Original Article

Co-Infection of HBV in Partially/Non-Vaccinated Diagnosed HCV Positive Patients

Raza Muhammad Khan[1] and Asmatullah Khan[2]

ABSTRACT

Objective: To determine the frequency of co-infection of HBV in partially/non-vaccinated diagnosed HCV positive patients.

Study Design: Descriptive / cross-sectional study.

Place and Duration of Study: This study was conducted at the Department of Medicine, DHQ Teaching Hospital Bannu, Khyber Pakhtunkhwa from Feb 2015 to Aug 2015.

Materials and Methods: Data was collected from 371 patients already diagnosed as HCV positive for more than 1 year, through a preset questionnaire, to note their vaccination status against HBV. Those patients who were partially or non-vaccinated, were screened for HBsAg by ELISA, to document the co-infection.

Results: Out of 371 HCV positive patients, 201 patients were males (54.2%) and 170 (45.8%) were females. Only 89 (23.99%) patients were vaccinated (49 males and 40 females) while the rest 282 were either non-vaccinated (260 patients) or partially vaccinated (22 patients). So overall 282 (76.01%) HCV positive patients were lacking proper vaccination against HBV, and merely 89 (23.99%) patients were properly vaccinated against HBV. Out of those 282 HCV positive patients, who were either non-vaccinated or partially vaccinated, 14 (4.96%) patients were found to be HBsAg positive by ELISA (co-infection).

Conclusion: The frequency of vaccination against HBV was very low in this high risk adult group patients (18-60 years) already infected with HCV. Only 89 (23.99%) patients were properly vaccinated, which is an alarming situation. Out of these 282 HCV positive patients lacking proper vaccination against HBV, 14 (4.96%) patients were found to be HBsAg positive by ELISA (co-infection). This co-infection can be prevented by proper planing by health care provider to improve vaccination.

Key Words: Hepatitis C virus (HCV), Vaccination status (vaccinated/non-vaccinated/partially vaccinated), Hepatitis B virus (HBV), Bannu.

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INTRODUCTION

Hepatitis Cis an infectious disease caused by the hepatitis C virus(HCV), previously called as "non-A non-B hepatitis". It is estimated that 130–170 million people i.e.; 3% of the world's population are living with chronic hepatitis C[1]. About 3–4 million people are infected per year, and more than 350,000 people die yearly from hepatitis C related diseases[1]. Its prevalence is higher in some countries in Africa and Asia e.g.; Egypt (22%), Pakistan (4.8%) and China (3.2%)[1].

[1.] Department of Medicine, DHQ Teaching Hospital / Bannu Medical College, MTI, Bannu, Khyber Pakhtunkhwa.
[2.] Department of Neurosurgery, Khalifa Gul Nawaz Teaching Hospital, MTI, Bannu, Khyber Pakhtunkhwa.

Correspondence: Dr. Raza Muhammad Khan, Assistant Professor of Medicine, DHQ Teaching Hospital / Bannu Medical College, MTI, Bannu, Khyber Pakhtunkhwa.
Contact No: 0333-9742570
Email: m-reyan33@yahoo.com

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Hepatitis B (HBV) infection is caused by Hepatitis B Virus (HBV)/ Dane particle, previously called as "Serum Hepatitis". The disease has caused epidemics in parts of Asia and Africa and it is endemic in China[2]. About a third of the world population has been infected at one point in their lives including 350 million who are chronic carriers[3, 4]. National and regional prevalence ranges from over 10% in Asia to under 0.5% in the United States and northern Europe. As of 2010, China has 120 million infected people, India 40 million and Indonesia 12 million. According to WHO, worldwide, an estimated 2 billion people are infected with the HBV, more than 240 million have chronic liver disease and 600000 people die every year due to acute or chronic consequences of hepatitis B[3].

Both hepatitis **C**[1] and **B**[,2,3,4] are becoming a major health challenge for the world in general and government of Pakistan and KPK in specific.

