ABSTRACT

of the dissertation submitted for the degree of Doctor of Philosophy (PhD)
in the educational program 8D10102 – Medicine
by Arina Sakenovna Yespotayeva
"Features of the course of chronic viral hepatitis
in patients undergoing hemodialysis"

Relevance of the research topic

Chronic viral hepatitis B and C (CVH) remain important in nephrology practice because of liver damage, the development of cirrhosis, and complications of portal hypertension in patients with chronic kidney disease. Patients receiving maintenance hemodialysis (MHD) constitute a distinct group: the combination of kidney failure, viral infection, and comorbidities complicates diagnosis, prognostic assessment, and the choice of treatment strategy.

Regular use of vascular access, invasive interventions, and a history of blood transfusions necessitate infection control in dialysis centers. An assessment of the prevalence of viral hepatitis among patients undergoing hemodialysis is required to plan preventive measures.

The clinical assessment of CVH in patients undergoing hemodialysis requires a comprehensive approach. Transaminase levels do not always reflect the severity of liver damage, and the interpretation of laboratory findings is complicated by concomitant metabolic and hematological disorders. Virological testing, noninvasive assessment of fibrosis, and identification of signs of portal hypertension are therefore of particular importance.

Modern antiviral therapy has expanded treatment options for patients with CVH and kidney failure. However, national data on infection prevalence, clinical and laboratory features, and disease outcomes are needed to organize care in the Republic of Kazakhstan. Comparing population and clinical findings provides a basis for an assessment and follow-up algorithm that coordinates the work of nephrologists, hepatologists, and infectious disease specialists.

Aim of the study

To comprehensively assess the epidemiological indicators, clinical and laboratory features, and outcomes of viral hepatitis in the general population and among patients receiving maintenance hemodialysis in the Republic of Kazakhstan, and to develop a management algorithm for this patient group.

Objectives of the study

1. To analyze the prevalence of chronic viral hepatitis B and C in the general population and among patients receiving kidney replacement therapy in the Republic of Kazakhstan, using data from the Unified National Electronic Health System.
2. To determine the prognostic significance of the timing of confirmation of a viral hepatitis diagnosis for overall survival in patients receiving maintenance hemodialysis.
3. To identify the clinical and laboratory features of chronic viral hepatitis in patients receiving maintenance hemodialysis, including the pattern of complications and the stage of liver fibrosis, compared with individuals without kidney failure.
4. To develop and substantiate an integrated management algorithm for patients with chronic kidney disease and viral hepatitis in order to optimize diagnosis, therapy, and prevention of complications.

Object and subject of the study

The object of the study comprises patients with end-stage chronic kidney disease receiving maintenance hemodialysis in the Republic of Kazakhstan.

Materials and methods

The study was conducted in several interrelated stages. The population stage involved a retrospective analysis of data from the Unified National Electronic Health System (UNEHS) of the Republic of Kazakhstan for 2014–2019; a cohort of 82,700 patients with recorded hepatitis B and C diagnoses was established. Demographic characteristics, the etiological distribution of infection, and epidemiological indicators were examined.

The next stage examined a national cohort of 9,310 patients who received kidney replacement therapy in 2014–2018. Viral hepatitis was recorded in 500 patients. Prevalence, distribution by infection type, and survival were assessed according to the timing of the first registration of hepatitis relative to the initiation of hemodialysis.

Patients were grouped according to whether the diagnosis was registered before or within the first 120 days of hemodialysis, or more than 120 days after its initiation. The registration date reflects the first appearance of the corresponding diagnosis in the database and may not coincide with the date of infection acquisition or seroconversion. This grouping was used to describe the timing of diagnosis and analyze its association with outcomes.

The clinical stage involved a retrospective review of the medical records of 317 patients with CVH for 2015–2024: 164 patients received maintenance hemodialysis, and 153 formed the comparison group without hemodialysis. Medical history, clinical manifestations, virological and biochemical parameters, ultrasound findings, noninvasive fibrosis assessments, and signs of portal hypertension were analyzed. Comparative analyses of the groups and survival assessments were performed.

