

THE EVOLUTION OF SOME BIOCHEMICAL MARKERS AT PATIENTS WITH B HEPATITIS VIRUS

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Keywords: B hepatitis virus, age groups, biochemical markers, percentage distribution

Abstract: The study aimed at the mathematics processing of some biochemical indicators in subjects infected with heptatitic virus of B type, that were investigated in S.C. Dorna Medical S.R.L. Vatra Dornei Lab, between December 2011 – February 2012, through echeloning on different categories of age the experimental results and the calculation of procentual weighting, related to the whole patients, both for physiological values, as for those that outgrow the superior ceiling of normality interval. Biochemical profile of the realized study signalize the highest prevalence of hepatitis B in female sex, in the case of majority of studied markers, the most significant share registering in 40-59 years old category.

INTRODUCTION

The chronic hepatitis and the cirrhosis, whose main etiological factor is represented by the hepatitis viruses, represent a main problem of public health in worldwide, both through their weight, as well as through multiple complications that appear during the disease's evolution (**Lavanchy, 2005**).

B Hepatitis is a liver infection caused by a virus of adenovirus type which is transmitted through blood or blood derivatives contaminated during the transfusions, through other secretions of infected patients (saliva, milk, vaginal secretions), through sexual contact with an infected person, by using some pins or similar tools contaminated. Unlike the A hepatitis virus, the B virus may cause both an acute form of hepatitis, as well as one chronic, the B hepatitis being one of the most frequent chronic affection in the world and knowing 4 evolutionary stages namely: the immune tolerance phase (responsiveness), the immune clearance phase (immunoreactive, chronic hepatitis), the low viral replicative phase (inactive carrier of B hepatitis virus) and the reactivation phase (**Villeneuve, 2005; Tran, 2011**).

The present work aims the analysis of some biochemical indices in patients with B hepatitis, through procentual analyze of the distribution, on different categories of age, of those parameters.

MATERIALS AND METHODS

Between December 2011 – February 2012 were made a number of 8182 biochemical tests on patients with B hepatitis virus within the S.C.Dorna Medical S.R.L. Vatra Dorna's lab, determining the activity of transaminases, of total and direct bilirubin, of alcalin phosphatase and γ -glutamyl-transferase and the serum proteins' electrophoresis.

To accomplish the biochemical tests were used the Hitachi 917 automatic analyzer and for proteins electrophoresis the Line Electrophoresis Genio.

RESULTS AND DISCUSSIONS

It is known the fact that, depending on pathological process that it determines with predominance, the biochemical samples of liver exploration can be divided in several categories namely those that signalize the existence of a chronic inflammatory process in liverish mesenchyme, that correspond on morphological plan of some limfoplasmocitar infiltrations in interstitium, those that indicate a growth of hepatocytes' membrane permeability, which gives points to a liver functional insufficiency or which denotes the existence of a hepatic cholestasis (**Cucuianu et al., 1998**).

Of the 8182 biochemical tests, the alanin-aminotransferase was determined on 2980 cases, presenting a share of 36.43%, the aspartat-aminotransferase on 2721 cases, with a share of 33.26%, the direct bilirubin, respectively total having an addressability of 7.62%, the γ -glutamyl-transferase of 8.28%, while the alkaline phosphatase and the serum proteins' electrophoresis were found in a 3.78% percentage, respectively 3.01% (Fig.1). As for the

distribution on sexes, the balance pitched in favour of male sex with 56.19% from the 8182 patients whose analyses were processed (Fig.2).

