

A Comparative Assessment of Immunological Parameters in HIV-HCV Coinfected Patients on Art-With and Without Treatment for HCV.

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Abstract: Among HIV-HCV co-infected patients all patients cannot afford the treatment of HCV. The aim is to study the natural history of disease in HIV-HCV co-infected patients on Anti Retroviral Therapy (ART) who could not take treatment for HCV. We hypothesized that Anti Retroviral Therapy will help in decreasing the disease progression of HCV and there will not be much difference in prognosis who are additionally treated with anti HCV drugs.

Methods: 145 patients are included in this study who are HIV HCV co-infected who are on ART. Only 40 patients has been treated for HCV in some point of their life. We compared the immunological profile of two groups and paired t test was used to compare it. CD4 count was calculated by Fluorescence Activated Cell sorter.

Results: Mean CD4 count was higher in treated group ($p=0.0013$) showing better immunological status in treated patients. HCV RNA count ($p=0.0001$) was also higher in non treated group.

Conclusion: There is a better immunological profile in HCV treated than in non treated patients indicating the importance of early treatment for hepatitis C in HIV-HCV co-infection.

Keywords: HIV-HCV Co-infection, treatment, CD4 count, HCV RNA.

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I. Introduction

Acquired immuno deficiency syndrome (AIDS) was first recognized in the United States in the summer of 1981. The current Centre for disease control (CDC) classification system for human immunodeficiency virus (HIV) infected adolescents and adults categorizes persons on the basis of clinical conditions associated with HIV infection and CD4+ T lymphocyte counts. HIV disease is a spectrum ranging from primary infection, with or without the acute syndrome, to the asymptomatic stage, to advanced stages associated with opportunistic diseases.¹

When a person is affected two or more different disease-causing organisms it is called co-infection. Infection with the hepatitis C virus (HCV) is the most common co-infection in people with HIV and hepatitis C is categorized as an HIV-related opportunistic illness. Complications related to HIV/HCV co-infection have become an increasingly important medical issue and consequences from HCV infection are now the leading cause of death in people with HIV. It is estimated that approximately 1.2 million people in the U.S. are infected with HIV and more than 4 million are infected with hepatitis C. As many as 30% of people with HIV may also be co-infected with hepatitis C.²

Hepatitis C virus (HCV) is one of the five hepatitis virus (A-E) which infect human liver. It is an enveloped single-stranded positive sense RNA virus belonging to the genus Hepacivirus within the family Flaviviridae. It has six major genotypic groups of variants (1-6) and hundreds of quasi-species showing variation in their molecular composition. Different variants are found in different geographical regions of the world. The genotype 1, 2 and 3 have a worldwide distribution. HCV is a significant cause of liver disease in those who are HIV positive. Cirrhosis due to HCV is probably as high as 22% at the time of death in HIV-HCV co-infection patients.³

Due to shared risk factors, approximately one-third of patients with human immunodeficiency virus-1 infection (HIV) are co-infected with chronic hepatitis C virus (HCV) infection.⁴With the successful implementation of highly active antiretroviral therapy (HAART) for patients with HIV infection, a rapidly fatal illness has been converted to an illness maintained as a chronic disease. With dramatic reductions in the prevalence of opportunistic infections, other diseases have become important health problems in the HIV-infected population. Hepatitis C virus (HCV) co-infection has emerged as a major source of morbidity and mortality. Patients with HCV-HIV co-infection appear to have accelerated progression to symptomatic liver disease and cirrhosis, and successful initiation of HAART may be limited by either HCV-related liver disease or hepatotoxicity of medications in concert with viral liver disease.⁵Of those infected with HCV, about 75 per cent become chronically infected, and of these, 7-18 per cent will develop cirrhosis over a 20 year period, and be at risk of hepatocellular carcinoma (1-6% per year) or liver failure (2-3% per year).⁶The prevalence of HCV infection in India is estimated to be between 0.5 and 1.5 per cent which is five times higher than the prevalence of HIV infection.⁷

