

ANNOTATION

to the dissertation work of Saussakova Saniya Baglanbayevna on topic “Modern approaches to assessing the quality of life of patients with chronic hepatitis B in the Republic of Kazakhstan”, for the degree of Doctor of Philosophy (PhD) in specialty 8D10103 – “Public Health”

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Relevance of the research. Viral hepatitis is one of the most important global health problems in the world. By 2030, it is planned to completely eliminate hepatitis as a public health threat, achieving a 90% reduction in new infections and a 65% reduction in mortality (WHO, 2016).

The issue of high incidence of viral hepatitis remains relevant in public health, including in Kazakhstan. In the country, due to routine immunization against viral hepatitis B over more than past 20 years, there has been a steady decrease in the incidence up to 59.8 times. However, the growth of its first identified chronic forms is a source of concern.

According to official data from the dispensary registration of patients, to date, about 57 thousand people with viral hepatitis B have been registered in Kazakhstan, of which about 25 thousand cases account for the chronic form. The highest incidence of chronic forms of viral hepatitis B (about 87%) is registered in the age group from 30 to 60 years (Ministry of Health of the Republic of Kazakhstan, 2020).

The relevance of studying the incidence of chronic viral hepatitis B is also associated with an increase in the detection of positive markers, despite the vaccination program in Kazakhstan, and an increasing degree of detection of complications (hepatocellular carcinoma, cirrhosis of the liver, etc.) (Konysbekova A. et al., 2017). In addition, one of the significant aspects of chronic viral hepatitis should include their impact on the social functioning of a person and the decline of his quality of life (Karacaer Z. et al., 2017).

In addition, the medical community in the country has long been actively discussing the need to optimize screening examinations to detect viral hepatitis B among the contingent of people at increased risk of infection. In accordance with the recommendations of the World Health Organization, hepatitis screening should be comprehensive to identify endemic regions, transmission routes, and resources needed for patient management (WHO, 2015).

Thus, based on the above, the study of the quality of life of patients, analysis of the burden of viral hepatitis B are important for assessing the health of this population group, existing and planned health care programs, as well as the effectiveness of investing government funds.

The aim of the research

Assessing of the burden of chronic hepatitis B and development of approaches

to assess the quality of life of patients with chronic hepatitis B.

Research objectives

1 to study the medical and social characteristics of patients with chronic hepatitis B;

2 to assess the quality of life of patients with chronic hepatitis B during treatment;

3 to determine the socioeconomic burden of chronic hepatitis B;

4 to develop recommendations for optimizing the quality of life and the detection of patients with chronic hepatitis B.

Materials and methods of research

1. The meta-analysis of literary sources. The data of published studies in the scientific international library systems, such as PubMed, Medline, ProQuest, Cochrane Central register of controlled trials, Clinicaltrials.gov and Web of Science, were analyzed. The meta-analysis of observational studies was carried out in accordance with the international PRISMA guidelines.

2. The study of medical and social characteristics of patients with chronic viral hepatitis B. The main method was a retrospective study. The materials of the research were the medical records of patients registered with D-registration in hepatological Centers for the period from 2003 to 2021. Age and sex structure, clinical and demographic characteristics, risk factors, and laboratory data were assessed.

3. The study of the quality of life of patients with chronic hepatitis B during treatment. The main method was a survey. Standardized questionnaires such as SF-36 and EQ-5D-5L were used.

At the planning stage, the sample size was calculated (according to the N.Fox method). Taking into account the sample size, 239 patients at the age from 18 to 83 years took participation into the research.

Regression analysis was used to evaluate associations/dependencies. A disperse multivariate ANOVA analysis was carried out in order to study the domains that show the dominant influence. The ROC model analysis was built.

4. The study of the socio-economic burden of patients with chronic viral hepatitis B. The materials of the study were the case-records of patients with chronic hepatitis B, without serious liver complications or with a compensated form of liver cirrhosis, who received antiviral therapy based on one of the antiviral therapy strategies. In order to assess cost-effectiveness, the expected net benefit to health care was calculated to estimate the difference in effects between strategies by dividing the difference in cost, taking into account the cost-effectiveness threshold.

