HEMATOLOGICAL AND BIOCHEMICAL MODIFICATIONS IN MALE PATIENTS WITH VIRAL HEPATITIS *B*

**ELENA TODIRAŞCU-CIORNEA[1], GABRIELA DUMITRU [1*],
ELENA VIOLETA AXINTE [2], ANCA MIRELA AMARIEI [3],
SILVIA DUMITRAŞCU [4]**

Abstract: The study systematizes the values of main hematological and biochemical parameters at male persons wearers of hepatic B virus, monitorized in the Emergency County Hospital Mavromati Botosani, by echeloning on age groups and then followed these ones deviation from the physiologic-ordinary interval. The results of clinic tests showed that, excepting the number of leucocytes and blood platelets, all the hematological and biochemical indicators kept in view got out of the normality interval's sphere, the highest pathological values registering at the older persons.

INTRODUCTION

The hepatic affections can be of alcoholic and non-alcoholic nature, the alcoholic hepatic disease being the most frequent of all the hepatic diseases (Rossi et al., 2015), including steatosis with or without fibrosis, the alcoholic hepatitis, cirrhosis and hepatocellular carcinoma, in the Western countries representing a relevant negative co-factor in the progression of chronic hepatic lesions of different etiologies (Rehm et al., 2009; Neff et al., 2011; Mathurin et al., 2012).

The hepatitis B is a global major disease and constitutes the most severe viral form of hepatitis, being one of the main causes of cirrhosis and of hepatocellular carcinoma, approximately 350 millions of people being, in present, wearers of this virus (Lee, 2002). The disease raises serious problems in the less developed countries, reason for what it is entailed the initiation of some new therapies which has to complete the current medication, antiviral and immunomodulator, inclusive the hepatic transplant (Peng et al., 2011).

The goal of hepatitis B treatment is to prevent cirrhosis, liver decompensation and hepatocellular carcinoma. In clinical practice, treatment response is determined by suppression of serum HBV DNA levels, hepatitis B *e* antigen seroconversion to hepatitis B *e* antibody, hepatitis B surface antigen loss, normalization of alanine aminotransferase levels and improvement in liver histology (Kwon and Lok, 2011).

The present study aims to follow up the evolution of some hematologic and biochemical indexes with diagnostic value at male persons diagnosed with hepatic B virus through these ones analyze on different age categories.

MATERIAL AND METHODS

The research was performed on 29 male persons monitored within the Gastroenterology Department of the County Hospital Mavromati Botosani, in 2008 March - September, to establish the diagnostic or for its confirmation, sampling the blood immediately after the ill's internment, determining the values of hematologic and biochemical indexes with clinical importance in the decelation and, eventually, the establish of evolutiv stage of viral hepatitis B.

Given the fact that the physiologic-ordinary interval for the hematologic and biochemical indexes is in strong correlation with the person's age, we resorted to the patients' repartition in four categories of age namely 21-30 years old, 31-40 years old, 41-50 years old and 51-60 years old, the obtained results being statistically processed, the values refund in the graphics below representing the arithmetical average of each indicator in part. For the accuracy of results and the determination of existing/non-existing of some significant difference from statistically point of view between the average of obtained results in the case of the sample of analyzed subjects and the average of ordinary values in the medical practice we calculated the standard error and the variation coefficient of the average, as well as the Student statistical signification test (Văleanu et al., 1990; Varvara, 2001; Zamfirescu and Zamfirescu, 2008).

The analyze of hematologic parameters was done with the help of Pentra 60 C+ automatic analyzer, and of those biochemical with the help of Hitachi 912 automatic analyzer.

RESULTS AND DISCUSSIONS

From the total of subjects taken into observation a percent of 21.06% corresponds to 21 - 30 years old group, so as the other 3 categories of age to occupy each one a weighting of 26.31% (Fig.1).