A hallmark feature of hepatitis C virus (HCV) infection is its propensity for lifelong chronic infection. The majority (65%-80%) of all infected individuals remain chronically infected and at risk of severe liver disease (cirrhosis, end-stage liver disease and liver cancer); however, the remaining 15%-40% spontaneously resolve their infections.⁸

The HIV and HCV transmission efficiency varies and transmission through percutaneous blood exposure is 10-fold higher for HCV compared with HIV.⁹ As a consequence of this the incidence rate of HCV infection is higher than HIV among people who inject drugs (PWID), and it is estimated that 50%-90% of all PWIDs are infected with HCV.¹⁰⁻¹⁴

Manipur lies adjacent to the Golden Triangle, where the borders of Myanmar, Laos and Thailand meet; most of its eastern boundary is formed by Myanmar, the second largest opium producer in the world. Manipur is on a major drug-trafficking route from the Golden Triangle; thus, illicit drugs are commonly available. Heroin and locally known as "number four" among IDUs, is considered to be the major injecting drug used in Manipur, although powder form of dextropropoxyphene (from capsules) is also increasingly used by IDUs for injections.¹⁵ Manipur is one of the seven high HIV prevalent states of India and among the HIV positive people HCV infection is one of the common co-infection because of common route of transmission.

In Manipur now most of HIV-HCV cases are having longer life and better quality of life than before after starting free HAART by NACO through Manipur AIDS Control Society (MACS) since April 2004. But the mortality of HIV-HCV still increasing in Manipur as most of them cannot afford HCV treatment and dies of liver complication because of poor socioeconomic condition.¹⁶ So, this study is to evaluate and compare the clinico-immunological outcome of HIV HCV coinfecting patients who are on ART, who took treatment for HCV and who could not afford to take because of low socioeconomic status.

The aim of this study is to assess and compare immunological response in HIV-HCV co-infected patients on ART who is treated for HCV and not treated.

II. Material And Methods

All cases of HIV-HCV co-infection patients, both male and female >18 years of age, who attended the centre of excellence (COE) OPD, ward and liver clinic at RIMS Hospital, Imphal, Manipur during the study period were included in the study group.

Study Design This was a hospital based Cross sectional study

Study setting: This study carried out in the department of medicine OPD, Liver clinic, ward and COE (centre of excellence) ART centre, Regional Institute of Medical Sciences, Imphal for one and half years from October 2015.

Study Duration: The study was carried out for 24 months starting from October 2015 to September 2017.

Sample size: The estimated sample size for the study was 145.

Sample size calculation: The sample size was calculated according to prevalence of HIV-HCV co-infection among HIV infected people in India. The prevalence of co-infection is 8 – 15%.¹⁷ So we included 145 patients who are HIV-HCV co-infected patients for study. Due to poor economic status of patients very less patients have taken treatment for HCV. We only got 40 patients in 145 who had taken treatment for HCV. So we compared the data according to that.

Inclusion criteria were 1) All HIV-HCV co-infected patients on HAART from ART (COE), Gastro-Enterology (GE) Clinic and Medicine OPD or ward. 2) Those patient who were willing to participate and given informed consent to this study. 3) Age \geq 18 years.

Exclusion criteria were 1) All mono-infection of HIV and Hepatitis c. 2) Patients co-infected with HBV infection. 3) Patients known to have malignancy, cardiovascular disease, diabetes mellitus and chronic liver diseases except hepatitis C virus infection. 4) Those patients who were not willing to participate in this study.

Study variables

- CD4 count
- CD8 count
- HCV RNA count

Study tools:

CD4 and CD8 cell count was calculated by Fluorescence Activated Cell sorter(Manufacture:BD Biosciences 2350 QumeDrive, San Jose,CA95131-1807,USAand HCV viral load was measured by Real Time PCR (manufacture: ROCHE and Thermo Scientific).