5. The development of recommendations for optimizing the quality of life and the detection of patients with chronic hepatitis B. As part of a cross-sectional study, a questionnaire was developed to determine the awareness of workers in beauty sphere about viral hepatitis B (103 participants). The prevalence of the viral hepatitis B marker, anti- HBcore, among the healthy population of Kazakhstan was also studied, and the relationship of positive serological markers of hepatitis B with risk factors and behavior in 5709 Kazakhstani blood donors in the age from 18 to 66 years was studied.

Scientific novelty

For the first time in public health of the Republic of Kazakhstan:

1. As a result of the meta-analysis of the quality of life, the negative impact of chronic hepatitis B on the physical and mental state of patients was proved.
2. The medical and social characteristics of patients with chronic hepatitis B were determined: average age, married, with higher education, employed, with a history of chronic diseases of the respiratory and digestive organs, treated before the onset of the disease in surgical and dental clinics, also cosmetic procedures that had viral hepatitis A in early childhood.
3. The quality of life of patients with chronic hepatitis B was assessed during treatment, and the factors that have the greatest impact on the change in the quality of life of these patients were identified (duration of the disease, social status of the patient, type of antiviral treatment).
4. The socio-economic burden of the disease was determined. The threshold value of the cost of treatment effectiveness is more than \$2000 per QALY in the case of the use of high-tech antiviral therapy drugs.
5. Evidence-based modern recommendations for optimizing the quality of life and the detection of patients with chronic hepatitis B are proposed.

Practical significance of the study

The practical significance of the work involves the possibility of health managers, using the results/conclusions/recommendations proposed as part of this research, to develop effective programs for the prevention, diagnosis and treatment of chronic hepatitis B in the Republic of Kazakhstan.

The analysis and results of the study are set out in “Ways to detect chronic hepatitis B” guidelines in the Republic of Kazakhstan”, amendments and additions were proposed to the order of the Ministry of Health of the Republic of Kazakhstan №113 “On approval of requirements for medical examination of donors, safety and quality in the production of blood products for medical use” (protocol of the Scientific Council of the Scientific and production center for transfusiology of the Ministry of Health of RK №3 dated 24.04.2022).

Theoretical significance of the study

The theoretical significance of the work is determined by its contribution to the modern understanding of the medical, social and economic aspects of chronic hepatitis B in the Republic of Kazakhstan. The focus of the research on the quality of life of patients with chronic hepatitis B adds to the existing body of knowledge about the impact of the disease on patients’ well-being. The development of recommendations for optimizing the detection of patients with chronic viral hepatitis B contributes to the development of more effective strategies for screening and diagnosing this disease, the initiation of timely treatment, which in turn can reduce complications and reduce the cost of patients’ treatment.

The factual material can be used in the development of the Roadmap and the National plan to combat viral hepatitis, as well as the conclusions and recommendations can be used in educational process at compiling lecture content and practical (case) assignments.

Basic provisions for defense

1. Patients with chronic hepatitis B are characterized by the following medical and social characteristics: of average age, married, with higher education, employed, with a history of chronic diseases of the respiratory and digestive organs, treated before the onset of the disease in surgical and dental clinics, also cosmetic procedures that had viral hepatitis A in early childhood.

2. The quality of life of patients who suffer from chronic viral hepatitis B did not depend on gender and age during treatment. The decline in the quality of life of patients during treatment was characterized by a decrease in the overall health index, in terms of reduced ability to work, deterioration in self-service, mobility, everyday pain and discomfort, and the emergence of depressive tendencies.

3. The socioeconomic burden of treating chronic viral hepatitis B is costly to the government budget, and the cost threshold for effective treatment is more than \$2000 per QALY for high-tech antiviral drugs.

