American Journal of Medicine and Medical Sciences 2025, 15(10): 3283-3286
DOI: 10.5923/j.ajmms.20251510.02

Comparative Study of Viral Hepatitis Markers and Some Opportunistic Infections in Patients Before and After Transplantation

Abdurakhimova D. R., Kasimova R. I., Kan N. G., Brigida K. S., Abdurakhmanova D. N., Musabaev E. I.

Scientific Research Institute of Virology of the Republican Specialized Center for Epidemiology, Microbiology, Infectious and Parasitic Diseases

Abstract The presented work presents a comparative analysis of molecular genetic and immunological parameters in patients with viral hepatitis before and after liver transplantation. The study included two groups: 30 patients who underwent liver transplantation within 3-6 months and 50 patients awaiting liver transplantation. The study covered parameters including the presence and quantitative indices of HBV DNA and HDV RNA, serological status for HBsAg, anti-HCV and anti-HDV IgG. The obtained results showed a significant decrease in HDV RNA and the absence of HBV DNA in patients after transplantation, indicating the effectiveness of the intervention. A decrease in the frequency of HBsAg detection was also found, which further emphasizes the success of antiviral therapy and transplantation. The high frequency of anti-HDV IgG in both groups indicates a wide spread of HDV infection in patients with end-stage liver disease. In the post-transplant period, patients have a higher frequency of reactivation of opportunistic infections, such as Epstein-Barr virus and cytomegalovirus, which is associated with the effect of immunosuppressive therapy. Of interest is also the increased frequency of detection of anti-HCV in patients after transplantation, indicating the possible impact of immunosuppression on the reactivation of HCV infection. Special attention is paid to the need for comprehensive monitoring of such patients, including regular virological monitoring and individualized antiviral and immunosuppressive therapy to improve survival and quality of life in patients with a transplanted liver.

Keywords Viral hepatitis B and D, Liver transplantation, HDV RNA, HBV DNA, HBsAg, anti-HCV, Opportunistic infections, Immunosuppression, Tenofovir, Tacrolimus, Post-transplant monitoring

1. Materials and Methods

Clinical data of liver transplant recipients were obtained based on discharge summaries and medical documentation from the transplant clinics. Information on patients who underwent surgery at the Fortis Clinic (India) was collected with the assistance of representatives from the Shinon company.

Serological and molecular-biological methods used for the study of viral hepatitis were based on the results of enzyme-linked immunosorbent assay (ELISA) using test systems from the "Diagnostic Systems" Scientific-Production Association (Russian Federation): "DS-IFA-HBsAg," "IFA-ANTI-HCV," and "IFA-ANTI-HDV." Molecular-genetic studies for the detection of HBV DNA and HDV RNA were carried out using the test systems "AmpliSens-HBV-FL," "AmpliSens-HDV-FL," and "AmpliSens-HBV-FL."

To detect DNA of Epstein-Barr virus (EBV), Cytomegalovirus (CMV), and Herpes Simplex Virus types 1 and 2 (HGV 6), the "AmpliSens EBV/CMV/HHV6-skrin-FL" test system was used. Analytical sensitivity was 5 copies of cells of the 10*5th degree.

The above-mentioned research methods were conducted at the reference laboratory of the Research Institute of Virology of the Republican Specialized Scientific-Practical Medical Center for Epidemiology, Microbiology, Infectious and Parasitic Diseases under the Ministry of Health of the Republic of Uzbekistan.

2. Results

The study included an analysis of molecular genetic and immunological parameters in two groups of patients: those who had undergone liver transplantation and candidates for transplantation. The data obtained are shown in Table -1 and include parameters such as the presence and amount of HBV DNA, HDV RNA, serological status for HBsAg, anti-HCV and anti-HDV IgG. The study revealed significant differences between the groups, demonstrating the effectiveness of liver transplantation in improving the virological and immunological status of patients.

Received: Jul. 24, 2025; Accepted: Aug. 20, 2025; Published: Oct. 9, 2025
Published online at http://journal.sapub.org/ajmms

Table 1. Comparative characteristics of molecular genetic and immunological parameters in the study groups

Indicator	Patients who have undergone liver transplantation (n=30)	Liver transplant candidates (n=50)	p
Presence of HDV RNA	6,7 ±4,6	96,0 ±2,8	p<0,001
HDV RNA quantitative	3950 ±735,9	281376 ±182218	P<0,05
HBsAg positive	23,3 ±7,7	100,0 ±0,0	p<0,001
Anti-HCV positive	10,0 ±5,5	3,3 ±3,3	p<0,001
Anti-HDV IgG п positive	96,7 ±3,3	100,0 ±0,0	P<0,05

The presence of HBV DNA was not detected in any patient after transplantation, while in candidates the virus was present in a significantly higher percentage of cases ($p<0.001$). Quantitative analysis of HBV DNA was also not determined in the main group, while in the comparison group it averaged 725.5 ±99.9.