Procedure methodology

Written informed consent was taken from the patient or their family members participating in the study. The privacy of the patient was be respected.

(1)Laboratory investigations;

- CD4 and CD8 count were done
- HCV RNA and genotype.

CD4 and CD8 cell count was calculated by using automated analyzer, Fluorescence activated cell sorter (FACS).

Statistical analysis

The data collected were checked for completeness and consistency and were analyzed using IBM SPSS software, version 21.0 for windows. Paired T test is used for comparison between two groups.

III. Result

The study was conducted in Regional Institute of Medical Sciences. Patients attendingthe medicine OPD, Liver clinic, ward and COE (centre of excellence) ART centre in Regional Institute of Medical Science.

Table 1: Distribution of the respondents by others biochemical parameters

CD4/CD8	Mean ± SD
CD4	271.4 ± 99.1
CD8	709.3 ± 110.3
HCV RNA quantitative	4082861 .1 ± 1119851.1

Table 2: Relation between HCV treated and non-treated HIV patients on parameters of CD4, CD8 and HCV RNA

CD4/CD8	HCV treated Mean ± SD	HCV not treated Mean ± SD	t-test
CD4	310.2 ± 87.3	250.2 ±100.2	t-3.2 df-142 p-0.0013
CD8	699.3 ± 95.2	712.3 ± 110.5	t-0.64 df-142 p-0.52
HCV RNA quantitative	2006581.2 ± 365322.3	6178936.7 ± 1052937	t-10.6 df-142 p-0.0001

In table 2, comparison of CD4, CD8 and HCV RNA of the two groups were done in mean with standard deviation. Test of significance was done using t-test and p-value of less than 0.05 was taken as significant.

The study results shows significant increase in immunological status in CD4 count (p-0.0013) after taking hepatitis C treatment. There is decrease in HCV RNA count also in treated group than non treated group(p-0.0001).

IV. Discussion

Although it is widely recognized that patients infected with HIV have increased risk of HCV co-infection. With the decline in AIDS-related deaths, non-AIDS causes of morbidity and mortality have become prevalent and for HIV-HCV co-infected individuals, the burden of disease is largely related to their HCV infection. A consensus of the influence of HIV on the natural course of HCV exists; however, how HCV influences the natural course of HIV is still debated and no final conclusions have been drawn.

This comparative study about immunological profile of HIV- HCV co-infected patients on ART- with and without treatment for hepatitis C helps us to understand about the natural history of HIV-HCV co-infection who are not treated for HCV infection. There are several studies which compares data of HIV mono-infected and HIV-HCV co-infected patients. But while reviewing literature there is no study which compares HIV-HCV co-infection on ART who has been treated for HCV and those who have been not treated. This study is relevant in the present scenario of India and especially in Manipur because of low socioeconomic status as they can't afford the treatment for HCV infection.

The results of immunological factors compared in this study are CD4 and CD8 T cells. In CD4 T cell count showed significant increase in those who had received treatment. The study results shows significant increase in immunological status in CD4 count (p-0.0013) after taking hepatitis C treatment. But CD8 T cells when compared doesn't showed any significance. The immunological finding is supported by the fact that the HCV RNA count in treated group which showed significant decrease than in non treated group(p-0.0001), so in treated group CD4 T cells showed increase in number and HCV RNA count showed lower than untreated group. It shows that there is an evident improvement in immunological status of treated patient when compared to treatment naïve patient.

V. Conclusion

This study showed that in patients with HIV-HCV co-infection who are on ART should start Hepatitis C treatment as early as possible to avoid long term hepatic complications like cirrhosis or hepatocellular carcinoma. The study result shows significant increase in immunological status by way of increase in CD4 count (p-0.0013) after being treated for hepatitis C infection. There is decrease in HCV RNA count also in treated group than treatment naïve group(p-0.0001).