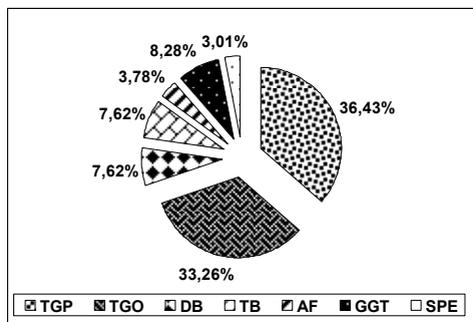


Fig. 1. The procentage distribution of the biochemical tests

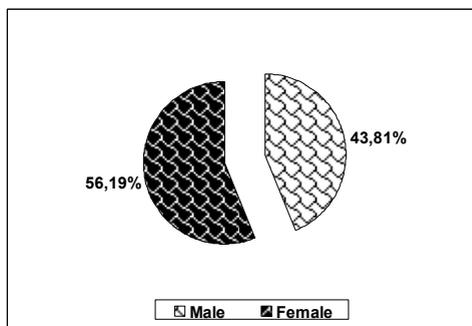


Fig. 2. The procentage distribution on sex

The alanin- and aspartat-aminotransferases (TGP and TGO) are widely used in medical practice for a sensitive indexes, although non-specific, of acute hepatocitar lesions, independently of any etiologic consideration, the activity's level of those enzymes can be due to and some possible diseases which induce immunodeficiency (hepatitis, including toxic-drug) or to the presence in immediately antecedents of some curative treatments with hepatotoxic (for example, ceftriaxone from cephalosporin's group) (Suankratay *et al.*, 2008).

The graphical representation of the alanin-aminotransferase's activity (Figs.3-4) highlights a non-uniform distribution of the patients on age categories, both in what concerns the ordinary values and those pathological, the smallest share, in the case of ordinary values, registering on 0 – 4 years categories age (1.51%), respectively 80 - 99 years (1.85%), while, in both cases, the biggest percentage is occupied by the 40 - 59 years subjects (34.22% in the case of ordinary-physiological limits and 48.63% in the case of those pathological).

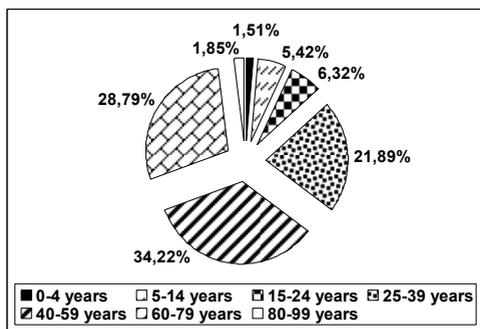


Fig. 3. The procentage distribution of TGP – normal values

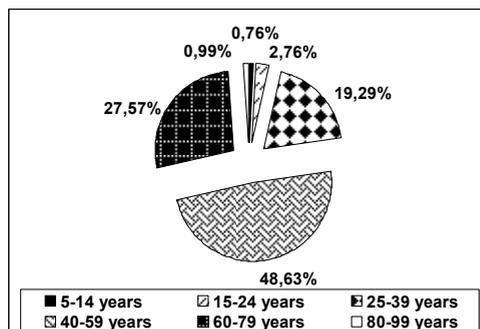


Fig. 4. The procentage distribution of TGP – pathological values

In what concerns the aspartat-aminotransferase it isn't established significant differences regarding the values' distribution on age categories, being able only to make reference to the fact that, on 25-39 years old group, the pathological cases are more numerous, occupying a 33.79% percentage at TGO comparatively with 27.57% at TGP (Figs.5-6).

Data from specialty literature mention the fact that, in different diseases of the liver, it is realized different spectrums of the lesional enzymes' activity, based on the hepatopathy's evolutionary stage and etiology (Pâslaru, 2004), a cellular synthesis that interests especially the enzymes with cytosolic localization, such as the alanin-aminotransferase, taking place in the case of a moderate lesion that affects only the permeability of hepatocitar's membrane.