Scientific novelty

1. Data from the Unified National Electronic Health System of the Republic of Kazakhstan were used to comprehensively assess the prevalence of chronic viral hepatitis in patients receiving maintenance hemodialysis. Prevalence was found to be substantially higher than in the general population, with HCV infection predominating.
2. The timing of confirmation of a chronic viral hepatitis diagnosis in patients receiving maintenance hemodialysis was found to have substantial prognostic significance for survival: the least favorable prognosis was observed when infection was detected before hemodialysis initiation or within the first 120 days of treatment.
3. The clinical and laboratory features of chronic viral hepatitis in patients receiving maintenance hemodialysis were identified, including higher frequencies of advanced liver fibrosis, cirrhosis, and complications of portal hypertension compared with patients not receiving kidney replacement therapy.
4. The most significant clinical and instrumental markers of liver disease progression in patients receiving maintenance hemodialysis were identified, including reduced albumin levels and platelet counts, a predominance of F3–F4 fibrosis stages, and high frequencies of portal hypertension, esophageal varices, and ascites.

Theoretical significance

1. New data were obtained on the prevalence of chronic viral hepatitis among patients receiving maintenance hemodialysis in the Republic of Kazakhstan, confirming substantially higher prevalence than in the general population and the predominance of HCV infection.
2. The clinical and laboratory features of chronic viral hepatitis in patients receiving maintenance hemodialysis were established, characterized by higher frequencies of advanced fibrosis, liver cirrhosis, and complications of portal hypertension.
3. The prognostic significance of the timing of confirmation of a chronic viral hepatitis diagnosis for survival in patients receiving maintenance hemodialysis was demonstrated.
4. Scientific understanding was expanded regarding the effects of chronic kidney failure and kidney replacement therapy on the clinical course of chronic viral hepatitis, the progression of liver fibrosis, and the development of complications.
5. An integrated approach to the management of patients with chronic viral hepatitis receiving maintenance hemodialysis was scientifically substantiated, taking into account the epidemiological, clinical, and prognostic features of this patient group.

Practical significance

1. An integrated management algorithm for patients with chronic viral hepatitis receiving maintenance hemodialysis was developed and proposed for practical use, with a focus on early detection of infection, timely assessment of fibrosis, and prevention of complications.
2. The need for mandatory polymerase chain reaction (PCR) screening in patients attending hemodialysis centers, regardless of the biochemical activity of the disease, was demonstrated; this can improve the detection of chronic viral hepatitis.
3. The most significant clinical, laboratory, and instrumental signs of liver disease progression in patients receiving maintenance hemodialysis were identified and may be used for risk stratification and optimization of follow-up.
4. The study findings may be used in the development of clinical protocols, standards of medical care, and educational programs for specialists in nephrology and gastroenterology.
5. Implementation of the proposed algorithm in dialysis center practice contributes to reducing the risk of late diagnosis, decreasing the frequency of complications, and improving patient survival.

Main propositions submitted for defense

1. The prevalence of chronic viral hepatitis among patients receiving maintenance hemodialysis in the Republic of Kazakhstan is substantially higher than in the general population, with HCV infection being the predominant etiological form.
2. The timing of confirmation of a chronic viral hepatitis diagnosis is an independent prognostic factor for survival in patients receiving maintenance hemodialysis.
3. In patients receiving maintenance hemodialysis, chronic viral hepatitis has a more severe clinical course, with high frequencies of advanced fibrosis, liver cirrhosis, and complications of portal hypertension.
4. The use of an integrated management algorithm incorporating mandatory PCR screening, noninvasive fibrosis assessment, early antiviral therapy, and a multidisciplinary approach improves the effectiveness of diagnosis and management of chronic viral hepatitis in patients receiving maintenance hemodialysis.

Implementation of the research findings

Implementation of the research findings in medical organizations is confirmed by the implementation certificates presented in the dissertation appendices labeled “В” and “Г”. The practical developments are intended to systematize the assessment and management of patients with chronic viral hepatitis undergoing hemodialysis.

Personal contribution of the doctoral candidate

The personal contribution of Arina Sakenovna Yespotayeva includes participation in the development of the scientific concept and study plan, analytical work with the literature and study materials, interpretation of the findings, and preparation of the dissertation text. The aim, objectives, and methodological approaches were developed jointly with the scientific supervisors.

The doctoral candidate searched, systematized, and critically analyzed the scientific literature on chronic viral hepatitis in patients undergoing hemodialysis. She participated in the organization and analysis of the research data, compared epidemiological indicators with the clinical, laboratory, and instrumental characteristics of the patients, and synthesized the identified differences and their clinical significance.