A prime hematologic indicator taken into study was represented by the erythrocytes sedimentation rate (ESR), test screening that offers relations on proteic structure of blood plasma, especially on the fibrogen, on the α_2- globulines şi γ-globulines. The specialty literature mentions the fact that, within the hepatocellular affections, the homeostatic modifications at the peripheral blood's level present conexe functional implications, which are manifested in forms all to the aggravating the more the liver's dysfunction is much severe (Paşparan, 2009). As it can be ascertained from Figure 2, the medium values of ESR at male persons investigated don't fit between the limits of normality interval (5 - 7 mm/h), all the subjects with hepatic B virus presenting values much lower, the more drastic decrease being at the age group of 51 – 60 years old $(2.2 \pm 0.2$ mm/h). It is known the fact that there is a correlation between the blood's deposition speed, on the one hand and the number of red cells, respectively the fibrinogen level, on the other hand. Thus, the rapport's modification between the plasmatic proteins may influence the ERS's value, in the sense that the proteins' dominance with high molecule (globulines and fibrogen) determines the increase of ERS's values, and the increase of red cells' density leads to the decreasing of this parameter's values (Misăilă and Dumitru, 2010). Our results respect the correlation between the fibrinogen concentration and the deposition speed, but don't evidence literally the relation towards the number of red cells, supplementary factor of influence. In the same time, the low values of ERS may be explained by the installation of anemia, which impedes the formation of erythrocytary aggregates slowing the erythrocytes sedimentation Rate (Paşparan, 2009).
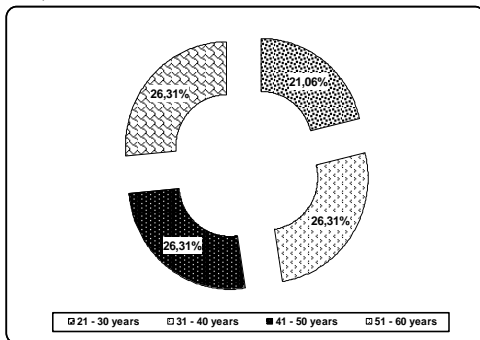

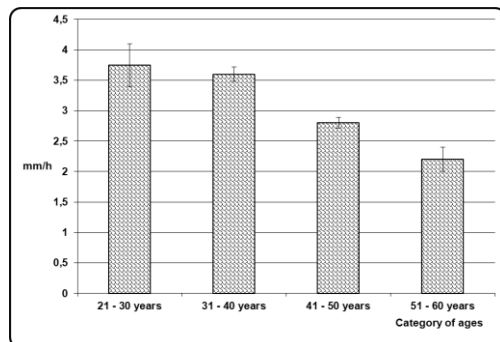Fig. 1. The procentual distribution of the patients on category of ages

Fig. 2. The ERS average values of on category of ages

Commonly, in hepatic diseases appear perturbations as well in what concerns the iron's ordinary metabolism, with consequences on hemoglobinosynthesis and on red cells' normochromic, as well as in the deposition and in the corresponding usage of folic acid and of vitamin $B_{12,}$ implied in the ordinary ageing of figurate elements in erythropoiesis, all these contributing to the association of liver disease with the anemia (Sulkowski, 2003; Andreana et al., 2004; Gupta et al., 2005; Cengiz et al., 2007; Grimaldi et al., 2008; Savage et al., 2008).

In the case of hemoglobin the physiological interval values are of 13 - 17g/dL blood. At the male persons investigated by us (Fig. 3), the hemoglobinic insufficiency is broader at the 41 - 50 years old category, reaching the threshold of 10.47 ± 0.053 g/dL blood, while, the other groups reached medium values between 11.72 ± 0.11 g/dL (at category of ages 21-30 years) and 12.64 ± 0.128 g/dL (at category of ages 51-60 years).