Although in other types of hepatitis (C hepatitis) was signalized the fact that it is possible the existence of an ordinary level of this transpherase under the terms of the appearance and the persistence of those cellular lesions that, though light, are decisive for the further evolution disease, can be correlated in a significant proportion with the disease's progression (Zeuzem *et al.*, 2006), in B hepatitis case it is known the fact that a high gradient of alanin-aminotransferase is in a significant association relation with the carcinoma liverish risk (Chen *et al.*, 2011). Both the factors that predict the spontaneous increases of this enzyme as well as the frequency of these episodes aren't known, especially at the patients with chronic B hepatitis which are asymptomatic (which have the level AgHB negative and the level TGP ordinary) (Kumar *et al.*, 2009), the necessity of knowing these ones deriving from the fact that a liverish carcinoma is preceded by a transitional estate abnormal ordinary of seric levels alanin-aminotranspherase (Chen *et al.*, 2011).

Therewith, the increase concentration of viremy is in strong dependence with the high levels of alanin-aminotransferase, a lusty episode of this enzyme's activity raising the virologic answer in the acute phase disease (Nair and Perrillo, 2001).

In the case of some necrosis, it is released from the cells and the mitochondrial enzymes, the aspartat-aminotranspherase being an enzyme with localization both cytosolic and mitochondrial, its activity increasing more comparatively with the alanin-aminotranspherase (Pașparan, 2009).

A research made by Petersen *et al.* (2014) show that the alanin-aminotranspherase can be a sensible marker in distinguishing with accuracy the light liverish fibrosis, and in mixture with other validated algorithms improves the performance of profiling the significant fibrosis.

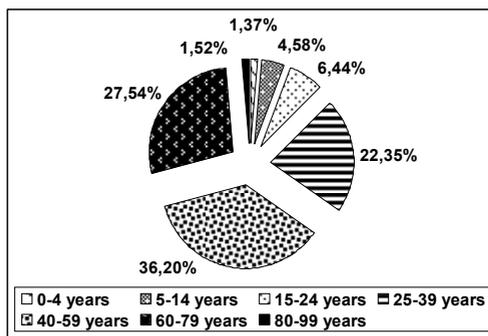


Fig. 5. The procentual distribution of TGO - normal values

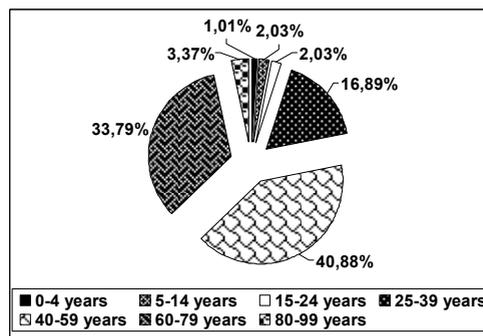


Fig. 6. The procentual distribution of TGO - pathological values

Apart from the hepatic transaminases, there are also other enzymes used in the evaluation of hepatic function, as the alcalin phosphatase - AF (considered specific indicator of the hepatic disfunction) and the γ -glutamyl-transpherase - γ -GT, the determination of plasmatic activity of latter one being a sensitive marker of hepatobiliar pathology, even if this analyze

doesn't allow the differentiation between the cholestasis pathologies and those hepatocellular (Negură, 2008).

The monitored patients in S.C. Dorna Medical Laboratory, during December 2011 – February 2012, presented a large specter of distribution of alcalin phosphatase activity's determinations on age groups. In what concerns the ordinary-physiologic values of alcalin phosphatase, from the seven age groups in which were distributed the investigated patients, the 25-39 groups and 60-79 years occupy approximately half of the total, so as to, the 40-59 years old group to have a maximum weight, of 38.84% (Fig.7). By comparison, the analyze of pathologic values (Fig.8), discloses a different behavior, the 40-59 and 60-79 years old categories being the most represented with a 39.7% percent, respectively 42.71%, at the opposite pole being the groups of 0-4 years old (1.46%) and 15-24 years old (4.41%).

