

THE EVOLUTION OF SOME HEMATOLOGICAL AND IMMUNOLOGICAL MARKERS AT PATIENTS WITH B HEPATITIS VIRUS

GABRIELA DUMITRU¹, CRISTINA IRIMESCU², ELENA CIORNEA^{1*}, IOANA PAULA CIOBANU³

Keywords: B hepatitis virus, age groups, hematological and immunological markers, percentage distribution

Abstract: The study aimed at the mathematics processing of some hematological and immunological indices in subjects infected with hepatitis virus of B type, that were investigated in S.C. Dorna Medical S.R.L. Vatra Dornei Lab, between December 2011 – February 2012. From the statistical study of the hematological and immunologic profile at patients with B hepatitis shows that the highest percent of immunological clinical investigations are recorded, generally, in the age categories of 40-59 years and 25-39 years, while the hematological tests predominates at the groups 40-59 years and 60-79 years.

INTRODUCTION

B Hepatitis is an extremely common disorder, with severe manifestations, so that in recent decades the world has taken a series of measures to prevent its occurrence and to mitigate the consequences of infection with B hepatitis virus. Thus, the emphasis increasingly on methods of immunoprophylaxis and routine screening through vaccination campaigns both in infants, to prevent HBV infections in childhood, and in children and adolescents who were not previously vaccinated or previously unvaccinated adults with increased risk of infection (Silverman *et al.*, 1991; West and Margolis, 1992; Thomas *et al.*, 2004).

B Hepatitis virus is an adenovirus that is transmitted by perinatal, percutaneous – *i.e.*, puncture through the skin, through direct contact with mucous membranes, through exposure to infectious blood or to body fluids that contain blood or through open cuts and sores (Shikata *et al.*, 1977; Bond *et al.*, 1981, Mast *et al.*, 2005), the literature data (Beasley *et al.*, 1982; 1983, McMahon *et al.*, 1985; Coursaget *et al.*, 1987; Tassopoulos *et al.*, 1987) highlighting that the risk of developing chronic HBV infection after acute exposure ranges from 90% in newborns of HBeAg-positive mothers, to 25%, respectively, to 30% in infants and children under 5 years-old and to less than 5% in adults (Lok and McMahon, 2009). In addition, immunosuppressed persons are more likely to develop chronic HBV infection after acute infection (Bodsworth *et al.*, 1989; Horwath and Raffanti, 1994).

Laboratory diagnosis of the HBV infection is based on the detection of viral antigens (HBs antigen, HBe antigen), of viral DNA and of specific antibodies (anti-HBs, anti-HBe, anti-HBc antibodies of IgM type and of totals anti-HBc) in patients serum (Mast *et al.*, 2005).

The present work aims the analysis of immunologic markers evolution of B hepatitis virus and of some hematological parameters in patients with hepatitis affection, through procentual analyze of the distribution, on different categories of age, of those parameters.

MATERIAL AND METHODS

Between December 2011 – February 2012 were made a number of 2012 hematological and immunological tests on patients with B hepatitis virus within the S.C.Dorna Medical S.R.L. Vatra Dorna's lab, determining the Quick time, the fibronogen, the INR, the HBs antigen, the antiHBs antibodies, the HBe antigen, the antiHBe antibodies and the antiHBc antibodies. To accomplish the hematological tests were used the Sysmex SF 3000 analyzer, for coagulations the Sysmex CA 1500 analyzer and for those immunological the Arhitect CI 4100 analyzer with chemiluminescence.

RESULTS AND DISCUSSIONS

For the hematological and coagulation tests (Fig. 1) were investigated a number of 1607 patients, on which were taken in study the Quick time, the INR (the value of protrombine index increased at ISI power – international standardized index which is assigned to tissue tromboplastine used to determin the protrombine time) and the fibrogen, each parameter filling

aproximatively one third of the total patients (30.8% for the Quick time and the INR, respectively 38.4% in the fibrogen's case).

