

Triple Coinfection – Thirteen Years' Experience at Tertiary Care Centre of Northern India

Parveen Malhotra¹, Vani Malhotra¹, Ankit Chahal¹, Pranav Malhotra², Chitrakshi Bhardwaj¹, Himanshu, Shivanshu¹, Rajasvi Khurana¹, Rahul Siwach¹, Avani Sharma¹, Abhishek Yadav¹

¹Department of Medical Gastroenterology and Gynaecology & Obstetrics, PGIMS, Rohtak, Haryana, India.

²Department of Psychiatry, PGIMS, Rohtak, Haryana, India.

Abstract

Background: Human immunodeficiency virus (HIV), hepatitis B and C viruses (HBV and HCV), and dual or triple infections are serious public health issues. While most medications have significantly improved the management of mono-infections, triple co-infection may be a greater challenge in the future. The aim is to determine triple Co-infection of hepatitis B, C and HIV at the Tertiary care centre of Northern India. **Material and Methods:** The present study was conducted at the Department of Medical Gastroenterology, Post Graduate Institute of Medical Sciences, North India. A total of 30,000 serum samples of Hepatitis B (11, 500), Hepatitis C (12000) and HIV (6500) confirmed patients were tested for co-infection with other viruses. **Results:** Out of the total pool of 30,000 patients, triple co-infection was seen only in 46 patients (0.15%), and except for one, all were male, the majority in the younger age group, sexually active and were intravenous drug abusers. Of the total pool of 30,000 patients, only 46 (0.15%) had triple co-infection. Of these 46 patients, 45 were male (97.77%), and 1 was female (2.23%). The largest number of patients were young males in the 20-30 years age group, i.e., 35 (76.08%), followed by the 30-40 years age group, with 6 patients (13.04%). There was predominance of patients belonging to rural background, i.e., 33 patients (71.73%), and only 13 patients (28.27%) resided in urban areas. In the marital analysis, 32 patients (69.56%) were unmarried, and 14 patients (31.44%) were married. Out of the total 46 patients, 35 (72.5%) gave a history of intravenous drug abuse, alcohol intake and were smokers. In the total study group of 46 patients, 28 (60.86%) had a history of previous surgery and tattooing. In the total pool of 46 patients, only 6 (13.04%) were admitted for having multiple sexual partners. Of 46 patients, 44 (95.65%) were non-cirrhotic, 1 (2.17%) had significant fibrosis (fibroscore >7 kPa), and 1 (2.17%) was cirrhotic. All 46 patients were on the HARRT with TLE regimen, containing tenofovir & lamivudine, which have antiviral activity against HBV. All of them were treated with oral directly acting antivirals (DAA's) for HCV. Of 46 patients, 43 (93.47%) achieved sustained virological response, similar to what is seen in mono-infected HCV patients. **Conclusion:** The HBV, HCV and HIV triple co-infection was extremely low, that too in the hotspot of HBV & HCV mono and dual infections and is a positive sign. It can be attributed to mandatory HBV vaccination of every HIV and HCV patient, along with a multi-pronged strategy of reducing high-risk behaviour. Moreover, early detection and treatment of mono-infections reduced the risk of developing dual or triple co-infections in the future.

Keywords: HIV, Hepatitis B, Hepatitis C, Intravenous drug abuse, Tattooing, Surgery.

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INTRODUCTION

Since most medications have significantly improved the treatment of mono infections, dual or triple infections with the human immunodeficiency virus (HIV), hepatitis B, and C viruses (HBV and HCV) represent a serious public health concern.^[1] Now, triple infections of HIV/HBV/HCV have become an important health issue,^[2] affecting the clinical course of the disease,^[3,4] and sharing common modes of transmission.^[5-7] Thus, People living with HIV (PLHIV) are at risk of dual or triple infections with HBV and HCV.^[8] Virological interactions and immunological mechanisms lead to prolonged effects of triple co-infections.^[4,9,10] Dual infections with HIV/HBV or HIV/HCV and triple infections with HIV/ HBV/ HCV are common problems among intravenous drug users (IDUs).^[11-13] Amongst the transmissible blood-borne viruses through the Parenteral route (blood transfusion and sexual intercourse), HIV, HBV and HCV are significant.^[13-15] However, due to variations in

hepatitis infection backgrounds and HIV transmission methods, the epidemiology of HIV-HBV-HCV triple infections varies,^[16] and may result in serious disease and death.^[17] When HIV, HBV, or HCV enter the human body, innate immunity is first recognised, followed by a cellular and humoral immune response,^[18-22] aimed at removing HIV, HBV, and HCV from the bodies of immunocompetent individuals. Immune-mediated hepatocyte damage results from this.^[23] Highly active