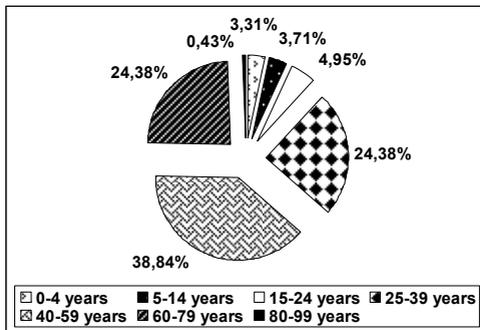


Fig.7. The procentage distribution of AF – normal values

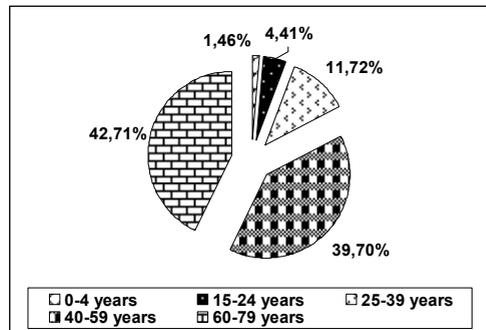


Fig.8. The procentage distribution of AF – pathological values

According to specialty literature data, in medical practice are used the AF and γ -GT dosages, whose level increase also in minor forms of cholestasis, when the conjugated bilirubin's level is ordinary or presents increases scarcely delineated (Cucuianu *et al.*, 1998). In the situation that the alcalin phosphatase's growth occurs concomitantly with that of γ -glutamyl-transpherase, it can be assumed the existence of a cholestasis process (Goldberg, 1980). The growth of seric activity of γ -GT is less specific for cholestasis, increased values of this enzyme can be meet in any hepatic affection. The growth degree of γ -GT activity is however less expressed in a chronic hepatitis without cholestasis phenomena (2-5 times more comparatively with the superior limit of the ordinary) than in a case in which the cholestasis is situated on the foreground (Zamfirescu-Gheorghiu and Popescu, 1991).

Cooper *et al.* quoted by McComb *et al.*, (1979) showed that the alcalin phosphatase's levels can remain in reference limits in the patients' serum with anicteric hepatitis, although the seric levels were proved to be in strong connection with the biliar duct's inflammation at patients with hepatitis (Bodlaj *et al.*, 2010). It is necessary to bear in mind of the fact that the low levels of seric alcalin phosphatase before the beginning of interferon treatment of hepatitis, during it and after it seems to be associated with a higher risk of disease backsliding (Bodlaj *et al.*, 2010).

The quest in dynamic of AF behavior and of γ -GT can bring definitions regarding the pathologic process that led to the activity's increase of those enzymes. Anyway, the progressive growth of AF and γ -GT to a patient without jaundice infers the development of a malignant process that must be documented through imaging and radiological exploration of digestive tube (Mircea *et al.*, 1981). On the other hand, in cases in which the hepatic tumor compresses or

stymies the choledochal cysts, it will developed all the manifestations of an extra hepatic cholestasis (mechanical jaundice), and the progressive growth of AF and γ -GT activity is associated with hiperbilirubinemy (the conjugated bilirubin) and with the biliar acids' growth in serum (**Merican et al., 1993**).

The distribution of the subjects on age groups points us, both in ordinaries values' case as in those pathological, a predominant of patients with the age between 40 and 59 years old (43.25%, respectively, 56.39%) (Figs.9-10).