References

- [1]. Alexander J. AIDS. In: Kasper DL, Fauci AS, Longo DL, Jameson JL, Loscalzo J, editors. Harrison principle of internal medicine. 18th ed. New York: MC Graw Hill; 2012.p.1215-18.
- [2]. Franciscus A. Guide to HIV-HCV Co-infection. Available on www.hcvadvocate.org/hepatitis/factsheets-pdf/Coinfection/20Guide.pdf. Accessed Oct 15, 2015.
- [3]. Ghany M, Strader D, Thomas D, Seeff L. Diagnosis, management, and treatment of hepatitis C: an update. *Hepatology*. 2009;49(11):1335-74.
- [4]. Resino S, Bellon J, Asensio C, Micheloud D, Miralles P, Vargas A, et al. Can serum hyaluronic acid replace simple non-invasive indexes to predict liver fibrosis in HIV/Hepatitis C coinfecting patients. *BMC infect dis*. 2010;10(1):864-8.
- [5]. Eyster ME, Diamondstone LS, Lien JM, Ehmann WC, Quan S, Goedert JJ. Natural history of hepatitis C virus infection in multitransfused hemophiliacs: Effect of co-infection with human immunodeficiency virus. The multicenter hemophilia cohort study. *Journal AIDS* 1993;6(1):602-10.
- [6]. Grebely J, Dore GJ. What is killing people with hepatitis C virus infection. *Semin liver dis* 2011;31(2):331-9.
- [7]. Puri P, Anand AC, Saraswat VA, Acharya SK, Dhiman RK, Aggarwal R, et al. Consensus statement of hcv task force of the indian national association for study of the liver (INASL). Part I: Status report of HCV infection in India. *J clin exp hepatol* 2014;4(2):106-16.
- [8]. Hoofnagle JH. Course and outcome of hepatitis C. *Hepatology* 2002; 36(1): 21-29.
- [9]. Sulkowski MS, Thomas DL. Hepatitis C in the HIV-Infected Person. *Ann intern med* 2003; 138(13): 197-207.
- [10]. Garten RJ, Lai S, Zhang J, Liu W, Chen J, Vlahov D, et al. Rapid transmission of hepatitis C virus among young injecting heroin users in Southern China. *Int j epidemiol* 2004; 33(15): 182-188.
- [11]. Quan VM, Go VF, Nam LV, Bergstrom A, Thuoc NP, Zenilman J, et al. Risks for HIV, HBV, and HCV infections among male injection drug users in northern Vietnam: a case-control study. *AIDS Care* 2009;21(17):7-16.
- [12]. Alter MJ. Epidemiology of viral hepatitis and HIV coinfection. *J Hepatol* 2006;44(13):6-9.
- [13]. Thomas DL, Vlahov D, Solomon L, Cohn S, Taylor E, Garfein R, et al. Correlates of hepatitis C virus infections among injection drug users. *Medicine (baltimore)* 1995;74(4):212-20.
- [14]. Villano SA, Vlahov D, Nelson KE, Lyles CM, Cohn S, Thomas DL. Incidence and risk factors for hepatitis C among injection drug users in Baltimore, Maryland. *J clin microbiol* 1997;35(13):3274-7.
- [15]. Chakrapani V, Newman P, Shunmugam M, Dubrow R. Social-structural contexts of needle and syringe sharing behaviours of HIV-positive injecting drug users in Manipur, India: a mixed methods investigation. *Harm reduction journal* 2011;8(1):9-14.
- [16]. Kermode M, Nuken A, Medhi GK, Akoijam BS, Sharma HU, Mahanta J. High burden of hepatitis C & HIV co-infection among people who inject drugs in Manipur, Northeast India. *Indian j med res* 2016;143(3): 348-56.
- [17]. Chandra N, Joshi N, Raju Y.S.N, Ajit K, Teja V D. Hepatitis B and/or C co-infection in HIV infected patients: A study in a tertiary care centre from south India. *Ind j med res* 2013;138(1):950-4.

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