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Some Features of Biochemical Blood Analysis in Patients with Hepatocellular Carcinoma Associated with Viral Hepatitis B and C

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INTRODUCTION:

Hepatocellular carcinoma is the fifth most frequent and third most frequent cause of death from cancer, with a prevalence of about 1 million cases per year [1]. Hepatocellular carcinoma is the second leading cause of death from cancer in men and sixth among women in the world [2]. The incidence ranges from 2/100 000 in Europe and up to 30/100 000 cases per year in endemic regions for viral hepatitis B and C (Southeast Asia and Africa). Men suffer 4-10 times more often than women. Any patient with chronic liver disease is at high risk for hepatocellular carcinoma. In liver cirrhosis, the prevalence of hepatocellular carcinoma is 2-60% [3].

About 80% of cases of hepatocellular carcinoma are associated with chronic viral hepatitis. In chronic viral hepatitis B, the risk of hepatocellular carcinoma increases by 5–15 times, and in chronic viral hepatitis C - by 11.5–17 times, compared with individuals without chronic viral hepatitis [4]. According to data obtained during a 30-year follow-up in liver cirrhosis caused by chronic viral hepatitis C, the risk of developing hepatocellular carcinoma annually increases by 1-4% [5].The age at which hepatocellular carcinoma debuts varies greatly in different parts of the world. The development of hepatocellular carcinoma after 60 years is typical for the countries of North America, the European Union and Japan. Whereas in most African and Asian countries, hepatocellular carcinoma is detected in 30-60 years. A study conducted on 18,031 patients from 14 countries of the world showed the average age at which hepatocellular carcinoma debuted for Japan was 69 years, for Europe 65 and for North America 62 years, for South Korea 59 years and for China 52 years, respectively [6]. Data from a cohort study of 1552 patients in Africa, published in 2015, showed an average age of hepatocellular carcinoma onset of 45 years [7]. It should be noted that, unlike other more common neoplasms that tend to reduce the incidence, the incidence of hepatocellular carcinoma is increasing [8]. Hepatocellular carcinoma is often asymptomatic, and the onset of symptoms can signal the development of a serious illness. In this case, hepatocellular carcinoma is often diagnosed already in stage B or C. It should be noted that in some patients with small tumors decompensated cirrhosis is often noted [9].

Clinical signs and symptoms of liver cirrhosis, which is often present in patients with hepatocellular carcinoma and obscures the presence of antecedent early hepatocellular carcinoma [10].

Keywords: Viral hepatitis B, viral hepatitis C, hepatocellular carcinoma, biochemical blood test

MATERIALS AND RESEARCH METHODS

This work includes the results of a retrospective and prospective analysis of the case histories of patients diagnosed with hepatocellular carcinoma of the Republican Specialized

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The patients were divided into 3 groups. Group 1 included patients with hepatocellular carcinoma, positive tests for viral hepatitis B. Group 2 consisted of patients with hepatocellular carcinoma, and positive tests for viral hepatitis C. Group 3 included patients with hepatocellular carcinoma, in whom serological markers for viral hepatitis were negative.

The criteria for inclusion in-group 1 were the presence of hepatocellular carcinoma, confirmed by ultrasound and computed tomography and / or magnetic resonance imaging and histological confirmation of the diagnosis, as well as the presence of positive test results for viral hepatitis B.

The exclusion criteria were negative markers of viral hepatitis B, the presence of concomitant hepatitis C, human immunodeficiency virus, age under 18 years.

The criteria for inclusion in-group 2 were the presence of hepatocellular carcinoma, confirmed by ultrasound and computed tomography and / or magnetic resonance imaging and histological confirmation of the diagnosis, as well as positive ELISA results for antibodies to viral hepatitis C and / or positive values of the polymerase chain reaction ribonucleic acid of viral hepatitis C.

The exclusion criteria were negative markers for viral hepatitis C, the presence of concomitant hepatitis B, human immunodeficiency virus, age under 18 years.

The criteria for inclusion in-group 3 were the presence of hepatocellular carcinoma, confirmed by ultrasound and computed tomography and / or magnetic resonance imaging and histological confirmation of the diagnosis, negative markers for viral hepatitis and human immunodeficiency virus, age less than 18 years.