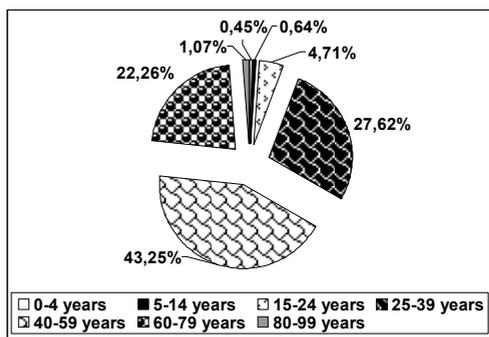


Fig.9. Percentual distribution of γ -GT - normal values

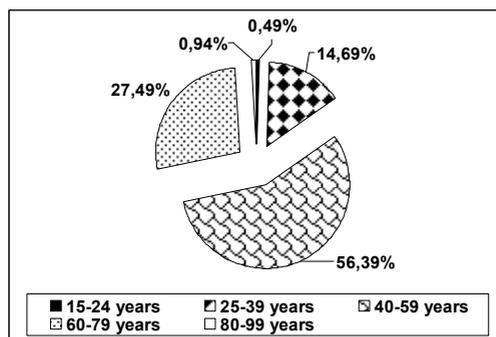


Fig.10. Percentual distribution of γ -GT - pathological values

It is known the fact that the hepatitis pathology is characterized through hepatitis parenchymatosis cells' alteration, registering commotions of different types of metabolism, with stalwart biochemical modifications (**Paramo and Rocha, 1993**). Hereby, according to literature data, in hepatocellular jaundices takes place the reversible occlusal or irreversible of hepatic parenchyma, that determines a growth both of the conjugated bilirubin and of that non-conjugated, the hepatic dysfunction affecting the capture, the glicuronoconjugation and the bilirubin excretion (**Pavel, 1982; Mihele, 1997**). In the same time, the bilirubin's values increase based on the degree in which is disturbed the bile's elimination, as a result of the necrosis of some hepatocytes, it can be created communications between the blood capillaries and the biliar canalicules. Therewith, the hepatitis architecture's alteration, caused by the necrosis, sclerosis processes' alternation and nodular regeneration, characteristic for cirrhosis, create also conditions for the bile's regurgitation in sinusoidal capillaries (**Iwamura, 1982; Cucuianu et al., 1998**).

From Figures 11-14, comes out the fact that, both in the case of ordinary values as in the pathologic, in what concerns the total and direct bilirubin (TB and DB) aren't observed semnificative differences regarding the distribution in function of age, the maximum weight registering also at the 40-59 years old group (39.3% for total bilirubin and 38.23% for direct bilirubin – ordinary values, respectively 34.21% and 40.76% for total and direct bilirubin in pathological values' case).