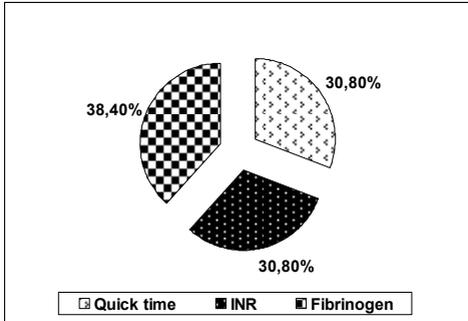


Fig. 1. The procentage distribution of the hematological tests

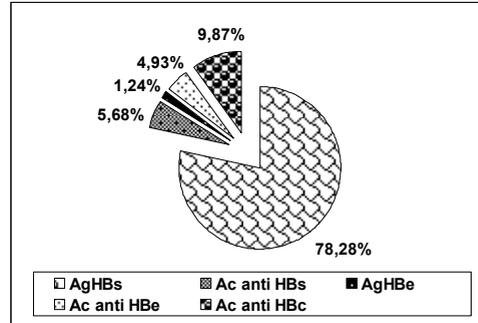


Fig. 2. The procentage distribution of the immunological tests

In what concerns the immunological tests, the number of investigated cases was of 405, the HBs antigen representing 78.28%, the antiHBs antibodies 5.68%, the HBe antigen 1.24%, the antiHBe antibodies 4.93%, while the antiHBc antibodies occupied 9.76% from the total determinations (Fig. 2).

Low values of Quick time are presented in numerous diseases (blood diseases, liver diseases) in absentia of K vitamin, after a treatment with anticoagulant drugs. The blood's coagulation samples are made when are suspected different diseases in which the blood's coagulation is either too slowly, fact that predispose at hemorrhage, either too fast, situation that favors the forming of thrombi in blood vessels (Misăilă and Dumitru, 2010). A time protombine substantially prolonged in B hepatitis implies the necessity of emergency management of antiviral treatment (Girke et al., 2008).

After the effectuated investigations we observe a bigger frequency on 60-79 years old group (61.81%), followed then by the category of 40-59 years (18.18%) and 25-39 years old (9.29%). The interpretation of pathologic values is based on the treatment's monitoring and the therapeutic interval (Fig. 3).

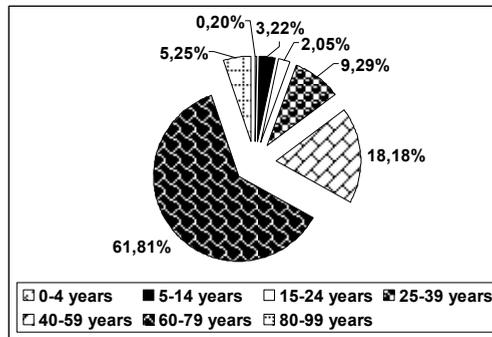


Fig. 3. Quick time - normal values

The injured liver can produce increased quantities of fibrogen, as well as of other collective proteins designated inductances of acute phase (the C reactive protein, the

hepatoglobin, the ceruloplasmina and the transpherina). While the liver can produce ordinary quantities or high of fibrinogen, the molecules by itself can be abnormal qualitative (respectively structural and functional), reflecting slicker disorders of proteic stasis. These molecules of fibrogen, abnormally from functional point of view, can concur at hemostasis, frequently debased at patients with chronic liverish affections (Cucuianu *et al.*, 1994).

From Figures 4-5, we can observe that, in the case of ordinary-physiologic limits, the patients with the highest addressability are those with ages between 40-59 years old (35%), while, in the case of the subjects that overtake the superior limit of normality ceiling, the biggest weight is occupied by the 60-79 years old categories (42.3%), respectively 40-59 years old (37.18%), the most rare met being the groups of age for children which don't have significant modifications.

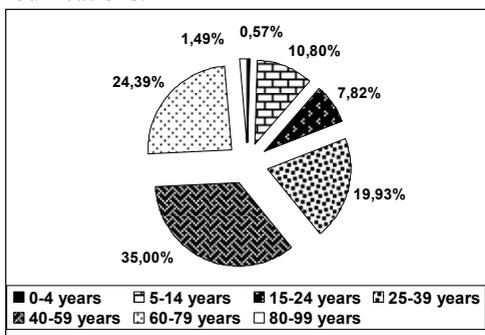


Fig. 4. Procentage distribution of fibrinogen – normal values

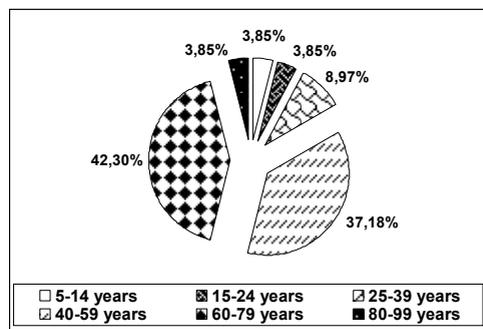


Fig. 5. Procentage distribution of fibrinogen – pathological values

The liverish B virus contains more antigens with different roles in hepatitis' evolution. The HBs antigens represent the serologic marker election of infection with HVB. Its persistence more than 6 months defines the statute of carrier, it can be also detected in chronic infections.