Address for correspondence: Dr. Parveen Malhotra, Department of Medical Gastroenterology and Gynaecology & Obstetrics, PGIMS, Rohtak, Haryana, India.
E-mail: drparveenmalhotra@yahoo.com

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antiretroviral treatment (HAART) has transformed HIV and AIDS from a chronically fatal illness into a manageable chronic infection.^[24,25] Due to their known antagonistic effects about HIV and hepatitis infections, dual or triple infections with hepatitis viruses may undermine the benefits of HAART.^[26] Therefore, dual or triple infections with HIV and hepatitis viruses need care.

MATERIALS AND METHODS

This study was conducted by the Department of Medical Gastroenterology at Post Graduate Institute of Medical Sciences, Rohtak, India, over a period of thirteen years, i.e., from 1st April 2013 to 31st March 2026, for determining the Triple co-infection in patients. A total of 30,000 confirmed cases of Hepatitis B (11,500), Hepatitis C (12,000) and HIV (4000) were enrolled in the study after proper consent and then tested for co-infection with other viruses. Venipuncture was used to aseptically draw around 5 millilitres of whole blood. After allowing the blood to coagulate, the serum was separated by centrifugation at room temperature and analysed for HIV, HBV, and HCV using an enzyme-linked immunosorbent assay. In all enrolled patients, a detailed history, physical examination, and clinical examination were performed. Every patient underwent complete biochemical examination, which included complete hemogram, liver & renal function tests, viral screen, viral load, ultra-sonogram of the abdomen, Fibroscan and upper Gastrointestinal endoscopy and Triple-

phase computed tomography scan, wherever indicated.

RESULTS

A total of 11,500 confirmed patients of HBV, 12,000 patients of HCV and 6500 of HIV infected patients were screened for other two virus co-infections. Of the total pool of 30,000 patients, only 46 (0.15%) had triple co-infection. Of these 46 patients, 45 were male (97.77%), and 1 was female (2.23%). The largest number of patients were young males in the 20-30 years age group, i.e., 35 (76.08%), followed by the 30-40 years age group, with 6 patients (13.04%). There was predominance of patients belonging to rural background, i.e., 33 patients (71.73%), and only 13 patients (28.27%) resided in urban areas. In the marital analysis, 32 patients (69.56%) were unmarried, and 14 patients (31.44%) were married. Out of the total 46 patients, 35 (72.5%) gave a history of intravenous drug abuse, alcohol intake and were smokers. In the total study group of 46 patients, 28 (60.86%) had a history of previous surgery and tattooing. In the total pool of 46 patients, only 6 (13.04%) were admitted for having multiple sexual partners. Of 46 patients, 44 (95.65%) were non-cirrhotic, 1 (2.17%) had significant fibrosis (fibroscan score>7 kPa), and 1 (2.17%) was cirrhotic. All 46 patients were on the HARRT with TLE regimen, containing tenofovir & lamivudine, which have antiviral activity against HBV. All of them were treated with oral directly acting antivirals (DAA's) for HCV. Of 46 patients, 43 (93.47%) achieved sustained virological response, similar to what is seen in mono-infected HCV patients.

Table 1: Showing Prevalence of Triple Co-infection

Total Patients (HBV, HCV, HIV)	Triple Co-infected (HBV, HCV, HIV)	Mono or Dual Co-infected
30,000	46 (0.15%)	29,954 (99.84%)

Table 2: Showing Age group distribution in both the genders in Triple Co-infected Patients

Age Group (46 Patients)	Male (45 patients)	Female (1 patient)
0-10 yrs	0 (0%)	0 (0%)
11-20 yrs	0 (0%)	0 (0%)
21-30 yrs	35 (76.08%)	0 (0%)
31-40 yrs	6 (13.04%)	0 (0%)
41-50 yrs	3 (6.66%)	0 (0%)
51-60 yrs	1 (2.22%)	1 (100%)
61-70 yrs	0 (0%)	0 (0%)
71-80 yrs	0 (0%)	0 (0%)

