The aim of this study is to identify the frequency and severity of liver damage using ultrasound elastometry in chronic viral hepatitis B (HBV) among the population of different regions of Azerbaijan. Objects and methods. The study involved patients residing in Baku, Sumgait and certain regions of Azerbaijan and seeking medical care at the Medical Centre “Medikus clinic” in Baku. There were examined 639 participants with HBV, 398 men and 241 women. They were divided into 5 age groups: 1st group included individuals aged from 18 to 29, 2nd group involved patients aged 30-39, 3rd group included patients aged 40-49, 4th group was formed by 50-59 year old patients and 5th group included individuals of 60 years and older. In order to verify the HBV diagnoses, specific laboratory investigation methods and their evaluation criteria were applied. The study was carried out by ELISA using the Access 2 Immunoassay System (Beckman Coulter). The participants were diagnosed as HBV positive, when their indicator equaled to 5 IU/ml. The study was conducted on by applying the “Rotor Gene Q” (Germany). Elastometry was performed by using 2D – Supersonic Aixplorer SWE (France). The examination was carried out according to the Cut–offs scale, and liver fibrosis was determined according to the METAVIR scale (sensitivity of the method is more than 80%, specificity is more than 90%). The level of hepatic tissue density was estimated in cRa. The density value of more than 5 kPa was regarded as pathological. Ultrasound elastometry of the liver will enable to assess the intensity of its fibrosis and predict its possible complications, which, along with other preventive measures, will significantly reduce disability and mortality. Results. The data on the liver elastometry indicators of men and women with confirmed diagnosis of chronic HBV, regardless of their region of residence are presented. In male patients, there is an obvious reliable association between an increase in the stiffness of the liver tissue and an increase in the age of the individuals (1 - 5.3±0.4 kPa; 2 – 5.4±0.2; 3 – 6.3±0.6; 4 – 8.2±0.8; 5 – 10.8±0.8 (p<0.001)). Among women under 50 years, the hepatic tissue stiffness index values corresponded the normal ones (less than 5 kPa), and then significantly increased, then in the last age group it decreased unreliably (1 – 4.4±0.2; 2 – 4.2±0.1; 3 – 4.2±0.1; 4 – 9.7±1.4 (p<0.001); 5 – 8.3±1.2). Comparing the results obtained, it can be stated that in males with HBV, gender and age play a significant role in the development of liver fibrosis. In all age groups, this indicator was higher than the standard. Among women under the age of 50, the process does not develop, but it sharply picked up the growth rate after 50 years, and then stabilized. In men, the discussed indicator was higher compared to women. Conclusion. Chronic HBV has a significant negative effect on the indicator of assessing the degree of development of fibrous tissue. The age of 50 years in patients with chronic HBV is an important factor, which in many cases, without gender differences, significantly increases the rate of formation of fibrous tissue in the liver.

Key words: chronic viral hepatitis B, liver elastometry, fibrous tissue.

Introduction

Chronic viral hepatitis B (HVB) is still remaining as one of the pressing health problems in most countries due to its growing prevalence that results in disability and mortality [1]. The HBV presence is accompanied by the development of a number of pathological processes, and, in particular, cardiovascular diseases, type 2 diabetes mellitus, disorders of lipid and carbohydrate metabolism. There is also a growing occurrence rate of hepatitis transformation into non-alcoholic fatty liver disease (NAFLD), cirrhosis of the liver (CP), hepatocellular carcinoma (HCC) [2, 3, 4]. The latest highly reliable, non-invasive andatraumatic investigation techniques are believed to play a critical role in early detection and timely correction of therapeutic tactics. Therefore, early detection of fibrous changes is among healthcare priorities. Liver fibrosis refers to a number of structural and functional changes in various chronic liver diseases [5]. Among the investigation methods for assessing the severity of liver damage, ultrasound elastometry seems as the most informative, accessible and non-invasive imaging technique based on determining the stiffness of liver tissue by measuring the velocity of a low-frequency elastic transverse wave shearing through the liver. The stiffer the tissue is, the higher the velocity of the transverse wave shearing we observe. The findings are measured in kilopascals (kPa) and can vary from 1.5 to 7.5 kPa. The normal value is about 5 kPa [6, 7, 8].

The aim of this study is to identify the frequency and intensity of liver tissue damage by ultrasound elastometry in patients with chronic viral hepatitis B (HBV) residing in various regions of Azerbaijan.