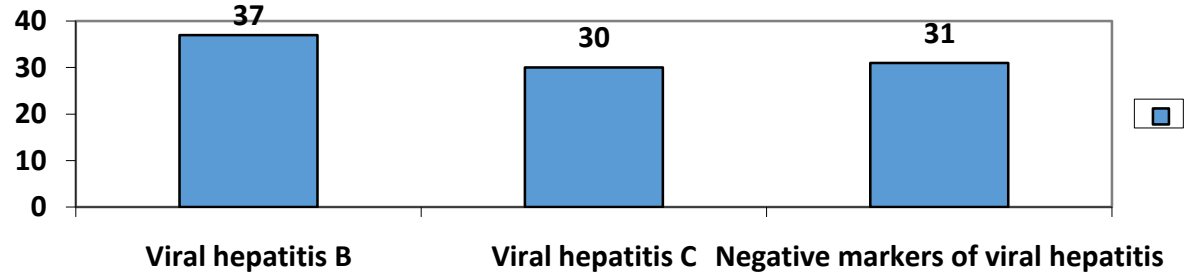
The study included the results of a biochemical blood test.

The stages of hepatocellular carcinoma were established in accordance with the international classification according to the TNM system adopted in our country.

Statistical analysis was performed using Excel 16.0 software. For each series of results, the arithmetic mean (M) and the error of the mean (m) were calculated. Comparison of the two samples was carried out using the xi-square. When comparing the mean values, the Student's t-test was used. The level of reliability of statistical indicators was taken as $p < 0.05$.

RESULTS AND DISCUSSION

Group 1 with hepatocellular carcinoma and positive markers of chronic hepatitis B consisted of 37 patients, group 2 with hepatocellular carcinoma, positive markers of hepatitis C had 30, and group 3 included 31 patients with hepatocellular carcinoma and negative markers of viral hepatitis (Picture 1).



Picture 1
Distribution of patients into groups, based on the presence or absence of markers of viral hepatitis B and C

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In the analysis, hepatocellular carcinoma was more common in men (62.77 %) than in women in 35 (37.23%) people.

At the same time, the number of men prevailed in all groups with viral hepatitis. However, in the group of patients without viral hepatitis, the numerical advantage was on the side of women. (Table 1).

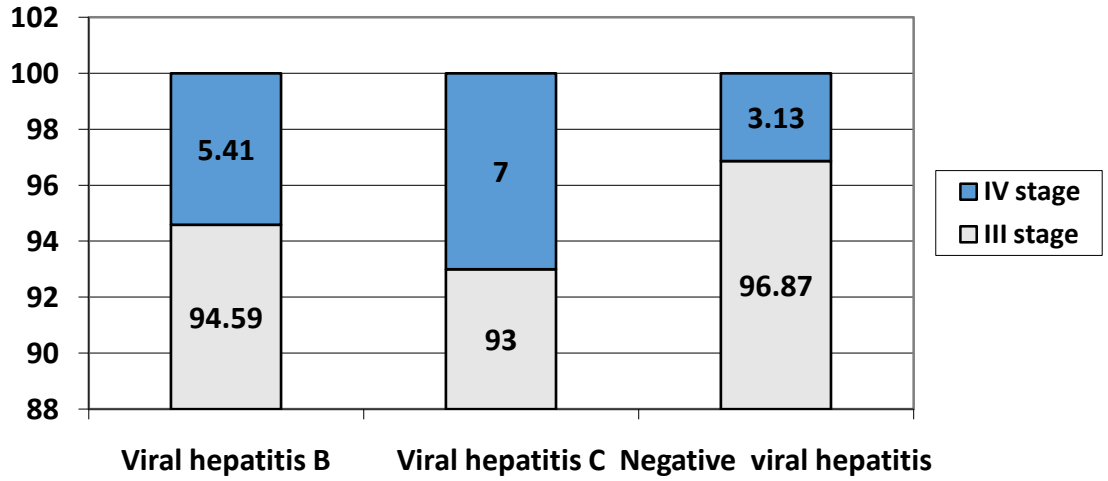
Table 1
Distribution of patients by gender and age

Groups	**Gender**				**Age M±m**
	Male		**Female**		
	n	%	n	%	
1 group n=37	27	72,97	10	27,03	46,7±5.18
2 group n=30	25	83,33	5	16,67	64,22±5.27
3 group n=31	11	35,48	20	64,52	54,41±5.6

When analyzing the age structure, 67.02% of patients were over the age of 50 years in the group with chronic viral hepatitis B, 96.6% in the group with chronic viral hepatitis C and 64.52% in the group without hepatitis.