According to one study in Pakistan, prevalence of HBV infection among healthy adults, blood donors and non-donor, was 2.4% and that for HCV infection was 3.0%[5]. The condition is even worse in Khyber Pakhtunkhwa (KPK) and FATA areas. In one study, 224 out of 7148 i.e.; 3.13% blood donors were positive for anti-HCV antibodies by ICT[6]. In another study, 57 patients out of

1269 (4.49%) patients were HBs-Ag positive and 88 patients(6.93%) patients anti-HCV antibodies positive[7].
According to Government of KPK, 1553 Hepatitis B and 6214 Hepatitis C patients were treated in year 2011-12 under Hepatitis Control Programme[8].
Both hepatitis B and C viruses are hepatotropic and have the same mode of transmission. Co-infection with these two viruses can occur especially in area of high prevalence.
Hepatitis "B" virus co-infection can occur in those HCV-positive patients who are not vaccinated against HBV infection. Dual chronic infection with HCV and HBV is common in areas endemic for either virus like Chinafor HBV[2].
In one study in Taiwan, co-infection with HBV in active HCV infection was noted in161 patients (HBsAg positive) out of 321 (50.16%)[9].Co-infection with HBV or Hepatitis A virus (HAV) in patients with chronic HCV infection is associated with increased morbidity and mortality[10,11]
Complications like Acute Fulminant Hepatitis, Hepatocellular Carcinoma and Cirrhosis are more common and earlier in those HCV patients who are co-infected with Hepatitis B, HIV and alcoholics[12].
No local data is available regarding hepatitis B and C co-infection in KPK. Dual chronic infection with HCV and HBV is common in areas endemic for either virus.
Peg-Interferon alfa 2a & 2b along with Ribavirin are antiviral which can be used for co-infection caused by HCV & HBV[1]. It is equally effective in patients with HCV mono-infection and in those with chronic HCV-HBV infection.[9] 9 million U of standard IFN 3 times weekly for 3 months could clear HCV in 31% of patients with HCV-HBV coinfection.[13]
Standard IFN and Ribavirin could cause sustained HCV eradication at rates comparable to those in patients with HCV alone and, interestingly, up to 21% of their patients lost the hepatitis B surface antigen[14].

MATERIALS AND METHODS

This descriptive, cross sectional study was conducted at Department of Medicine, DHQ Teaching Hospital Bannu KPK, 6 months from Feb 2015 to Aug 2015.
Sample Size: 371 HCV positive patients who were analyzed for HBV vaccination (taking 40.5%[15] as frequency of true vaccination rate against HBV, keeping 5% margin of error and 95% confidence interval, using WHO sample size calculator). Out of it, the 282 patients not vaccinated were tested for HBV infection. Consecutive, Non-probability Sampling used.
Inclusion Criteria: All "HCV" positive patients (Anti-HCV Abs positive by ELISA, diagnosed for last one year, noted from clinical record), not vaccinated for HBV, of Either gender, and aged above 18 and under 60 years.
Exclusion Criteria: Those patients with a history of previous Hepatitis "B" infection (who have cleared the virus either spontaneously or by treatment), vaccinated patients, patients with End-stage liver disease, patients terminally ill, and patients with dementia/mentally retarded were not included because, as they were either already infected, naturally immuned/vaccinated to HBV, would not benefit from future planned vaccination or would give recall bias.
Data Collecting Procedure: The study was conducted after approval from hospitals ethical and research committee/ board. All the patients who were HCV positive not vaccinated for HBV and meeting the inclusion criteria, as per operational definitions, presented to the Department of Medicine, DHQ Teaching Hospital Bannu, through emergency or OPD, were included in the study. All patients were first counseled for interview. The purpose and benefits of the study were explained to all patients, and a written informed consent was obtained from all who agreed to participate in the study. A detailed medical history (used as a diagnostic tool) was taken from all the patients, regarding duration of HCV infection and hepatitis "B" vaccination status. A structured questionnaire was distributed among patients (study population), as data collection tool having all variables of interest.
All the patients were interviewed on the basis of questionnaire and they were categorized as Vaccinated, Partially vaccinated or Non-vaccinated Hepatitis "B".
Those HCV positive patients who were partially/ non-vaccinated were screened for HBsAg by ELISA from hospital laboratory of DHQ Teaching Hospital Bannu, if they were not screened in the past after 1 year of acquiring HCV infection, to document the co-infection.
All the information including name, age, gender, address, vaccination status and co-infection were recorded in that pre-designed Proforma. Only a complete Proforma was subjected to analysis. Strict exclusion criteria was applied to control confounders and bias in the study results.
Statistical Analysis: Data obtained was entered into SPSS version 10 and analyzed in descriptive statistics. Mean $\pm$ SD were calculated for numerical/ quantitative variables like age. Frequencies and percentages (%) were calculated for categorical/ qualitative variables such as gender, vaccination status and co-infection. Vaccination status and co-infection were stratified among age and gender to see the effect modifiers. All results were presented in the form of tables, charts.