HBsAg was determined in a significantly lower percentage of patients after transplantation compared to candidates, in whom it was detected in 100% of cases ($p<0.001$).

All patients in both groups took tenofovir as antiviral therapy. However, in the group after transplantation, greater adherence to treatment was observed. This may explain the more pronounced improvement in virological parameters in this group. Greater adherence to treatment in patients after transplantation may be associated with more careful monitoring of these patients and their increased motivation to comply with the therapy regimen to preserve graft function. The high frequency of anti-HDV IgG detection in both groups indicates the high prevalence of HDV infection among patients with severe liver disease. This emphasizes the importance of considering HDV infection in treatment planning and management of patients both before and after liver transplantation [3].

A significant decrease in the frequency and amount of HDV RNA in transplant patients compared to candidates indicates the effectiveness of transplantation in controlling HDV infection. This may be due to several factors. First, removal of the infected liver during transplantation significantly reduces the viral reservoir in the body. Second, the use of antiviral therapy in the post-transplant period helps suppress viral replication [4].

However, the presence of HDV RNA in some patients after transplantation indicates the possibility of reinfection or persistence of the virus. This suggests the need for further monitoring and, possibly, additional treatment of this group of patients. For effective management of patients with HDV infection after liver transplantation, regular virological examination with an individual approach to therapy is necessary. Continuation of antiviral therapy after liver transplantation is an important component of treatment. Despite significant improvement in virological parameters after liver transplantation, there is a need for further monitoring and possibly additional treatment of patients with persistent HDV infection. This is necessary to prevent disease progression and improve long-term transplantation outcomes. A comprehensive approach to the management of such patients, including regular monitoring of virological parameters and individualized therapy, will optimize treatment outcomes and improve the prognosis for patients with HDV infection after liver transplantation [1].

The results of the study revealed an interesting pattern in the presence of antibodies to the hepatitis C virus (anti-HCV) in patients after liver transplantation and in transplant candidates.

A small proportion of patients who underwent liver transplantation were found to have antibodies to the hepatitis C virus. At the same time, among transplant candidates, the frequency of anti-HCV detection was statistically significantly lower ($p<0.01$).

Of particular interest is the presence of anti-HCV in patients after liver transplantation, which encourages a more in-depth study of the role of immunosuppressive therapy in this process.

In our study, a comparative analysis of the incidence of some opportunistic infections in patients before and after liver transplantation was performed. The results demonstrate significant differences between the groups and changes over time, which is of great clinical importance for the management of patients with a transplanted liver (Fig-1).

When comparing patients who underwent liver transplantation with transplant candidates, significant differences in the frequency of detection of a number of viral infections were revealed. In patients after transplantation, Epstein-Barr virus (EBV) was detected in the blood significantly more often 36.7% ±8.8% versus 20.0% ±5.7% in candidates ($p < 0.05$). A similar trend was observed for cytomegalovirus (CMV), which was detected in 10.0% ±5.5% of patients after transplantation compared with 4.0% ±2.8% in applicants ($p<0.05$).

These data may indicate an increased risk of reactivation of latent viral infections in patients receiving immunosuppressive therapy after transplantation [5].

It is interesting to note that the frequency of detection of herpes virus type 6 (HGV-6) was significantly lower in patients after transplantation (3.3% ± 3.3%) compared to candidates (10.0% ±5.5%) ($p < 0.001$). This may be due to the characteristics of the immune response to this virus or to the effectiveness of antiviral prophylaxis used in patients after transplantation.