At the time of diagnosis of hepatocellular carcinoma, cirrhosis was observed in 67% of cases in the general group. It should be noted that liver cirrhosis was more common in the group with chronic viral hepatitis B (75.68%) and chronic viral hepatitis C (83.33%), while in the group with hepatocellular carcinoma with negative viral markers cirrhosis liver was found only in 38.71% of cases ($p < 0.05$). Nevertheless, 24.32% of patients in the group with hepatocellular carcinoma associated with chronic viral hepatitis B and in 16.67% of patients in the group with hepatocellular carcinoma associated with chronic hepatitis C virus cirrhosis was not observed, which explains the effect of the presence of hepatitis B viruses themselves and C in hepatocytes for oncogenesis of hepatocellular carcinoma.

The majority of patients according to the TNM classification were stage III. This indicates a rather late diagnosis of hepatocellular carcinoma (Picture 2).



Picture 2
Patient distribution according to TNM classification

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The data of biochemical analyzes in the studied groups are presented in table 2.

Table 2

The results of a biochemical blood test in the studied groups

Groups / **Indicators**	**iral hepatitis B and hepatocellular carcinoma n=37 M ± m**	**iral hepatitis C and hepatocellular carcinoma n=30 M ± m**	**Hepatocellular carcinoma with negative specific markers of hepatitis n=31 M ± m**	**Normal indicators**
Total bilirubin (μmol / liter)	25,49±3,2	24,71±2,68	18,12±1,82	2,0-21,0
Alanine aminotransferase (unit / liter)	93,54±10,5	76±10,46	59,87±6,92	0-64
Aspartate aminotransferase (units / liter)	131,78±13,89	92,7±11,08	66,81±7,12	0-62
Creatinine (mmol / liter)	44,29±4,15	78,67±9,39	47,78±7,3	44-80
Urea (mmol / liter)	5,06±0,42	7,61±1,17	4,8±0,35	1,7-8,3
Residual nitrogen (mmol / liter)	2,52±0,23	2,96±0,26	2,28±0,16	0-4
Albumin (gram / liter)	35,23±1,58	34,98±1,79	37,85±1,77	30-55
Amylase (units / liter)	114,93±12,05	93,46±18,31	91,9±11,82	0-220
Total protein (gram / liter)	64,35±1,88	65,22±1,54	67,0±1,3	66-87
Glucose (mmol / l)	5,01±0,27	5,17±0,17	5,27±0,19	4,2-6,4

When analyzing the results of biochemical parameters, there were no statistically significant differences in the level of total bilirubin in patients with hepatocellular carcinoma associated with viral hepatitis B and in patients in the group with hepatocellular carcinoma associated with viral hepatitis C ($p > 0.05$). However, when comparing this indicator in the group of hepatocellular carcinoma associated with chronic viral hepatitis B, as well as in the group of hepatocellular carcinoma associated with chronic viral hepatitis C with the group of patients with hepatocellular carcinoma and negative markers of viral hepatitis, a statistically higher level of total bilirubin was noted in the groups with chronic viral hepatitis B ($p<0.05$) and with chronic viral hepatitis C ($p<0.05$).