RESULTS

A total of 371 patients with HCV positive were included in the study. Among them, 201 (54.18%) were male and 170 (45.82 %) were female, with male to female ratio of 1.18: 1.0. Their age ranged between 18 and 60 years, and the mean age was 37.15±14.009 years. 89 (23.99%) patients were completely vaccinated, while 282 (76.01%) patients were either non-vaccinated (260 patients i.e.70.08%) or partially vaccinated (22 patients i.e.5.93%), as per operational definition.

Table No.1: Summarized descriptive statistics of study population (n=371)

Vaccination Status	Age Group									Total Patients
	18-25 years			26-55 years			56-60 years			
	M*	F	T	M	F	T	M	F	T	
Vaccinated	16	13	29	27	22	49	06	05	11	89
Non-vaccinated	50	43	93	68	59	127	22	18	40	260
Partially Vaccinated	03	03	06	07	06	13	02	01	03	22
Total Patients	69	59	128	102	87	189	30	24	54	371

***M= Male F= Female T= Total**

Out of 371 (n=371) HCV positive patients, 201 patients were males (54.2%) and 170 (45.8%) were females. Only 89 (23.99%) patients were vaccinated (49 males and 40 females) while the rest 282 were either non-vaccinated (260 patients i.e. 70.08%, 140 males and 120 females) or partially vaccinated (22 patients i.e. 5.93%, 12 males and 10 females) (table 2). So overall 282 (76.01%) HCV positive patients were lacking proper vaccination against HBV, and merely 89 patients were properly vaccinated against HBV.

Out of those 282 (n=282) HCV positive patients, who were either non-vaccinated or partially vaccinated, 14 (4.96%) patients were found to be HBsAg-positive by ELISA (co-infection) and 268 (95.04%) were HBsAg-negative by ELISA (table 3). Cross-tabulation between vaccination status and co-infection is shown in table 4 which showed that all the 14 HBsAg-positive patients (co-infected) were those who were not vaccinated at all (8 males and 6 females). Co-infection in table 3, while combined vaccination status &co-infection in table 4.

Table No.2: Frequency of vaccination status of patients (n=371):

Vaccination status	Frequency	Percentage
Non-vaccinated	260	70.1%
Partially Vaccinated	22	5.9%
Vaccinated	89	24.0%
Total	371	100.0%

Table No.3: Frequency of co-infection of patients (N=282):

Parameters	Frequency	Percentage
HBsAg –VE by ELISA	268	95.035%
HBsAg +VE by ELISA	14	4.965%
Total	282	100%

Table No.4: Co-Infection in non-/partially vaccinated patients (N=282):

Vaccination status	Co-Infection by HBV			Total
	Not checked	HBs Ag-ve by ELISA	HBsAg+ve by ELISA	
Non-vaccinated	-	246	14	260
Partially Vaccinared	-	22	0	22
Vaccinated	89	-	-	89
Total	89	268	14	371

P value= 0.000

DISCUSSION

Hepatitis Cis aninfectious disease of the liver. It is a word health problem. It is estimated that 130–170 million people i.e.; 3% of the world's population are living with chronic hepatitis C[1]. Hepatitis C is the leading cause of liver transplantation and is primary cause of cirrhosis (27%) and Liver cancer (25%)[16]. Novaccineagainsthepatitis Cis available. Its spread and transmission can be decreased by adopting preventive measures.