Similar decreasing were registered also in the case of the medium values of hematocrite (the normally values are 38 - 50%), the insufficiency in this case reaching to $35.6 \pm 0.509\%$ at the 41-50 years old group and $37.25 \pm 0.629\%$ at 21-30 years old group (Fig.4), thing which can be explained by the fact that the decreasing of hemoglobinic synthesis gets to a hematocritic insufficiency.
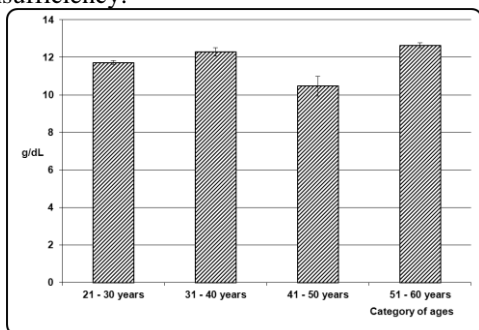
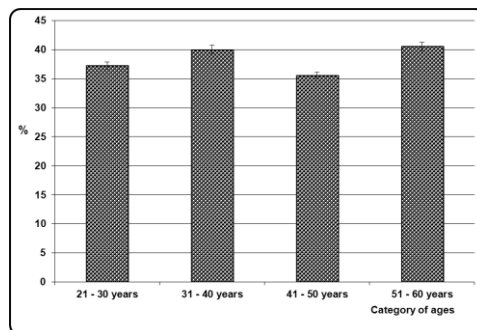|	
Fig. 3. The hemoglobin average values on category of ages	**Fig. 4. The hematocrit average values on category of ages**

In what concerns the fibrinogen quantity, it can be ascertained that this one decreases at all the groups investigated (the normal values for males oscillate between 150 and 360 mg/dL), the lowest value being registered at 51-60 years old group (97.2 ± 0.374 mg/dL), the rest of the groups presenting values that oscillated between 122 ± 0.316 mg/dL and 145.4 ± 0.244 mg/dL (Fig. 5), the viral hepatitis B, according to literature data (Brujan et al., 2006), being characterized by decreasing of ERS and fibrinogen concentration.
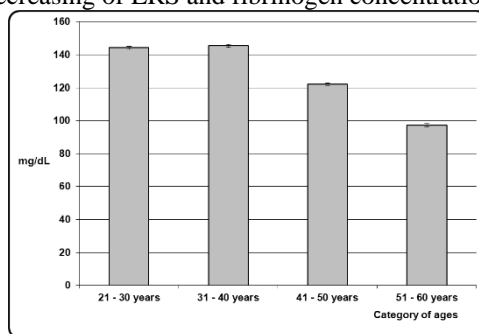
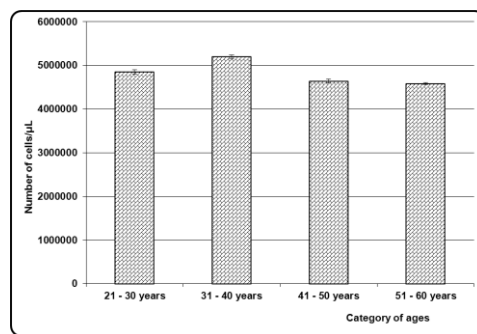|	
Fig. 5. The fibrinogen average values on category of ages	**Fig. 6. The average values of red cells number on category of ages**

From Figure 6 comes out that it doesn't exist significant differences in what concerns the number of red cells at male persons with hepatic B virus, all the age categories presenting values under the inferior limit of the normality ceiling characteristic for the respective age, the 51-60 years

old group registering a minimum average value of 4584000 ± 26570.66 red globules/μL blood, while, at 31-40 years old group, was dignified a medium average of 5200000 ± 35355.34 red globules/μL.

Data from the specialty literature mention the fact that leucopenia with selective neutropenia is common to viral infections, inclusively hepatic, case in which it may be come to agranulocitose all-gravely through medullar inhibition, concomitantly and compensatory installing a relative limfocitose – the ordinary response of the organism in numerous viral infections (Brujan and colab., 2006 cited by Paşparan, 2009), the medium values of the leucocytes number (Fig. 7) at all the investigated patients being situated in the physiologic-ordinary interval (4210 - 7450 white globules/μL blood).

A similar situation it's met also in the case of thrombocytes, the minimum average value being highlighted at the 41-50 years old category (172600 ± 2070/μL blood), and the maximum at the 21-30 years old category (276500 ± 3898/μL blood).