The main propositions, conclusions, and practical recommendations were formulated, and a management algorithm for patients with CVH receiving maintenance hemodialysis was developed, with the direct participation of the doctoral candidate. She prepared the dissertation text and participated in preparing scientific publications and materials for presenting the study findings. The results were discussed and the conclusions refined jointly with the scientific supervisors and co-authors.

Conclusions

1. According to the Unified National Electronic Health System of the Republic of Kazakhstan, the prevalence of chronic viral hepatitis showed a sustained upward trend during 2014–2019, with hepatitis C virus infection predominating (56.6%). Among patients receiving maintenance hemodialysis, the prevalence of viral hepatitis (5.4%) was three to four times that in the general population, with hepatitis C virus infection predominating (73.8%).

2. Survival analysis in the cohort of patients receiving maintenance hemodialysis demonstrated that the timing of diagnostic confirmation has critical prognostic significance: a hepatitis diagnosis established before hemodialysis initiation or within the first 120 days was associated with significantly poorer survival.

3. Compared with patients not undergoing hemodialysis, the clinical and laboratory features of chronic viral hepatitis in patients receiving maintenance hemodialysis included:

- a predominance of HCV infection (92.7% vs 79.1%) and genotype 1b (67.8% vs 44.6%), and a more frequent history of blood transfusions (39.0% vs 20.3%);
- more frequent dyspeptic syndrome (47.6% vs 34.0%) and arterial hypertension (84.8% vs 69.3%), and lower albumin levels and platelet counts;
- more frequent detection of heterogeneous liver echotexture and diffuse changes in the liver parenchyma (56.1% vs 34.0%), and hepatosplenomegaly;
- a higher frequency (threefold) of advanced F3–F4 fibrosis (56.7% vs 30.1%) and a 2.4-fold higher frequency of F4 liver cirrhosis (25.0% vs 10.5%);
- more frequent complications, including portal hypertension (54.9% vs 26.1%), esophageal varices (45.7% vs 20.9%), ascites (32.9% vs 13.1%), and splenomegaly (43.3% vs 24.8%).

4. Based on the identified epidemiological, clinical, and laboratory features and the pattern of complications, an integrated management algorithm was developed for patients with chronic viral hepatitis receiving maintenance hemodialysis. It incorporates mandatory PCR screening regardless of transaminase levels, prioritized use of noninvasive fibrosis assessment with specific cut-off values, early initiation of antiviral therapy taking altered pharmacokinetics into account, and interdisciplinary collaboration between specialists.

Practical recommendations

An integrated management algorithm for patients with chronic viral hepatitis receiving maintenance hemodialysis was developed and proposed for practical use, with a focus on early detection of infection, timely assessment of fibrosis, and prevention of complications.

The need for mandatory PCR screening in patients attending hemodialysis centers, regardless of the biochemical activity of the disease, was demonstrated; this can improve the detection of chronic viral hepatitis.

The most significant clinical, laboratory, and instrumental signs of liver disease progression in patients receiving maintenance hemodialysis were identified and may be used for risk stratification and optimization of follow-up.

The study findings may be used in the development of clinical protocols, standards of medical care, and educational programs for specialists in nephrology and gastroenterology.

Implementation of the proposed algorithm in dialysis center practice contributes to reducing the risk of late diagnosis, decreasing the frequency of complications, and improving patient survival.

Publications related to the dissertation

Nine scientific works have been published on the dissertation topic: three articles in publications recommended by the Committee for Quality Assurance in the Sphere of Science and Higher Education of the Ministry of Science and Higher Education of the Republic of Kazakhstan; one article in an international peer-reviewed journal indexed in Scopus, with a percentile rank of 71; and five publications in international conference proceedings.

Two certificates of entry of information into the State Register of Rights to Copyright-Protected Objects were obtained. The research findings are reflected in scientific publications and conference materials.

Length and structure of the dissertation

The dissertation comprises 115 pages of typescript and consists of an introduction, a literature review, a description of the materials and methods, the original research findings, a discussion, conclusions, practical recommendations, a bibliography of 124 references, and five appendices. The dissertation is illustrated with 23 figures and 37 tables.