At children, both the effectuated tests and their results are in small percentage (1.08%), as you get older increasing both the addressability and the apparition of B virus infections. When they are discovered, 60-80% of AgHBs carriers already show some signs of hepatic destruction. At subjects taken into study, the highest weight is met at 25-39 years old categories, respectively 40-59 years old (37.58% and 33.68% in the case of ordinary values, respectively 28.58% and 48.57% in the case of pathologic values) (Figs. 5-6).

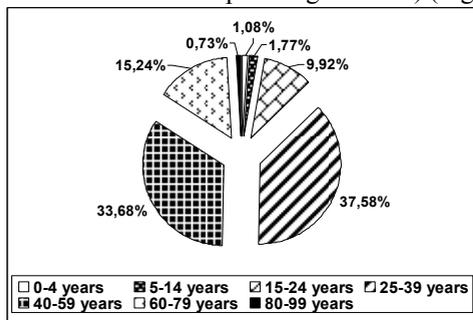


Fig. 5. Procentage distribution of HBs antigen – normal values

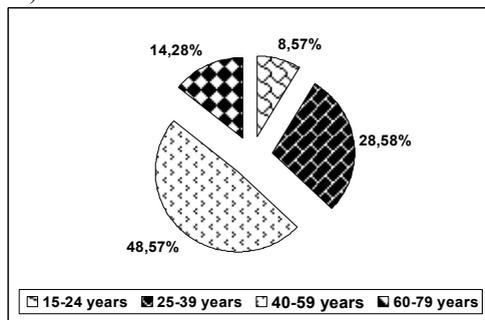


Fig. 6. Procentage distribution of HBs antigen – pathological values

The presence of antibodies indicates the recovery after an infection with B liverish virus, the absence of contagiousness and of immunity towards a subsequently infection with this virus. The antiHBs antibody can be considered also an immunity marker post-immunization for B liverish virus. The apparition of seroconversion from AgHBs at AchBs denotes the evolution to cure disease and the settlement of immunity. Within the consignment taken into analyze by us, the group age most met remains the 40-59 years old, with a percentage of 78.94% (Fig. 7).

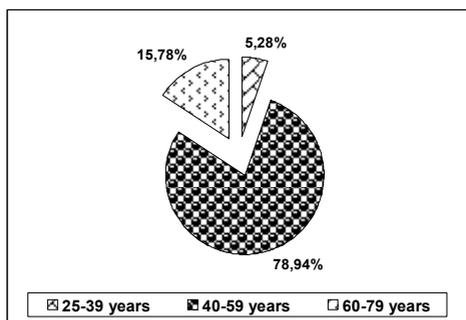


Fig. 7. Proportional distribution of antibodies antiHBs – normal values

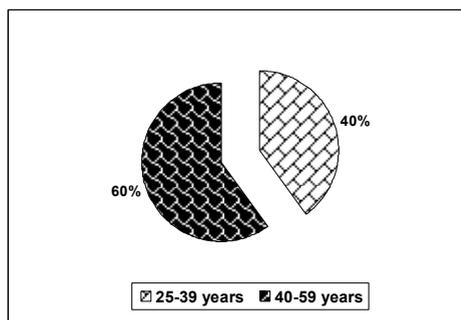


Fig. 8. Proportional distribution of antigen HBe – normal values

The literature data (McMahon *et al.*, 2001) reveals that HBeAg can be detected in the serum of persons with acute or chronic hepatitis, which correlates with the presence of a high level of viral replication and high infectivity. On the other hand, although it was revealed HBeAg positive, the presence of antiHBe antibodies correlates with a decrease in viral replication and infectivity.

The HBe antigen is useful in the determination of infection’s resolution. Its persistence more than 20 weeks infers the evolution, possibly, into chronic hepatitis, and the absence of HBe antigen doesn’t represent a clue of benign disease, non-gradually. There are possible the AgHBe absence and the DNA-HVB presence at patients infected with a mutant of B liverish virus, that doesn’t synthetizes AgHBe.

At same the time, although the seric levels of AgHBs were negative correlated with the severe fibrosis at the patients with AgHBe positive, these represent two index that aren’t affected by the number of residual hepatocytes and, consequently, can be positively correlated with the liverish fibrosis’ severity caused by the infections with B hepatitis’ virus, data from specialty literature concluding that the seric levels of AgHBs has a predictive capacity with accuracy (Hong *et al.*, 2014).

The patients with high addressability remain hereinafter those with the age between 40-59 years old (60%) (Fig. 8).