When analyzing the data of cytolytic syndrome, an increased level of alanine aminotransferase was noted in the groups with viral hepatitis. When comparing groups of patients with hepatocellular carcinoma associated with chronic viral hepatitis B and hepatocellular carcinoma associated with chronic viral hepatitis C, the level of alanine aminotransferase in the first was higher than in the second. When comparing groups of patients with hepatocellular carcinoma associated with chronic viral hepatitis B and

hepatocellular carcinoma without viral markers, the level of alanine aminotransferase was higher in the group with hepatocellular carcinoma associated with chronic viral hepatitis C. However, no statistically significant differences were found when comparing these groups. At the same time, a significantly higher level of alanine aminotransferase was revealed in the group with hepatocellular carcinoma associated with chronic viral hepatitis B, compared with the group of hepatocellular carcinoma without viral hepatitis ($p<0.05$).

A slightly different picture was in relation to the level of aspartate aminotransferase, which was increased in all three studied groups. When comparing the level of aspartate aminotransferase in the groups of patients with hepatocellular carcinoma associated with chronic viral hepatitis B and C and the group without viral hepatitis, the level of aspartate aminotransferase in the first group was statistically higher ($p<0.05$ and $p<0.05$, respectively). When comparing the group of patients with hepatocellular carcinoma associated with chronic viral hepatitis C and the group without viral hepatitis, the level of aspartate aminotransferase in the latter was lower, but there were no statistical differences ($p> 0.05$). Elevated levels of alanine aminotransferase and aspartate aminotransferase in patients with hepatocellular carcinoma associated with chronic viral hepatitis, compared with a group of patients with negative viral hepatitis, may be associated with viral liver damage, immune-mediated liver damage by viral hepatitis B and C.

Half of the patients showed a decrease in total protein (50%). The average values of the amount of albumin were within the normal range. There were no statistically significant differences in these indicators in the studied groups ($p> 0.05$).

The blood sugar level in all three groups was within the normal range; no statistically significant differences were found ($p> 0.05$).

The amylase level in the study groups was within the normal range, no statistically significant differences were found ($p> 0.05$).

The average values of urea were within the normal range in all groups. However, when comparing the group with hepatocellular carcinoma associated with chronic hepatitis C virus with the groups with hepatocellular carcinoma associated with chronic viral hepatitis B and the group without viral hepatitis, the urea level was statistically higher ($p <0.05$ and $p <0$, 05 respectively). When comparing groups with hepatocellular carcinoma associated with chronic viral hepatitis B and the group with hepatocellular carcinoma without hepatitis, there were no statistically significant differences ($p> 0.05$). Residual nitrogen in all groups was within normal limits.

When comparing the group with hepatocellular carcinoma associated with chronic viral hepatitis B with the groups with hepatocellular carcinoma associated with chronic viral hepatitis C and the group of patients with hepatocellular carcinoma without viral hepatitis, there were no statistically significant differences ($p> 0.05$). However, when comparing the group of patients with hepatocellular carcinoma associated with chronic hepatitis C virus and the group of patients with hepatocellular carcinoma without hepatitis, the differences were statistically significant ($p <0.05$).

The average creatinine values in all three compared groups were also within the physiological norm. There were no statistically significant differences in the groups of patients with hepatocellular carcinoma associated with chronic viral hepatitis B and hepatocellular carcinoma without viral markers ($p> 0.05$). In contrast, when comparing the group of patients with hepatocellular carcinoma associated with chronic hepatitis C virus with the group of patients with hepatocellular carcinoma associated with chronic hepatitis C virus and

hepatocellular carcinoma without viral hepatitis, the level of creatinine in the group with hepatitis C was statistically higher (p <0, 05 and p <0.05, respectively).

CONCLUSIONS:

1. In this study, hepatocellular carcinoma was more common in men than in women. It should be noted that hepatocellular carcinoma in men was more common in the groups with viral hepatitis, while women predominated in the group of patients with negative viral markers.

2. The presence of liver cirrhosis was statistically higher in the groups with chronic viral hepatitis compared to the group of patients with hepatocellular carcinoma without viral hepatitis.

3. The level of bilirubin in the group of hepatocellular carcinoma associated with viral hepatitis was statistically higher compared with hepatocellular carcinoma of non-viral etiology.

4. The level of alanine aminotransferase was statistically higher in the group with hepatocellular carcinoma associated with viral hepatitis B compared to non-viral etiology.