4. The importance of developing and implementing approaches to assessing the quality of life of patients with chronic viral hepatitis B play a fundamental and crucial role in improving the overall well-being of this group of patients, which is due to guaranteeing optimal patient health and mitigating the socio-economic and psychological consequences of this disease.

Approbation of the dissertation

Main principles of the dissertation work are presented in:

1. International scientific and practical conferences of students and young scientists “Insurance medicine. Science and education” (Nur-Sultan: NJSC “Astana Medical University”, December 21-22, 2020).

2. International online conference “Modern Science. Management and Research Standards III” (Prague, April 22-23, 2021).

3. International scientific and practical conference of students and young scientists (Nur-Sultan: NJSC “Astana Medical University”, December 09-10, 2021).

4. 5th Global Public Health Conference – GLOBEHEAL 2022 «Future of Global Health in changing world» (Shri-Lanka, 2022 – 24th-25th February).

5. 6th Global Public Health Conference – GLOBEHEAL 2023 «Building Bridges for Future Public Health Preparedness and Response» (Shri-Lanka, 2023 – 23rd-25th February).

Personal contribution of the dissertation student

Independently collected material, conducted a survey of patients in the regions, took part in the development of proposals for amending the regulatory legal acts.

The collection of literary data on the topic of the dissertation was individually carried out, the data obtained was analyzed and summarized, and their statistics was processed.

Participated in the development of methodological recommendations. The contribution of the author to the dissertation is confirmed by publication in scientific journals and participation in scientific conferences on the issues of the dissertation.

Implementation into practice

The results of the dissertation work are put into practice in the following

organizations:

1. “Clinic of family doctors”, Astana (act of implementation on the methodological recommendations “Ways to detect chronic viral hepatitis B in the Republic of Kazakhstan” dated 28.03.2023).

2. RSE on the REM “Research and production center for transfusiology” of the MH of the RK (act of implementation on the methodological recommendations “Ways to detect chronic viral hepatitis B in the Republic of Kazakhstan” dated 04.01.2023).

3. RSE on the REM “Republican blood center” of the MH of the RK (act of implementation on the methodological recommendations “Ways to detect chronic viral hepatitis B in the Republic of Kazakhstan” dated 23.02.2023).

4. SUE on the REM “Regional blood center” of the Akmola region (act of implementation on the methodological recommendations “Ways to detect chronic viral hepatitis B in the Republic of Kazakhstan” dated 13.02.2023).

5. SUE on the REM “Zhambyl regional blood center” of the healthcare management of the akimat of Zhambyl region (act of implementation on the methodological recommendations “Ways to detect chronic viral hepatitis B in the Republic of Kazakhstan” dated 23.02.2023).

6. SUE on the REM “Regional blood center” of the healthcare management of the akimat of the West Kazakhstan Region (act of implementation on the methodological recommendations “Ways to detect chronic viral hepatitis B in the Republic of Kazakhstan” dated 20.02.2023).

7. PSE on the REM “Regional blood center” of the healthcare management of the Abay Region (act of implementation on the methodological recommendations “Ways to detect chronic viral hepatitis B in the Republic of Kazakhstan” dated 06.02.2023).

8. PSE on the REM “East Kazakhstan regional blood center” of the healthcare management of the East Kazakhstan region (act of implementation on the methodological recommendations “Ways to detect chronic viral hepatitis B in the Republic of Kazakhstan” dated 15.02.2023).

9. PSE on the REM “Atyrau regional blood center” of the healthcare management of Atyrau region (act of implementation on the methodological recommendations “Ways to detect chronic viral hepatitis B in the Republic of Kazakhstan” dated 17.02.2023).

10. PSE “Regional blood center” of the healthcare management of the akimat of the Karaganda region (act of implementation on the methodological recommendations “Ways to detect chronic viral hepatitis B in the Republic of Kazakhstan” dated 20.01.2023).