The antiHBe antibodies appear after the AgHBe disparition and remain detectable for years, denoting the lowering of contagiousness level and inferring a good prognostic in what concerns the resolution of the acute infection. In our patients’ case, remains constantly hereinafter the age group between 40-59 years old with an occupation degree of 75% from total (Figs. 9-10).

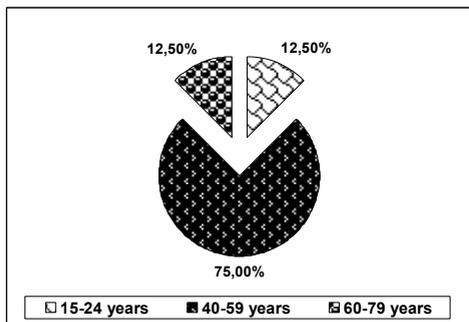


Fig. 9. Procentual distribution of antibodies antiHBe – normal values

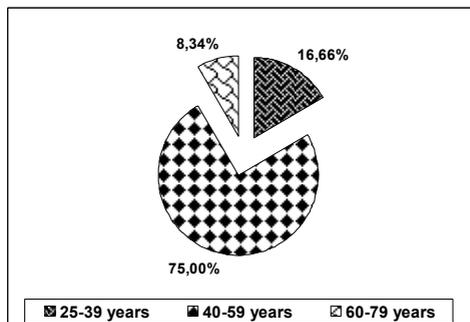


Fig. 10. Procentual distribution of antibodies antiHBe – pathological values

The antiHBe antibodies increase early in acute hepatitis, at 4-10 weeks from the AgHBs apparition, once with the start of clinic manifestations and it persists for years or even for the rest of the life.

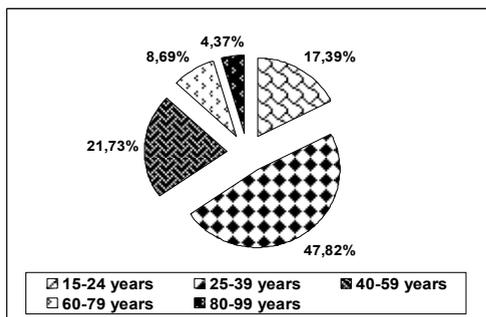


Fig. 11. Procentual distribution of antibodies antiHBe – normal values

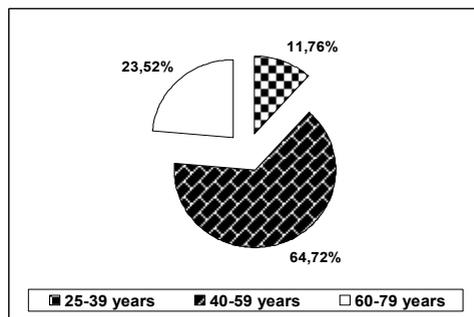


Fig. 12. Procentual distribution of antibodies antiHBe – pathological values

In chronic infection with B liverish virus, the antiHBe and AgHBs antibodies are always present, the antiHBs antibodies being absents. In the case of ordinary-physiologic limits, the addressability to S.C.Dorna Medical S.R.L. Laboratory is from patients with age between 25-39 years old (47.82%), while, the patients with antiHBe antibodies positive are those with the age between 40-59 years old (64.72%) (Figs. 11-12).

CONCLUSIONS

The patients with B acute viral hepatitis presented medium levels a lot diminished of the fibrogen, betraying like this the hemostasis' alteration, which gets head at the patients with liverish cirrhosis.

From the patients' study with addressability for AgHBs we observe that the group of age the most frequent is between 25-39 years old, fallowed by the groupe of 40-59 years old.

A lot of the patients with positive results at AgHBs detection test didn't continued the AgHBe, Ac antiHBe, Ac antiHBc, Ac antiHBs screening.