5. The urea level was statistically higher in the group with hepatocellular carcinoma associated with viral hepatitis C compared with the group of patients with hepatocellular carcinoma associated with viral hepatitis B and hepatocellular carcinoma of non-viral etiology.

6. Residual nitrogen was statistically higher in the group of patients with hepatocellular carcinoma associated with viral hepatitis C.

7. A more pronounced picture in the biochemical analysis of blood in patients with hepatocellular carcinoma against the background of viral hepatitis is due to prolonged liver damage by chronic viral hepatitis B and C.

REFERENCES

[1] Di Bisceglie AM, Sterling RK, Chung RT, Everhart JE, DienstagJL,Bonkovsky HL, et al. -Serum alpha-fetoprotein levels in patients with advanced hepatitis C: results from the HALT-C Trial.JHepatol -2005-43-P. 434-441
[2] Ferlay J, Soerjomataram I, Dikshit R, et al. -Cancer incidence and mortality worldwide: sources, methods and major patterns in GLOBOCAN 2012. -Int J Cancer- 2015-136-P.359–86
[3] Zhang BH, Yang BH, Tang ZY- Randomized controlled trial of screening for hepatocellular carcinoma. - J Cancer Res ClinOncol- 2004- 130 (7)-P. 417422].
[4] Tsai WL, Chung RT. -Viral hepatocarcinogenesis. -Oncogene. -2010-29(16)-P. 2309–2324
[5] El-Serag HB- Epidemiology of viral hepatitis and hepatocellular carcinoma. -Gastroenterology -2012-142- P.1264–1273
[6] Park , JW et al.- Global patterns of hepatocellular carcinoma management from diagnosis to death: the bridge study.- Liver Int. -2015-35-P.2155-2166
[7] Yang, J. D. et al.- Hepatocellular carcinoma occurs at an earlier age in Africans, particularly in associationwith chronic hepatitis B. -Am. J. Gastroenterol. -2015-110-P.1629-1631
[8] Siegel RL, Miller KD, Jemal A.- Cancer statistics, 2018- CA Cancer J Clin.-2018 --68(1):P.7-30