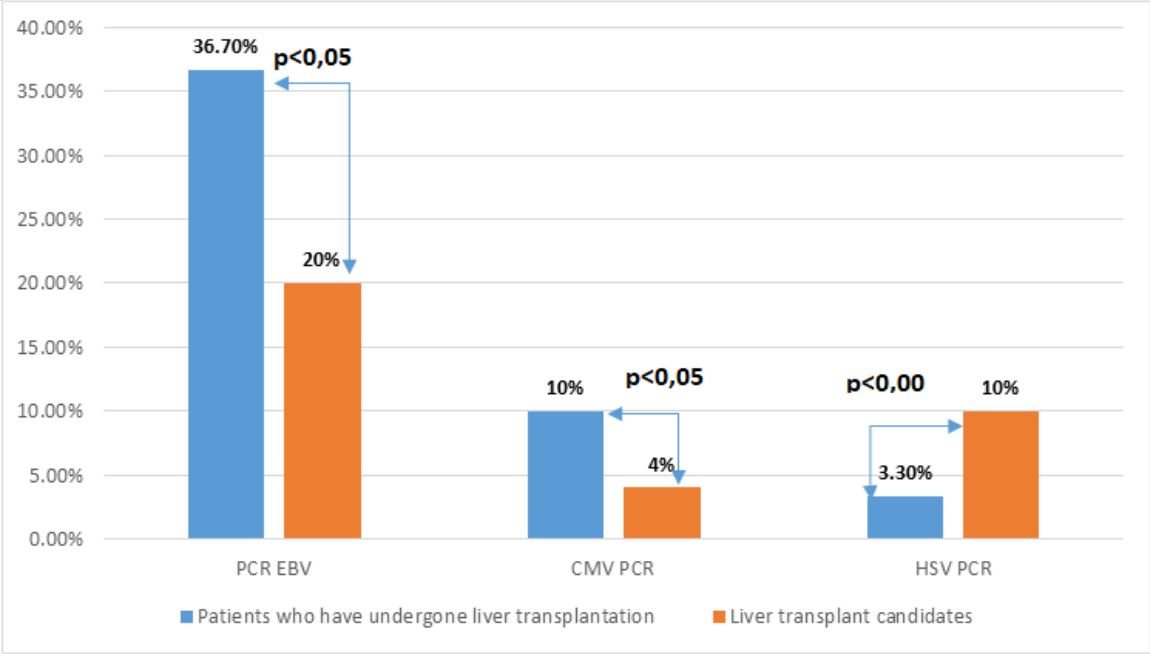

Figure 1. Comparative analysis of the incidence of some opportunistic infections in the compared groups

3. Discussion

Thus, the results of the study demonstrate a significant improvement in virological and serological parameters in patients after liver transplantation compared to transplant candidates. The effectiveness of transplantation in combination with antiviral therapy is manifested in the elimination of HBV DNA and a decrease in the frequency of HBsAg detection in patients after transplantation. The high prevalence of HDV infection among patients with severe liver disease highlights the need for a comprehensive approach to treatment and monitoring both before and after transplantation. A decrease in the detection rate and amount of HDV RNA after transplantation indicates the effectiveness of this method in controlling HDV infection, but requires further monitoring and an individual approach to therapy. The presence of anti-HCV in patients after transplantation with a low prevalence in candidates indicates a complex interaction between immunosuppressive therapy and viral hepatitis. This highlights the need for careful monitoring and an individualized approach to immunosuppressive therapy in patients after liver transplantation. Immunosuppression, being an integral part of post-transplant patient management, can affect the body's immune response, including the production and maintenance of antibodies to the hepatitis C virus. Immunosuppressive therapy, necessary to prevent graft rejection, can have a significant impact on the course of viral hepatitis. In the case of hepatitis C, immunosuppression can promote viral reactivation or accelerate disease progression in infected patients. The use of calcineurin inhibitors such as tacrolimus and cyclosporine, which are the mainstay of immunosuppressive therapy after liver transplantation, may create favorable conditions for the replication of the hepatitis C virus. This is explained by the fact that the suppression of the immune response reduces the body's ability to control the viral infection. It is important to note that the risk of HCV reactivation is especially high in the first two years after transplantation, when immunosuppression is most intense. This emphasizes the need for careful monitoring of patients during this period.

The study paid special attention to opportunistic infections, which pose a significant threat to patients after liver transplantation. It was found that CMV and Epstein-Barr virus were detected significantly more often in patients after transplantation. These data indicate an increased risk of reactivation of latent viral infections against the background of immunosuppressive therapy.

It is known that immunosuppression, which is necessary to prevent transplant rejection, can reduce the body's ability to control latent viral infections, which leads to their reactivation. This emphasizes the importance of careful monitoring of the virological status of patients after transplantation and timely administration of antiviral therapy, if necessary.

To optimize treatment results and improve the long-term prognosis of patients with viral hepatitis after liver transplantation, a comprehensive approach is needed, including regular monitoring of virological parameters, individualized antiviral and immunosuppressive therapy, as well as careful observation of patients, especially in the first years after transplantation. Particular attention should be paid to the prevention and timely treatment of opportunistic infections, which can significantly complicate the course of the post-transplant period and negatively affect the survival of the transplant and the patient.

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