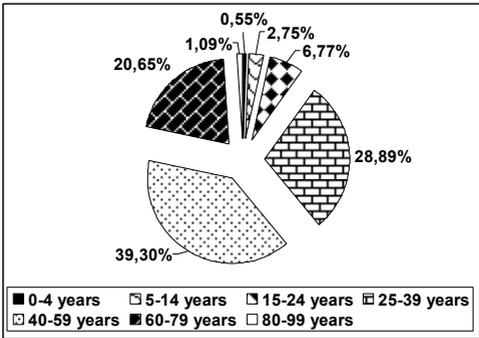


Fig. 11. Percentual distribution of TB - normal values

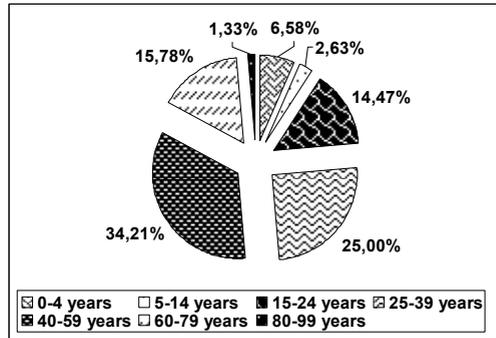


Fig. 12. Percentual distribution of TB - pathological values

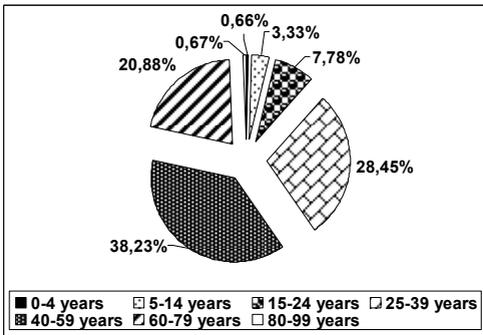


Fig. 13. Percentual distribution of DB - normal values

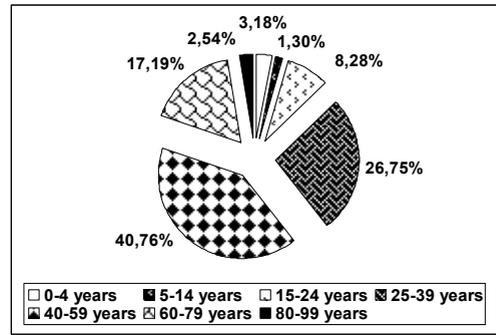


Fig. 14. Percentual distribution of DB - pathological values

The liver synthesizes besides own proteins, structural, a good deal of plasmatic proteins: the albumin, the α -2-globulin-ceruloplasmin, the α - and the β -lipoproteins, a good deal of proteic factors of the coagulation (the prothrombin, the proconvertin, the proaccelerin, the fibrogen), and in the mezenchimal cells are synthetised the immunoglobulins (IgM, IgG) (Cucuianu *et al.*, 1998).

The seric protein's electrophorese can be tested when the symptoms denote an inflammatory affection, an autoimmune disease, an acute or chronic infection, a kidney derangement or of the liver or proteins losses.

The total proteins' electrophorese it is less influenced by the factors that depend so much of the other biochemic determinations: the temperature of the environment, the physical effort, the modification of body position (clino- or ortostatism), the patient's medication. This analyze doesn't present daily variations and at same the time the results remain unchanged for more time.

In what concerns the electrophorese of seric proteins at the patients taken into observation in S.C. Dorna Medical S.R.L. Laboratory (Figs.15-16) we can highlight only the fact that the biggest weight is occupied by 40-59 years category both in the case of ordinary values (45.09%) and also pathological (36.18%), while, the groups age with the lowest frequency are those for children 0-4 years old and aged people 80-99 years old (0.67%).

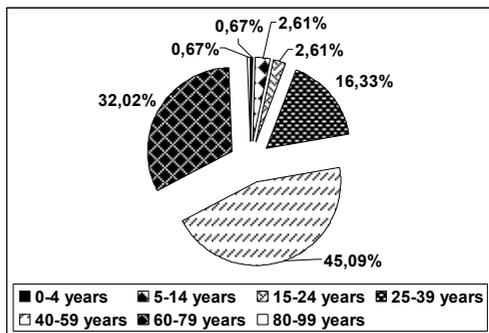


Fig.15. Proteins electrophoresis – normal values

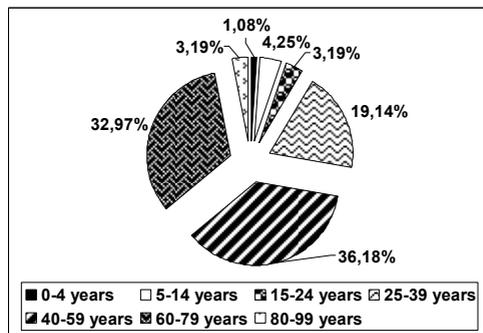


Fig.16. Proteins electrophoresis – pathological values

CONCLUSIONS

The liverish affections at the analyzed patients affect in particular the female.

From the effectuated researches on biochemical tests, results the highest frequency at the 40-59 years old category, followed then by the 60-79 years old group.

In what concerns the enzymes with diagnostic value, alanin- and aspartat-aminotransferase presented a higher activity for the subjects with B acute hepatitis, the γ -glutamyl-transferase and the alcalin phosphatase registering values of the activity a little more moderate.

The medium values of the total bilirubin increase once with the ageing and are a lot over the ordinary value, which expresses the occlusal of liverish parenchyma.

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