In what concerns the statistical signification of the obtained results, the hematologic parameters' values registered by us, are, in their majority, significant (0.01<p <0.05) and distinctly significant (0.001<p<0.005), while the hemoglobin and the fibrinogen in the case of 41-50 years old group and 51-60 years old group, respectively leucocytes and thrombocytes in the case of 31-40 years old groups , 41 -50 years old and 51-60 years old are significantly strong (p<0.001), and the ERS from the 31-40 years old group is insignificantly statistic (p>0.5).
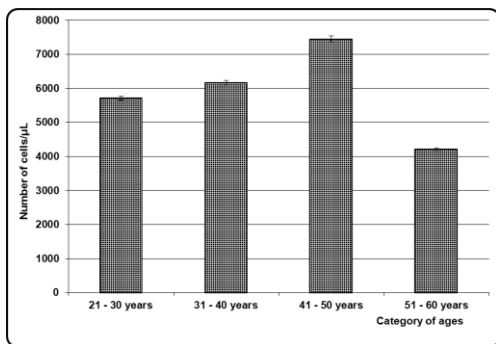

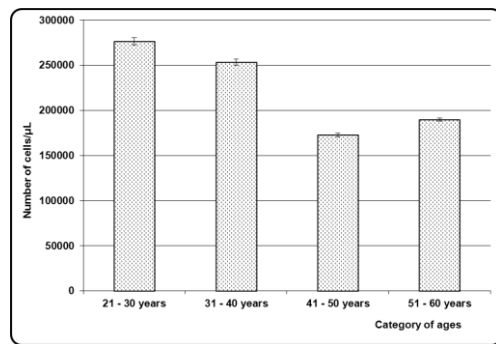**Fig. 7. The average values of leucocytes number on category of ages**

Fig. 8. The average values of thrombocytes number on category of ages

Hereinafter we calculated the medium values of the erythrocytary constants: MCV (mean cell volume) - indicator by virtue on which it is done the correct classification of the anemia types, MCH (mean cell hemoglobin) - constant which offers informations about the quantity of hemoglobin and MCHC (mean cell hemoglobin concentration) - parameter which expresses the rapport between the hemoglobin quantity and the total erythrocytary volume (Misăilă and Comănescu, 1999).

From the analyze of medium erythrocytary volume's values (Fig. 9) it is ascertained that, beside the patients with ages between 51-60 years old, which is situated in the normality interval's limits (88.5 μm^3/eritrocit), at all the others, the MCV values are pathologic (approximately 77 μm^3/eritrocit).

In a similar way varies also the medium erythrocytary hemoglobin (at the 51-60 years old category registering a physiologic value of 27.6 pg hemoglobin/erythrocyte) given the fact that the

MCH modifications go in parallel with those of the MCV, the easy increasing under the ordinary minimum threshold of the reference interval (25-32 pg Hb/ red cell) at the patients up to 50 years old being possible to be associated with feriprive hipochrome anemia (Manole et al., 2005).

The moderately reduced values of MCHC, at all the age categories (31.48 g Hb/100 mL erythrocytary weight at 21-30 years old category, 30.7 g Hb/100 ml erythrocytary weight at 31-40 years old category, 29.41 g Hb/100 mL erythrocytary weight at 41-50 years old category and 31.16 g Hb/100 mL erythrocytary weight at 51-60 years old category) may lead to a diagnostic of hypochromic anemia (Fig. 11).
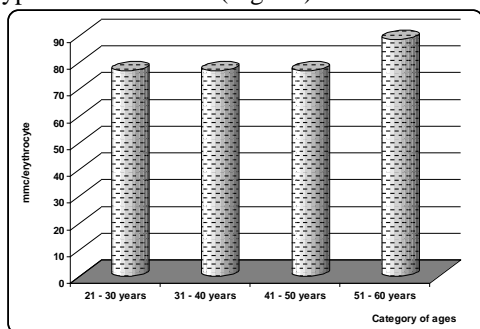