[9] Giannini E. G. et al.- Surveillance for early diagnosis of hepatocellular carcinoma: How best to do it? 2013.- 19- 47-P. 8808–8821
[10] Barghini, V., Donnini, D.,Uzzau, A., &Soardo, G. - Signs and Symptoms. Hepatocellular Carcinoma -2013- Future Outlook.
[11] Bekchanov D; Kawakita H; Mukhamediev M; Khushvaktov S; Juraev M. Sorption of cobalt (II) and chromium (III) ions to nitrogen- and sulfur-containing polyampholyte on the basis of polyvinylchloride /Polymers for Advanced Technologies 2021 https://doi.org/10.1002/pat.5209
[12] Davron, B., Mukhtar, M., Nurbek, K., Suyun, X., Murod, J. Synthesis of a New Granulated Polyampholyte and its Sorption Properties. *International Journal of Technology*. Volume 11(4), pp. 794-803. ., (2020) https://doi.org/10.14716/ijtech.v11i4.4024
[13] Mukhamediev, M.G., Bekchanov, D.Z. New Anion Exchanger Based on Polyvinyl Chloride and Its Application in Industrial Water Treatment. Russ J ApplChem 92, 1499–1505 (2019). https://doi.org/10.1134/S1070427219110053
[14] Mukhamediev, M.G., Auelbekov, S.A., Sharipova, Z.T. et al. Polymer complexes of gossypol and their antiviral activity. Pharm Chem J 20, 276–278 (1986). https://doi.org/10.1007/BF00758817
[15] Ikramova, M.E., Mukhamediev, M.G., Musaev, U.N. Complexation of hydrazine- and phenylhydrazine-modified nitron fibers with iodine/ Plasticheskie Massy: SintezSvojstvaPererabotkaPrimenenie, (12), стр. 41–45 (2004)
[16] Gafurova, D.A., Khakimzhanov, B.S., Mukhamediev, M.G., Musaev, U.N. Sorption of Cr(VI) on the anion-exchange fibrous material based on nitron. Russian Journal of Applied Chemistry, 75(1), стр. 71–74, (2002)
[17] Rustamov, M.K., Gafurova, D.A., Karimov, M.M. et al. Application of ion-exchange materials with high specific surface area for solving environmental problems. Russ J Gen Chem 84, 2545–2551 (2014). https://doi.org/10.1134/S1070363214130106
[18] Bazarova D. Some problems of counteracting crimes related to laundering of illegal proceeds in Uzbekistan Journal of Advanced Research in Dynamical and Control Systems. Volume 11, Issue 7, 2019, Pages 873-885
[19] Ismailova, Z., Choriev, R., Ibragimova, G., Abdurakhmanova, S., &Abdiev, N. (2020). Competent model of Practice-oriented education of students of the construction profile. Journal of Critical Reviews. Innovare Academics Sciences Pvt. Ltd. https://doi.org/10.31838/jcr.07.04.85
[20] Ismailova, Z., Choriev, R., Musurmanova, A., &Aripjanova, M. (2020). Methods of training of teachers of university on advanced training courses. Journal of Critical Reviews. Innovare Academics Sciences Pvt. Ltd. https://doi.org/10.31838/jcr.07.05.85
[21] Ismailova, Z., Choriev, R., Salomova, R., &Jumanazarova, Z. (2020). Use of economic and geographical methods of agricultural development. Journal of Critical Reviews. Innovare Academics Sciences Pvt. Ltd. https://doi.org/10.31838/jcr.07.05.84
[22] Isakov, A., Tukhtamishev, B., &Choriev, R. (2020). Method for calculating and evaluating the total energy capacity of cotton fiber. IOP Conference Series: Earth and Environmental Science, 614(1), 012006
[23] Davirov, A., Tursunov, O., Kodirov, D., Baratov, D., &Tursunov, A. (2020). Criteria for the existence of established modes of power systems. IOP Conference Series: Earth and Environmental Science, 2020, 614(1), 012039
[24] Obidov, B., Choriev, R., Vokhidov, O., &Rajabov, M. (2020). Experimental studies of horizontal flow effects in the presence of cavitation on erosion-free dampers. IOP Conference Series: Materials Science and Engineering, 883(1), 012051

[25] Khasanov, B., Choriev, R., Vatin, N., &Mirzaev, T. (2020). The extraction of the water-air phase through a single filtration hole. IOP Conference Series: Materials Science and Engineering, 2020, 883(1), 012206
[26] Shokhrud F. Fayziev The problem of social stigma during a pandemic caused by COVID-19 International Journal of Advanced Science and Technology Vol. 29, No. 7, (2020), pp. 660-664 http://sersc.org/journals/index.php/IJAST/article/view/13965/7188
[27] FayziyevShokhrudFarmonovich Medical law and features of legal relations arising in the provision of medical services. International journal of pharmaceutical research Volume 11, Issue 3, July - Sept, 2019 P. 1197-1200 doi:10.31838/ijpr/2019.11.03.088 http://www.ijpronline.com/ViewArticleDetail.aspx?ID=11016
[28] Bryanskaya Elena, FayzievShokhrud, Altunina Anna, MatiukhaAlena Topical Issues of an Expert Report in the Process of Proving in a Criminal Examination. International Journal of Engineering and Advanced Technology (IJEAT) ISSN: 2249 – 8958, Volume-9 Issue-1, October 2019 5345-5349 DOI: 10.35940/ijeat.A2946.109119
[29] https://www.ijeat.org/wp-content/uploads/papers/v9i1/A2946109119.pdf
[30] FayzievShokhrud (2019) Legal Aspects of Transplantology in the Republic of Uzbekistan. Systematic Reviews in Pharmacy, ISSN: 0976-2779, Vol: 10, Issue: 2, Page: 44-47 doi:10.5530/srp.2019.2.08
[31] http://www.sysrevpharm.org//fulltext/196-1575419211.pdf?1586863081
[32] Tulaganova, G.Some issues of observance of international legal norms of fight against legalization of criminal incomes in the Republic of UzbekistanJournal of Advanced Research in Dynamical and Control Systems 12(2 Special Issue), c. 143-155