical values			
		Pathological (g%)			
		30 - 35 years old		35 – 40 years old	
		x± Es	CV%	x ± Es	CV%
Hemoglobin	**13-17**	**6,97 ± 0,152**	**2,18**	**6,75 ± 0,070**	**1,03**

Table 3

Erythrocytes number (n) in female patients blood with Cooley's anemia

Cells type	Normal (n/mm^3)	Statistical values			
		Pathological (n/mm^3)			
		30 - 35 years old		35 – 40 years old	
		x± Es	CV%	x ± Es	CV%
Erythrocytes	**4500000**	**3266666,67 ± 305505,05**	**9,35**	**3633333,33 ± 208166,6**	**5,72**

Table 4

Erythrocytes number (n) in male patients blood with Cooley's anemia

Cells type	Statistical values				
	Normal (n/mm^3)	Pathological (n/mm^3)			
		30 - 35 years old		35 – 40 years old	
		x±Es	CV%	x ±Es	CV%
Erythrocyte	5000000	4200000 ± 200000	4,76	4150000 ± 212132,03	5,11

Table 5

Thrombocytes number (n) in female patients blood with Cooley's anemia

Cells type	Statistical values				
	Normal (n/mm^3)	Pathological (n/mm^3)			
		30 - 35 years old		35 – 40 years old	
		x ± Es	CV%	x ± Es	CV%
Thrombocytes	150000 – 350000	260000 ± 18027,76	6,93	280000 ± 10000	3,57

Table 6

Thrombocytes number (n) in male patients blood with Cooley's anemia

Cells type	Statistical values				
	Normal (n/mm^3)	Pathological (n/mm^3)			
		30 - 35 years old		35 – 40 years old	
		x ± Es	CV%	x ± Es	CV%
Thrombocytes	150000 – 350000	285000 ± 20000	7,01	240000 ± 14142,135	5,89

Table 7

Leucocytes number (n) in female patients blood with Cooley's anemia

Cells type	Normal (n/mm^3)	Statistical values Pathological (n/mm^3)			
		30 - 35 years old		35 – 40 years old	
		x ± Es	CV%	x ± Es	CV%
Leucocytes	4000-9000	15000 ± 5000	33,333	20000 ± 2000	10

Table 8

Leucocytes formula at female patients with Cooley's anemia

Cells type	Normal values		Pathological values	
	Relative value	Absolute value	Relative value	Absolute value
Non-segmented neotrophils	3%	230/mm^3	2%	350/mm^3
Segmented neutrophils	57%	4200/mm^3	53%	9275/mm^3
Eozinophils	2,7%	200/mm^3	1%	175/mm^3
Monocyts	5%	380/mm^3	3%	525/mm^3
Limphocytes	33%	2500/mm^3	41%	7175/mm^3

Table 9

The number of leucocytes (n) in the blood of malepatiebts with Cooley's anemia

Cells type	Normal (n/mm^3)	Statistical values Pathological (n/mm^3)			
		30 - 35 years old		35 – 40 years old	
		x ± Es	CV%	x ±Es	CV%
Leucocytes	4000-9000	13333,33 ± 3055,05	22,91	18000 ± 2828,427	15,71

Table 10

The leucocytes formula at male patients with Cooley's anemia

Cells type	Normal values		Pathological values	
	Relative value	Absolute value	Relative value	Absolute value
Non-segmented neutrophils	3%	230/mm^3	2%	313/mm^3
Segmented neutrophils segmentate	57%	4200/mm^3	50%	7833/mm^3
Eozinophiles	2,7%	200/mm^3	1%	156/mm^3
Monocytes	5%	380/mm^3	3%	470/mm^3
Limphocytes	33%	2500/mm^3	43%	6736/mm^3

Table 11

The fibrinogen concentration in the blood of patients with Cooley's anemia

The biochemical indicator biochimic	The values statistical analysed				
	Normal (g%)	Pathlogical (g%)			
		30 - 35 ani		35 – 40 ani	
		x ± Es	CV%	x ±Es	CV%
Fibrinogen	0,2-0,4	0,17 ± 0,060	35,29	0,20 ± 0,1	50

Table 12

The fibrinogen concentration in the blood of male patients with Cooley's anemia

The biochemical indicator	Valorile prelucrate statistic				
	Normal (g%)	Pathological(g%)			
		30 - 35 years old		35 – 40 years old	
		x ± Es	CV%	x ±Es	CV%
Fibrinogen	0,2-0,4	0,1 ± 0	0	0,2 ± 0,141	70,5

Tabelul 13

The imunoglobuline G concentration in blood of female patients with Cooley's anemia

The biochemical indicator	Normal (mg%)	The statistical values			
		Pathological (mg%)			
		30 - 35 years old		35 – 40 years old	
		x ± Es	CV%	x ±Es	CV%
IgG	800-1600	1000 ± 150	15	1600 ± 100	6,25

Table 14

The imunoglobuline G concentration in blood of male patients with Cooley's anemia

The biochemical indicator	Normal (mg%)	The statistical values			
		Pathological (mg%)			
		30 - 35 years old		35 – 40 years old	
		x ± Es	CV%	x ±Es	CV%
IgG	800-1600	1100 ± 100	9,09	1400 ± 282,84	20,20

Table 15

The imunoglobuline A concentration in blood of female patients with Cooley's anemia

The biochemical indicator	Normal (mg%)	The statistical values			
		Pathological (mg%)			
		30 - 35 years old		35 – 40 years old	
		x ± Es	CV%	x ±Es	CV%
IgA	100-360	106 ± 10,392	9,80	112 ± 12	10,71

Table 16
The concentration of imunoglobuline A in blood of male patients with Cooley's anemia

The biochemical indicator	Normal (mg%)	The statistical values			
		Pathological (mg%)			
		30 - 35 years old		35 – 40 years old	
		x ± Es	CV%	x ±Es	CV%
IgA	100-360	110 ± 5	4,54	115 ± 7,071	6,14

Table 17
The imunoglobuline M concentration in blood of female patients with Cooley's anemia

The biochemical indicator	Normal (mg%)	The statistical values			
		Pathological (mg%)			
		30 - 35 years old		35 – 40 years old	
		x ± Es	CV%	x ±Es	CV%
IgM	84-170	680 ± 20	2,94	384 ± 29,461	7,67

Table 18
The imunoglobuline M concentration in blood of male patients with Cooley's anemia

The biochemical indicator	Normal (mg%)	The statistical values			
		Pathological (mg%)			
		30 - 35 years old		35 – 40 years old	
		x ± Es	CV%	x ±Es	CV%
IgM	84-170	780 ± 20	2,56	362 ± 16,970	4,68