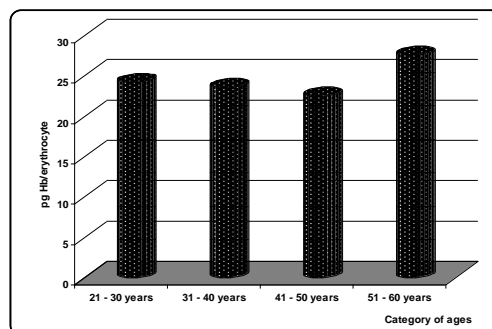**Fig. 9. The mean cell volume (MCV) on category of ages**

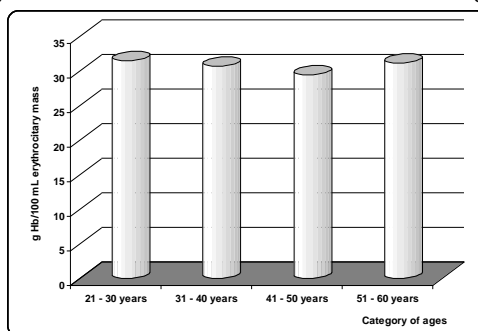**Fig. 10. The mean cell hemoglobin (MCH) on category of ages**

Fig. 11. The mean cell hemoglobin concentration (MCHC) on category of ages

It is known the fact that the hepatic cells' suffering which leads to the decrease of the permeability of hepatocytes' membrane, but not necessary to the necrosis of these cells, it is detected on the increase in serum of some cellular enzymes. The serum level of the activity of these lesion enzymes varies based on the number of affected hepatocytes, on the lesion gravity of each cell, on the speed with which were produced the lesions and on the elimination speed from serum of the respective enzymes (Cojocaru, 2005), as a result, in the different diseases of the liver, realizing different specters of the lesional enzymes' activity, based on the etiology and on the evolutiv stage of hepatopaty (Pâslaru, 2004).

Data from literature denote an association between the increase of the aminotranspherases' activity and the installation of a cytolyses estate, Nair et al., 2001 highlighting a significant increase of the alanin-aminotranspherase's activity (ALAT) in the hepatic affections comparatively with that of the aspartat-aminotranspherase's (ASAT). At the male persons with

viral hepatitis B taken into study, the two enzymes registered medium values a lot increased at all age categories, comparatively with the ordinary interval's limits (Figs. 12-13). Thus, the 21-30 years old group registered a medium value of the ALAT of 74.85 ± 1.142 U/L, while, at the same age group, the medium value of ASAT enzyme was of 64.55 ± 0.86 U/L. The 41-50 years old group reached the maximal average thresholds both in the case of ALAT (121.64 ± 0.526 U/L), as well as ASAT (106 ± 0.706 U/L), while in the case of the last analyzed age category (51-60 years old) ALAT registered a medium value of 86.708 ± 0.731 U/L, while ASAT had the medium value of 74.86 ± 0.824 U/L. The rapport ASAT/ALAT turned out to be sub-unitary for each age group in part, the literature data (Negură, 2008) associating these values with the acute hepatitis diagnostic, the increase of aminotranspherase's activity during the antiviral therapy being a good clue of the efficiency of the applied therapy. In the same time, it should be taken into view that, during the disease's evolution, although the cirrhosis was installed and takes place the firm progression of the disease to hepatocellular carcinoma (Popescu, 2005) the aminotranspherases can present a palette of values registered in the reference interval's limits.
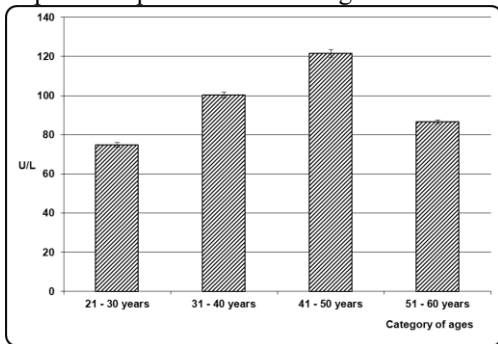