Material and methods

The study included patients living in Baku, Sumgait and certain regions of Azerbaijan and seeking medical care at the Medical Centre “Medikus clinic” in Baku. The study involved 639 patients with HBV, 398 men and 241 women, divided into 5 age groups: 1st group included patients aged from 18 to 29, 2nd group included patients aged 30-39, 3rd group included patients aged 40-49, 4th group was formed by 50-59 year old patients and 5th group included individuals of 60 years and older. In order to verify the HBV diagnoses, specific laboratory investigation methods and their evaluation criteria were applied. The study was carried out by ELISA using the Access 2 Immunoassay System (Beckman Coulter). The participants were diagnosed as HBV positive, when their indicator equaled to 5 IU/ml. The study was conducted on by applying the “Rotor Gene Q” (Germany). Elastometry was performed by using 2D – Supersonic Aixplorer SWE (France). The examination was carried out according to the Cut–offs scale, and liver fibrosis was determined according to the METAVIR scale (sensitivity of the method is more than 80%, specificity is more than 90%). The level of hepatic tissue density was estimated in cRa. The density value of more than 5 kPa was regarded as pathological. Ultrasound elastometry of the liver will enable to assess the intensity of its fibrosis and predict its possible complications, which, along with other preventive measures, will significantly reduce disability and mortality. Results. The data on the liver elastometry indicators of men and women with confirmed diagnosis of chronic HBV, regardless of their region of residence are presented. In male patients, there is an obvious reliable association between an increase in the stiffness of the liver tissue and an increase in the age of the individuals (1 - 5.3±0.4 kPa; 2 – 5.4±0.2; 3 – 6.3±0.6; 4 – 8.2±0.8; 5 – 10.8±0.8 (p<0.001)). Among women under 50 years, the hepatic tissue stiffness index values corresponded the normal ones (less than 5 kPa), and then significantly increased, then in the last age group it decreased unreliably (1 – 4.4±0.2; 2 – 4.2±0.1; 3 – 4.2±0.1; 4 – 9.7±1.4 (p<0.001); 5 – 8.3±1.2). Comparing the results obtained, it can be stated that in males with HBV, gender and age play a significant role in the development of liver fibrosis. In all age groups, this indicator was higher than the standard. Among women under the age of 50, the process does not develop, but it sharply picked up the growth rate after 50 years, and then stabilized. In men, the discussed indicator was higher compared to women. Conclusion. Chronic HBV has a significant negative effect on the indicator of assessing the degree of development of fibrous tissue. The age of 50 years in patients with chronic HBV is an important factor, which in many cases, without gender differences, significantly increases the rate of formation of fibrous tissue in the liver.

Key words: chronic viral hepatitis B, liver elastometry, fibrous tissue.
18-29 years, 2nd – 30 – 39 years, 3rd – 40 – 49 years, 4th – 50-59 years and 5th -60 years and over. In order to verify the presence of HBV, specific laboratory investigation methods and their evaluation criteria were applied. The study was carried out by ELISA using the Access 2 Immunoassay System (Beckman Coulter). For hepatitis B virus, the reliable indicator equalled 5 IU/ml. Tissue elastometry was performed by 2D–Supersonic Aixplorer SWE (France). The assessment was carried out according to the Cut-offs scale, and liver fibrosis was evaluated according to the METAVIR scale (sensitivity of the method is higher than 80%, specificity is higher than 90%). The stiffness of hepatic tissue density was measured in kPa. The density value of more than 5 kPa was regarded as pathological.

Statistical data processing was carried out by the Microsoft Excel–2010 program. The methods used included the calculation of correct distribution of averages, the reliability of differences calculated by the Student's t-criterion, the Mann–Whitney U test, as well as the calculation of the average value (M) and the error of the average value (m).

**Results and discussion**

One of the main objectives in this study was to measure and assess the elastography parameters in patients with chronic HBV in order to verify the features of the pathological process for further detailed analysis, taking into account the presence of comorbid conditions and their effect on metabolic processes. Below there are the data reflecting the liver elastography indicators among the male and female patients with a diagnosis of chronic HBV, regardless of the region of their residence.

Male patients were found to demonstrate a reliable association between an increase in the stiffness of the liver tissue and an increase in the age (1 – 5.3±0.6 kPa; 2 – 5.5±0.4; 3 – 7.3±1.2; 4 – 8.3±1.2 (p<0.05)); 5 – 5.6±0.5 (p <0.05)), and statistically significantly growth of the liver stiffness in the patients under 50 years. As for the women, this index was found within the normal range before the age of 50, and then after 50 years it grew up in more than 2.5 times and then, after 60 years, remained virtually unchanged (1 – 4.6±0.3; 2 – 4.8±0.8; 3 – 4.2±0.2; 4 – 10.5±1.9 (p<0.00); 5 – 10.7±2.7 (p>0.05)). Women residing in Baku, confirmed the peculiarities associated with a significant increase in the stiffness of liver tissue after 50 years that requires careful study and clear explanation. Moreover, the process of liver tissue stiffness does not reduce the pace of its development and can result in the formation of life-threatening complications. The studied index was slightly higher in the male patients under 50 years of age than among the female patients. This phenomenon is to be in the focus of further in-depth study paying special attention to the effects of comorbid diseases and metabolic disorders.

At the next stage of this study, we investigated the state of this issue in patients from Sumgait. The results obtained indicate that among the men, the index reflecting the liver tissue stiffness showed a very specific dynamics in age groups: it exceeded the reference values in the 1st group, while in the next two groups it was lower than normal, and in the patients over 50 years it rose increased almost twice (1 – 5.9±0.8; 2 – 4.8±0.5; 3 – 4.5±0.2; 4 – 8.4±1.5 (p<0.001); 5 – 14.1±8.6 (p<0.01)).