If these HCV-positive patients are also co-infected at the same time with HBV, HIV or are alcoholics, then the disease progress is more rapid and accelerated, leading to early hepatic failure, cirrhosis or hepatocellular carcinoma.

Management of chronic HCV patients also include screening of these patients for HBV infection, and if not infected/prior immuned/vaccinated, then proper vaccination of these patients against HBV with standard vaccination schedule[17,18]. This vaccination will protect against HBV as well as HDV infection.[18,19] No local data is available regarding hepatitis B and C co-infection in KPK. Dual chronic infection with HCV and HBV is common in areas endemic for either virus.

This preliminary study presents a detailed survey of 371 HCV-patients, both out patients and in-door patients, who were aged 18-60 years, with mean age 37.15+14.009 years, who were positive for anti-HCV positive by ELISA for >1year, noted from their clinical records, with compensated liver disease, according to inclusion criteria. Their vaccination status was inquired against HBV infection.

Out of 371, only 89 (23.99%) patients were vaccinated (49 males and 40 females) against HBV. This vaccination rate is slightly higher than the vaccination rate noted in a study in Texas[12], where it was 21.9% (vs.23.99%). While this vaccination rate is lower than the vaccination rate noted in a study in New York USA[15], where it was 40.5% (Vs 23.99).

Out of 371, a large portion of 282 (76.01%) patients were lacking proper vaccination against HBV according to standard schedule, they were either non-vaccinated (260 patients i.e.70.08%) or partially vaccinated (22 patients i.e.5.93%), as per operational definition.

These 282 patients were subjected to screening program for HBV co-infection. The method used was detection of HBsAg by ELISA.

The 22 patients who were partially vaccinated were all negative for HBsAg. It means that none of them has HBV co-infection. Though anti-HBs was not checked to see whether the partial vaccination has mounted some immunity against HBV or not, but it seemed that still they have some immunity against HBV due to this partial vaccination.

The 14 patients, all from 260 non-vaccinated patients (4.96% of 282), were positive for HBsAg by ELISA (Co-infected). This rate of co-infection is very low as compared to that noted in one study in Taiwan[9] (4.96

Vs 50.16), partially because of low prevalence /endmicity of HBV here and use of less sensitive test for screening for HBV infection (HBsAg by ELISA), which can neither detect occult/latent hepatitis B (HBsAg-negative and anti-HBc-positive) nor HBV infection in window period (HBsAg and anti-HBs both negative). This added risk to HCV-positive patients would have been prevented/decreased by proper vaccination against HBV infection, with standard schedule of vaccination.

CONCLUSION

This study has demonstrated that a large proportion of the HCV-positive patients lacked proper vaccination against HBV, where both the viruses have high prevalence, and HBV infection can occur to these patients (co-infection) when not vaccinated for HBV. Therefore, all those managing HCV-positive patients should also counsel and educate the patients, regarding preventive measures against both HCV/HBV infections, screen these patients for HBV infection, and if not co-infected, then properly vaccinate them against HBV, with standard schedule of vaccination, along with giving standard Treatment including recent antivirals for HCV.

Recommendations: In the view of the above study, we recommend:

- The guidelines that all HCV-positive patients should be screened and vaccinated for HBV, must be practiced.
- All the HCV free-treatment programs, which have already been started, should incorporate free vaccination against HBV as well, to prevent co-infection.

Author's Contribution:

Concept & Design of Study:	Raza Muhammad Khan
Drafting:	Asmatullah Khan
Data Analysis:	Raza Muhammad Khan
Revisiting Critically:	Raza Muhammad Khan
Final Approval of version:	Raza Muhammad Khan

Conflict of Interest: The study has no conflict of interest to declare by any author.

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