11. Kaskelen branch of the SUE on the REM “Regional blood center” of the healthcare management of the Almaty region (act of implementation on the methodological recommendations “Ways to detect chronic viral hepatitis B in the Republic of Kazakhstan” dated 01.02.2023).

Publications

12 scientific papers have been published on topic of the dissertation, of which:

- 2 articles in journals, indexed in bases of Web of Science and Scopus.

1. Saussakova S., Dauletova G., Nakipov Z., Sarsenbayeva G., Duisekova S., Sadibekova Z., Raissova K., Turgambayeva A. Health-Related Quality of Life in Patients with Chronic Hepatitis B: A Meta-Analysis of Observational Studies. *Iran J Public Health*. 2023;52(3):453-462.

2. Savchuk T., Grinvald Y., Ali M., Sepetiene R., Saussakova S., Zhangazieva K., Imashpayev D., Abdrakhmanova S. Antibodies to Hepatitis B core antigen prevalence study in Kazakhstan. *Immun Inflamm Dis*. Mar 2023;11(3):e793. doi: 10.1002/iid3.793. PMID: 36988253; PMCID: PMC10042129.

- 3 articles in publications recommended by the Committee for Quality Assurance in Education and Science of the Ministry of Education and Science:

1. Turgambayeva A.K., Saussakova S.B., Imashpayev D.M., Tebenova K.S., Asselah T. Evaluation of awareness of beauty employees about Hepatitis B viral infection. *Science and Healthcare*. 2022;3(24):88-94. doi:10.34689/SH.2022.24.3.012

2. Saniya Saussakova, Assiya Turgambayeva, Gaukhar Dauletova, Tarik Asselah. Management of Chronic Hepatitis B patients: HBsAg Kinetics. *Journal of Health Development*. 2022;3(48):44-50. doi:10.32921/2225-9929-2022-3-48-37-44

3. Saussakova S.B., Turgambayeva A.K., Nakipov Zh., Dauletova G., Tebenova K. Retrospective analysis of characteristics of patients with chronic hepatitis B. *Science and Healthcare*. 2023;1(25):86-93. doi:10.34689/SH.2023.25.1.011

- 6 abstracts in the materials of the international scientific and practical conferences:

1. Saussakova S.B., Golubev V.V., Nakipov Zh.B. The problem of chronic hepatitis B and new ways to solve it in Kazakhstan. Collection of abstracts of the international scientific-practical conference of students and young scientists “Insurance medicine. The science. Education” 21-22.12.2020, Kazakhstan, Nur-Sultan, NJSC “AMU”, p.120.

2. Saussakova S.B., Evdokimova E-M.P., Nakipov Zh.B. Measures to reduce viral hepatitis B among the decreed population group. Collection of abstracts of the international scientific-practical conference of students and young scientists “Insurance medicine. The science. Education” 21-22.12.2020, Kazakhstan, Nur-Sultan, NJSC “AMU”, p.121.

3. Saniya Saussakova, Assiya Turgambayeva. Patients with chronic hepatitis B: what is their health-related quality of life? Collection of abstracts of the III online conference “Modern science. Management and Standards scientific research”, Prague, April 22-23, 2021, p. 15.

4. Saussakova S.B. Quality of life and opportunities for its improvement in patients with chronic hepatitis B (with oral presentation). Collection of abstracts of the international scientific and practical conference of students and young scientists dedicated to the 30th anniversary of Independence of the Republic of Kazakhstan. 09-10.12.2021, 09-10.12. 2021, Kazakhstan, Nur-Sultan, NJSC “AMU”, pp. 26-27.

5. Saussakova SB, Turgambayeva AK. Quality of Life in Chronic Hepatitis B Patients (with oral presentation). Book Abstract of the 5th Global Public Health conference– GLOBEHEAL 2022 “Future of Global Health in a changing world” (Shri-Lanka, 2022 – 24rd-25th February), p. 50.