As for the women, the age dynamics of the hepatic tissue stiffness index was also very noticeable: very low indices were revealed in younger individuals under 40-49 years. Then, in the group aged 50-59 years, this index elevated in almost 2.5 times, and then in the women of 60 years and older it decreased just as sharply in almost 1.5 times. In both cases, the changes were statistically significant (1 – 3.9±0.2; 2 – 4.1±0.4; 3 – 4.2±0.2; 4 – 10.3±5.0 (p<0.05); 5 – 5.8±0.1 (p<0.05)).

In almost all age groups, this indicator was higher in men than in women. Among men living in the various regions of Azerbaijan, the index reflecting the state of liver tissue stiffness did not demonstrate statistically significant age-dependent dynamics before the age of 60, but in the group over 60 years this value doubled (1 – 5.1±0.2; 2 – 5.3±0.2; 3 – 5.3±0.4; 4 – 7.5±1.4; 5 – 13.0±3.1 (p<0.01)). It has also been detected that in all age groups the indices were higher than the reference values; the age factor was found as a contributor to the pathological changes resulting in the 1.5-fold increase in the index values in the individuals aged from 50 to59 years old compared with those of 40-49 years old, moreover the index was almost twice as high among the patients 60 years and older compared with the 50-59 year old patients.

Among the women, the average value of the index remained within the same range of values for the patients from 18 to 50 years, and then it sharply
doubled in the individuals aged 50-59 years. In 60 years and older, this index remained the same as for 50-59 year participants. In the women, the index exceeded the reference values only in the group over 50 years (1–4.2±0.1; 2–4.4±0.2; 3–4.2±0.2; 4–7.2±1.2; 5–7.0±1.2 (p≤0.05)).

Conclusion

In closing, it should be noted that the technique used in this study to assess fibrotic liver damage in individuals with chronic viral hepatitis B completely meets the requirements of specialists; this technique has been shown to be quite accurate to distinguish fibrosis stages [7, 8]. Determining the liver fibrosis index is of significant clinical importance for monitoring the dynamics of changes in patients with hepatitis, assessing treatment tactics and thus, predicting treatment outcomes. Therefore, the highly reliable result obtained can serve as a ground for solving an important medical and social task in early detection and successful treatment of hepatitis.

The study has demonstrated that HBV infection significantly impacts on the liver tissue changes resulting in stiffness. Moreover, this process begins much earlier in men than in women. In the presence of HBV in men, the pathological process is registered starting from the age of 18, while in women it is observed mainly in aged individuals. The analysis of individual regions of residence has shown that among the men with HBV diagnosis who reside in Baku, the liver fibrosis index is higher compared to the women. In the women, the age of 50 years is the boundary, striding across which is associated with the progressive elevation of the liver fibrosis index. Among the population of Baku with HBV diagnosis, the rate of liver tissue fibrosis in male individuals compared to female ones is significantly higher to the age of 50 year, and then the difference becomes insignificant. In Sumgait, the situation did not differ significantly from the picture presented above. The age and sex in patients with chronic HBV are risk factors that accelerate the development of liver tissue fibrosis that significantly worsens the functional state of the liver. Thus, the average liver fibrosis value in patients from various regions of Azerbaijan is correlated with age and sex.

Prospects for further research

In-depth investigation of the liver tissues fibrosis under comorbid conditions, including metabolic syndrome, type 2 diabetes mellitus, arterial hypertension, dyslipidemia in patient of various age groups can contribute to the clear vision of the triggering mechanisms of the liver tissues fibrosis.

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Результати. Наведено дані, що відображають показники еластометрії печінки серед чоловічого та жіночого населення незалежно від регіону проживання, із встановленим діагнозом хронічний НВВ. В осіб чоловічої статі очевидний достовірний зв’язок збільшення показника жорсткості печінкової тканини зі збільшенням віку обстежених осіб (1 - 5,3±0,4 кПа; 2 – 5,4±0,2; 3 – 6,3±0,6; 4 – 8,2±0,8; 5 – 10,8±0,8 (р<0,001)). Серед жінок показник жорсткості печінкової тканини до 50 років мав значення, що відповідали нормі (менше 5 кПа), а потім достовірно підвищувався, і в останній віковій групі недостовірно знижувався. (1– 4,4±0,2; 2 – 4,2±0,1; 3 – 4,2±0,1; 4 – 9,7±1,4 (р<0,001); 5 – 8,3±1,2). Порівняючи отримані результати, можна констатувати, що в осіб чоловічої статі за наявності НВВ стать та вік відіграють значну роль у розвитку фіброзу печінки. У всіх вікових групах цей показник був вищий за нормативний. Серед осіб жіночої статі до 50 років процес не розвивався, але різко набирав темпи зростання після 50 років, а потім стабілізувався. У чоловіків обговорюваний показник був вищим порівняно з жінками.

Висновки. Хронічний НВВ має значний негативний вплив на показник оцінки ступеня розвитку фіброзної тканини. Вік 50 років, у хворих на хронічний НВВ є важливим фактором, який у багатьох випадках без гендерних відмінностей значною мірою збільшує швидкість формування в печінці фіброзної тканини.