REFERENCES

1. **Beasley, R.P., Hwang, L.Y., Lin, C.C., Leu, M.L., Stevens, C.R., Szmuness, W., Chen, K.P. (1982):** *Incidence of hepatitis B virus infections in preschool children in Taiwan*, J. Infect. Dis., **146** (2): 198-204.
2. **Beasley, R.P., Hwang, L.Y., Lee, G.C., Lan, C.C., Roan, C.H., Huang, F.Y., Chen, C.L. (1983):** *Prevention of perinatally transmitted hepatitis B virus infections with hepatitis B virus infections with hepatitis B immune globulin and hepatitis B vaccine*, Lancet, **2** (8359): 1099-1102.
3. **Bodsworth, N., Donovan, B., Nightingale, B.N. (1989):** *The effect of concurrent human immunodeficiency virus infection on chronic hepatitis B: a study of 150 homosexual men*, J. Infect. Dis., **160** (4): 577-582.
4. **Coursaget, P., Yvonnet, B., Chotard, J., Vincelot, P., Sarr, M., Diouf, V., Chiron, J.P., Diop-Mar, I. (1987):** *Age- and sex-related study of hepatitis B virus chronic carrier state in infants from an endemic area (Senegal)*, J. Med. Virol., **22** (1): 1-5.
5. **Cucuianu, M., Trif, I., Cucuianu, A. (1994):** *Hemostaza. Biochimie, Fiziologie clinică*, Editura Dacia, Cluj-Napoca.
6. **Girke, J., Wedemeyer, H., Wiegand, J., Manns, M.P., Tillmann, H.L. (2008):** *Acute hepatitis B: is antiviral therapy indicated? Two case reports.*, Dtsch Med. Wochenschr. **133** (22): 1178-1182.
7. **Hong, M. Z., Huang, W.K., Min, F., Xu, J.C., Lin, Z., Fang, K.N., Pan, J.S. (2014):** *Enhanced HBsAg Synthesis Correlates with Increased Severity of Fibrosis in Chronic Hepatitis B Patients*, PLoS ONE **9** (1): e87344.
8. **Horvath, J., Raffanti, S.P. (1994):** *Clinical aspects of the interactions between human immunodeficiency virus and the hepatotropic viruses*, Clin. Infect. Dis., **18** (3): 339-347.
9. **Lok, A.S.F., McMahon, B.J. (2009):** *Chronic Hepatitis B: Update 2009*, AASLD Practice Guideline Update., Hepatology, **50** (3).
10. **Mast, E.E., Margolis, H.S., Fiore, A.E., Brink, E.W., Goldstein, S.T., Wang, S.A., Moyer, L.A., Bell, B.P., Alter, M.J. (2005):** *A comprehensive immunization strategy to eliminate transmission of hepatitis B virus infection in the United States - Recommendations of the advisory committee on immunization practices (ACIP)*, Part 1: *Immunization of infants, children and adolescents*, Morbidity and mortality weekly report, **54**: RR-16, 1-31.
11. **McMahon, B.J., Alward, W.L., Hall, D.B., Heyward, W.L., Bender, T.R., Francis, D.P., Maynard, J.E. (1985):** *Acute hepatitis B virus infection: relation of age to the clinical expression of disease and subsequent development of the carrier state*, J. Infect. Dis., **151** (4): 599-603.
12. **McMahon, B.J., Holck, P., Bulkow, L., Snowball, M. (2001):** *Serologic and clinical outcomes of 1536 Alaska Natives chronically infected with hepatitis B virus*, Ann. Intern. Med., **135**: 759-768.
13. **Misăilă, C., Dumitru, Gabriela (2010):** *Fiziologia animalelor și a omului. Lucrări practice*, Ed. Tehnopress, Iași.
14. **Shikata, T., Karasawa, T., Abe, K., Uzawa, T., Suzuki, H., Oda, T., Imai, M., Mayumi, M., Moritsugu, Y. (1977):** *Hepatitis B e antigen and infectivity of hepatitis B virus*, J. Infect. Dis., **136** (4): 571-576.
15. **Silverman, N.S., Darby, M.J., Ronkin, S.L., Wapner, R.J. (1991):** *Hepatitis B prevalence in an unregistered prenatal population. Implications for neonatal therapy*, JAMA, **266**: 2852-2855.
16. **Tassopoulos, N.C., Papaevangelou, G.J., Sjogren, M.H., Roumeliotou-Karayannis, A., Gerin, J.L., Purcell, R.H. (1987):** *Natural history of acute hepatitis B surface antigen-positive hepatitis in Greek adults*, Gastroenterology, **92** (6): 1844-1850.
17. **Thomas, A.R., Fiore, A.E., Corwith, H.L., Cieslak, P.R., Margolis, H.S. (2004):** *Hepatitis B vaccine coverage among infants born to women without prenatal screening for hepatitis B virus infection: effects of the Joint Statement on Thimerosal in Vaccines*, Pediatr. Infect. Dis. J., **23**: 313-318.
18. **West, D.J., Margolis, H.S. (1992):** *Prevention of hepatitis B virus infection in the United States: a pediatric perspective*, Pediatr. Infect. Dis. J., **11**: 866-874.

1“Alexandru Ioan Cuza” University of Jassy, Faculty of Biology, Romania

2 “S.C. Dorna Medical S.R.L.”, Vatra Dornei

3 University of Medicine and Pharmacy Tg. Mures, Romania

*ciornea@uaic.ro