6. Saussakova S.B. and Turgambayeva A.K. Characteristics of Patients with Chronic Hepatitis B in Kazakhstan: A Retrospective Study (with oral presentation) Book Abstract of the 6th Global Public Health Conference – GLOBEHEAL 2023 “Building Bridges for Future Public Health Preparedness and Response” (Shri-Lanka, 2023 – 23rd-25th February), p.34.

- 1 methodical recommendations “Ways to detect chronic hepatitis B” guidelines in the Republic of Kazakhstan” (MoM of Expert group of RSE on the REM “Salidat Kairbekova NRCHD” No. 335 dated 17.11.2022);

- 2 certificates of state registration of ownership of the object of copyright No. 31083 dated 10.10.2022, No. 31988 dated 01.24.2023.

Conclusions

1. Patients with chronic viral hepatitis B are characterized by the following medical and social characteristics: the average age was 48 years in the age range from 18 to 83 years, married (75.31%), with higher education (58.16%), employed (57.32%). 8.78% of patients were healthcare workers. The majority of patients indicated a record of dental treatment (90%), surgery (59.83%), in particular appendectomy (20%) and gynecological interventions (32.17%). Cosmetic procedures and viral hepatitis A were among patients in early childhood, 26.8% and 23.43%, respectively.

Most patients with chronic viral hepatitis B had a record of respiratory and digestive diseases: chronic cholecystitis (30.96%), chronic pancreatitis (15.48%), chronic gastritis (11.29%), and chronic bronchitis (7.11%).

The presence of concurrent diseases in patients with chronic viral hepatitis B is correlated with an increase in the age of patients from 40 years and above ($p < 0.001$).

2. It was established that the quality of life of patients suffering from chronic viral hepatitis B during treatment did not depend on gender and age ($p > 0.05$). There were infringements in the total physical - 37.6 points and mental components of the quality of life - 35.6 points.

Decline of total health index was determined ($p < 0.05$): deterioration in mobility by 3.1 points, decline in self-care by 2.08 points, down in daily activities by 2.92 points, worsening of pain-discomfort by 2.67 points, the occurrence of depressive tendencies by 2.3 points.

The change in the quality of life of patients in individual domains was differentiated depending on the duration of the disease with chronic viral hepatitis B.

The VAS index of quality of life differed in patients receiving various types of antiviral therapy: interferon 62.5 ± 5.35 points, combination therapy 54.39 ± 12.31 points, tenofovir 51.15 ± 14.07 points.

The study of patients with different social status during treatment revealed different indicators of VAS. The highest indicator of the general health index was observed in students (57.5 ± 11.37 points), working patients (54.93 ± 12.39 points), unemployed (48.33 ± 15.96 points), retirees (45.34 ± 13.36 points).

It was found that income ($p = 0.345$) and duration of treatment ($p = 0.337$) cannot predict how the quality of life of patients will change in the future.

3. The threshold value of the cost of treatment effectiveness was more than \$2000 per QALY in the case of high-tech antiviral drugs.

During analysis of the comparative effectiveness of therapy for chronic viral hepatitis B, tenofovir and interferon in combination can be distinguished as a treatment that demonstrates higher effectiveness compared to other drugs. The economic cost of this treatment strategy is \$9218.82 per patient.

The socio-economic burden of treating chronic viral hepatitis B is costly for the state budget. A less costly treatment strategy is to allocate a \$2000 treatment budget. But when using more than \$2000 of high-tech methods of treatment (the use of tenofovir, interferon), a high efficiency of treatment is noted.

4. Modern approaches to assessing the quality of life of patients with chronic viral hepatitis B are focused on the comprehensive improvement of their well-being. These approaches include practical recommendations and emphasize the importance of integrating innovative methods of disease detection, early diagnosis and personalized support plans tailored to the individual needs of patients, which contributes to improving their quality of life and reducing the social and economic burdens associated with the disease.

Practical recommendations

1. The results of the research and conclusions obtained by us are recommended for use by health managers for budget programs planning for the treatment of patients, to improve the diagnosis and testing of viral hepatitis B.