Fig. 12. The ALAT average activity
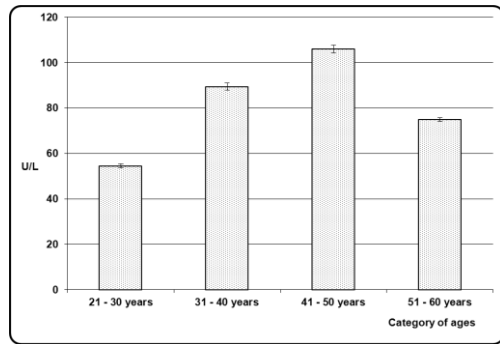on category of ages

Fig. 13. The ASAT average activity
on category of ages

The alkaline phosphatase's activity (FA) registered moderate increasing towards the superior limit of the reference interval (100-290 U/L), at all age categories taken into study. Thus, if the younger patients presented medium values of 342.875 ± 1.178 U/L (the 21-30 years old group) and 366.44 ± 0.591U/L (the 31-40 years old group), at all categories beyond 40 years the enzyme registered medium values net superior to admissed maximum limit (452.34 ± 0.808 U/L - at 41-50 years old group and 487.42 ± 0.538 U/L at 51-60 years old group).

And in what concerns the γ-glutamil-transpherase (GGT), enzyme indicator of cholestasis, the activity acted of a similar manner, laying out, at all age groups, medium values easy increased towards the superior limit of the ordinary interval (12-48 U/L). If at the 21-30 years old group the GGT activity reached the medium level of 52.95 ± 0.417 U/L, at 41-50 years old group and 51-60 years old group the medium thresholds of activity were significantly higher, the registered averages being of 68.92 ± 0.255 U/L, respectively 62.72 ± 0.315 U/L. From statistically point of view, the values of all serum enzymes were very significant (p<0.001) at all studied age categories.
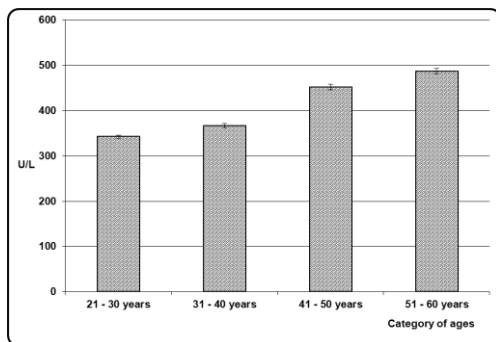
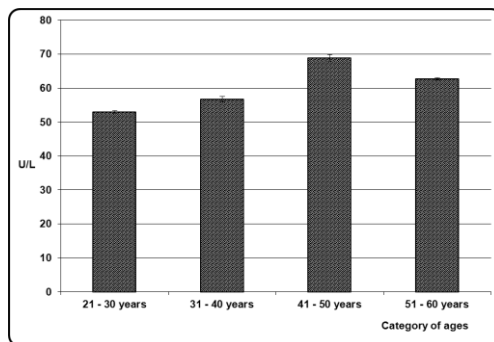**Fig. 14. The FA average activity on category of ages**

Fig. 15. The GGT average activity on category of ages

CONCLUSIONS

* At the investigated patients the number of leucocytes and thrombocytes are situated, generally, in physiologic limits.

* The erythrocytes sedimentation rate and the fibrinogen quantity register values situated under the inferior threshold of the reference interval.

* The hemoglobinic and hematocritic insufficiency reaches levels more marked at the patients from the 41-50 years old category.

* The enzymes with diagnostic value registered significant increasing of activity at all age categories, the aminotranspherases and the glutamil-transpherase being maximal at the 41-50 years old age category, while the alkaline phosphatase reaches superior quotes at the patients between 51 and 60 years old.

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[1] "Alexandru Ioan Cuza" University of Jassy, Faculty of Biology, Bvd. 20A Carol I, 700505, Romania

[2] Technological High School Petru Rares, Botosani, Calugareni Street, No 9, 710256, Romania

[3] Comprehensive School Nr. 1 Ramnicelu, Buzau

*gabriela.dumitru@uaic.ro