Table 3: Showing Distribution of various parameters in Triple Co-infected Patients

Total Patients (46)	Male (45)	Female (1)
Rural Background	32 (71.11%)	1 (100%)
Urban Background	13 (28.89%)	0 (0%)
Alcohol	35 (72.50%)	0 (0%)
Smoking	35 (72.50%)	0 (0%)
H/o Surgery	27 (60%)	1 (100%)
H/o Blood Transfusion	5 (11.11%)	0 (0%)
Tattooing	27 (60%)	1 (100%)
IV Drug abuser	40 (12.08%)	0 (0%)
Multiple Sex Partners	6 (13.33%)	0 (0%)
Dental Procedures	4 (8.88%)	0 (0%)
Non-Cirrhotic	43 (95.55%)	1 (100%)
HCV SVR Achieved	42 (93.33%)	1 (100%)

DISCUSSION

HIV dual or triple infections with HBV and/or HCV have

been documented globally. Still, limited data are available in the literature,^[8] and that was the reason for conducting the study. The predominance of sexually active young males in our

study group is in alignment with previous studies.^[27,28] Additionally, younger age groups are more likely to have isolated HBV and HCV co-infections.^[29-31] Our study group was mostly male, which is consistent with research by Gupta et al. and may be related to a greater incidence of sexual promiscuity.^[32] The one characteristic finding that was revealed was that the majority of patients were intravenous drug abusers, alcoholics, and smokers. The intravenous drug abuse is a well-established fact for isolated, dual or triple co-infection with HBV, HCV and HIV. The history of past surgery and tattooing was also seen in a significant percentage of patients, which has also been documented as a risk factor for causing isolated or co-infection with these viruses.

On analysing the status of viral predominance, HCV was predominant over HBV, which can be due to three reasons. First, HBV has an inherent tendency to remain in the inactive carrier state in the majority of patients. Secondly, it is well established that HCV inhibits HBV replication more effectively than HBV inhibits HCV. Thirdly, all patients were on HAART treatment with the TLE regimen, containing tenofovir & lamivudine, both of which have antiviral activity against HBV. The SVR achievement against HCV is similar among triple-, dual-, and mono-infected patients, and this was also observed in our study pool, which aligns with previous studies reported in the literature. Despite coming from a region that is a hotspot for both hepatitis B and hepatitis C, a significant feature of our large research population of 30,000 patients is the small number of patients with triple co-infection. In contrast to intravenous drug abusers, who have a greater risk of co-infection, HIV patients often have a lower likelihood of HBV/HCV co-infection if there is a sexual channel of transmission. Given the extremely low rate of triple co-infection found in our research group, it seems that there must have been a sexual method of transmission. As protocol, we always require vaccination for HBV in HCV or HIV patients. It prevents future HBV infection in these patients. It is well proven in literature that HIV, HBV or HCV mono-infected patients can develop co-infection in future. Moreover, total free treatment, including testing, has led to an exemplary high compliance rate, thus preventing the complications of co-infections in the future. Regular counselling of patients and family members throughout the course of illness helps reduce risk factors for the future development of co-infections. It is a multi-pronged strategy that is giving fruitful results. Another thing to consider is whether HBV, HCV, and HIV might interfere with one another in the human body. This has been shown in situations of HBV and HCV infection, where HCV is typically the prevalent virus. The triple co-infection leads to increased morbidity and mortality.^[33-35] Moreover, dual or triple infections may aggravate hepatotoxicity of HAART and the possibility of inception of an AIDS-defining illness, similar to infection with HIV only.^[36] Because of pharmacokinetic interactions with components of HAART regimens, managing any hepatitis virus requires several approaches, which is concerning.

CONCLUSION

The HBV, HCV and HIV triple co-infection was extremely low, that too in hotspot of HBV & HCV mono and dual infections and is a positive sign. It can be attributed to mandatory HBV vaccination of every HIV and HCV patient, along with a multi-pronged strategy of reducing high-risk behaviour. Moreover, early detection and treatment of mono-infections reduced the risk of developing dual or triple co-infections in the future.

Limitation of study- Our study group included the majority of patients who were uneducated or partially literate. They belonged to a poor socio-economic status, hence there are high chances that the percentage of multiple sex partners and intravenous drug abuse may be under-reported.

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Conflicts of interest

There are no conflicts of interest.

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