2. It is recommended to continue to working with the National register of patients with viral hepatitis in order to achieve complete accounting and effective coverage of treatment for patients with chronic viral hepatitis B. The registry's functionality should be enhanced as part of this project to include system to monitor treatment efficacy and quick identification of side effects like cirrhosis and liver cancer. In addition, the registry can be used to conduct research and analyze data that can help develop evidence-based strategies for the treatment and prevention of chronic viral hepatitis B.

3. In order to improve preventive measures for viral hepatitis, the roadmap for the prevention, diagnosis, treatment and prevention of the consequences of viral hepatitis for 2023-2027 should be continued developing. This will improve the control of viral hepatitis spread and reduce the number of cases in the future. As part of the development of the roadmap, attention should be paid to the following issues:

- *development and implementation of new methods of prevention, diagnosis and treatment of viral hepatitis.* This may include improving existing tests, developing new drugs and treatment technologies, and developing early disease detection programs.

- *improvement of educational programs for medical personnel and population.* This will help raise awareness about viral hepatitis, promote early detection of the disease, and reduce patient stigma.

- *development of measures to prevent the spread of viral hepatitis.* Inclusion of measures to reduce the risk of infection in various areas of life, such as health care, sexual behavior, a healthy lifestyle, as well as measures aimed at reducing the social vulnerability of risk groups, in the program for preventing the spread of viral hepatitis.

- *improvement of the monitoring and evaluation of the effectiveness of*

preventive measures. Development of mechanisms for monitoring and evaluating the effectiveness of preventive measures, including proper accounting of diseases, monitoring the quality of treatment and prevention, evaluating the effectiveness of programs, evaluating the results of treatment and the quality of life of patients.

- *creation of a network of expert centers on viral hepatitis, providing advice to hepatologists and general practitioners on the diagnosis and treatment of chronic viral hepatitis.* It is also an important step in improving the quality of medical care for patients with these diseases. These centers of expertise can be organized both nationally and regionally and provide services remotely or in local medical facilities. They should include highly qualified specialists in hepatology, immunology, molecular biology and other related fields, as well as have access to modern diagnostic and therapeutic methods. The work of such expert centers will contribute to earlier detection and more effective treatment of chronic viral hepatitis, as well as to increase the competence of doctors in this area.

4. Public health departments and hepatologists are recommended to develop and implement specialized questionnaires covering the physical and psychological state, the level of pain and social support. Conducting interviews with patients and experts, as well as creating an online platform for systematic monitoring of quality of life, will allow more accurately assessing the needs and effectiveness of medical and social support for patients. These measures can help improve the quality of life of this group of patients and provide them with the necessary care more purposefully.

5. In order to improve the epidemiological situation of viral hepatitis B, it is recommended to strengthen vaccination in risk groups and among persons at risk of infection. To do this, it is necessary to carry out targeted work to inform the population about the importance of vaccination against hepatitis B, organize free vaccination campaigns in areas where there is a high incidence, and also ensure the availability of vaccines in medical institutions.

6. Hepatologists to systematically monitor patients with chronic viral hepatitis B, including regular examinations and monitoring of viral load levels, conduct an individual assessment of patients and develop an optimal treatment plan, taking into account the characteristics of their condition and needs, taking into account not only physical, but also mental aspects of the quality of life of patients, conduct regular assessment of the quality of life of patients through the use of validated questionnaires. In addition, it is important to ensure that patients have access to support from psychologists, social counselors and other professionals to help them cope with the emotional and psychological difficulties associated with the disease.

7. Public health departments to develop and implement a system for monitoring and evaluating the effectiveness of the national strategy for the prevention, diagnosis and treatment of viral hepatitis.

Content and structure of the dissertation

The dissertation work is presented on 109 pages, consists of the following sections: introduction, literature review, research materials and methods, theoretical and practical parts of own research (5 sections), conclusion, practical recommendations. The manuscript includes 29 tables, 28 figures, 6 appendices. Reference list includes 165 sources, from of which 145 are on English language.