

HIGH PREVALENCE OF HEPATITIS B & C IN TB PATIENTS - WILL IT BE THE NEXT THREAT TO TUBERCULOSIS CONTROL?

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ABSTRACT

Background: Worldwide, tuberculosis & viral hepatitis are common diseases and both remain underdiagnosed and under-treated. Co-infection with tuberculosis and hepatitis is likely to make diagnosis, management and control of either disease difficult and challenging. **Objective:** To determine prevalence of HCV and HBV infection among PTB patients at Rahim Yar Khan, Pakistan. **Patients and Methods:** One hundred sputum smear positive pulmonary tuberculosis patients were screened for HCV and HBsAg. In this cross-sectional study, from 1st April to 31st December, 2010 results were analyzed by age, gender, marital, educational & socioeconomic status by using SPSS version 15. **Results:** Sociodemographic data showed that 66% patients were young between 15-49 years. Only 8 patients had history of blood transfusion, 4 had traveled abroad and none was drug abuser. Most of them were poor. Out of 100 patients (56 male and 44 female) 22% patients were positive for HCV and 3% for HBsAg. Prevalence of HCV infection was significantly higher in married (p value 0.03) and in those with history of blood transfusion (p value 0.004). No significant statistical difference of prevalence of HCV between male & female, urban & rural, educated & uneducated & in those who traveled abroad or not was found. **Conclusion:** Prevalence of HCV infection among the pulmonary tuberculosis patients at Rahim Yar Khan (22%) is alarmingly high as compared with general adult Pakistani population (approx. 4.7%).

Key words: Pulmonary TB, Viral Hepatitis, Hepatitis B, Hepatitis C

INTRODUCTION

Viral hepatitis is a serious public health concern worldwide. Hepatitis B virus (HBV) and hepatitis C virus (HCV) are found to be responsible for severe liver disease, including hepatocellular carcinoma and cirrhosis related end stage liver disease. According to WHO about 2000 million people have been infected with hepatitis B virus worldwide, of which more than 350 million are chronically infected, and half million people die annually as a result of hepatitis B virus infection. Some 130170 million people are chronically infected with hepatitis C virus, and more than 350,000 people are estimated to die from hepatitis C-related liver diseases each year.¹

Prevalence of viral hepatitis varies from country to country. HCV was first described in Pakistan as a cause of cirrhosis of liver in early nineties in northern areas of Pakistan.² Although no serious effort has been done to determine the actual burden of disease, however, on the basis of

available data from various studies, WHO ranked Pakistan amongst one of the worst afflicted countries.^{3,4} Umer et al reviewed the available data from various studies conducted in Pakistan. They found the frequency of HCV infection in blood donors and in the general population 3% and 4.7 %, respectively.⁵ In Pakistan, military recruits are screened for HCV before induction and studies showed a prevalence of 3.64% ± 0.31% in candidates for military recruitment.⁶⁻¹¹ In a recent systematic review of hepatitis C virus epidemiology in Asia, Australia and Egypt, it was found that 4.7% of adult population of Pakistan was infected with HCV.¹² In 2009, government officials reported to the Senate^{more} than 8 million people in Pakistan are suffering from deadly hepatitis C while more than 5.5 million are affected by hepatitis B.¹³

In a recently conducted countrywide survey of prevalence of hepatitis B & C in Pakistan, a total of 47043 persons were screened by Pakistan Medical Research Council (PMRC). Overall prevalence of hepatitis B (HBsAg) was 2.5% and hepatitis C (HCV) was 4.9%. During this survey, out of 773 persons screened from district Rahim Yar Khan, 35 were found positive for HBsAg (4.7%) and 51 were positive for HCV (6.6%).¹⁴ Ministry of Health (MOH), Pakistan started a hepatitis sentinel surveillance system in five large public hospitals in four provinces and Islamabad Capital Territory. As

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reported in 14th October issue of MMWR, during June 2010–March 2011, a total of 712 cases of viral hepatitis were reported by these five sentinel sites. Newly reported hepatitis C was the most common cause of viral hepatitis, accounting for 53.2% of cases, followed by acute hepatitis A (19.8%), acute hepatitis E (12.2%), and newly reported hepatitis B (10.8%). In addition, among patients, 28 (3.9%) had evidence of HBV and HCV co-infection, and 11 (14.3%) of those with HBV infection had evidence of co-infection with hepatitis D.¹⁵

Considering the fact that presence of chronic liver disease in patients with TB makes the job of management of TB more complicated and no data of prevalence of TB & HCV/HBV co-infection available at least in the area served by our institute. We decided to determine the prevalence of HBV & HCV in pulmonary tuberculosis patients in this part of world.

PATIENTS AND METHODS

This cross-sectional study was conducted at Department of Pulmonology, Sheikh Zayed Medical College / Hospital, Rahim Yar Khan, Pakistan from 1st April to December, 2010. One Hundred consecutive smear positive patients were included in this study. Department of Pulmonology is serving as a diagnostic & treatment center for 316244 people of Rahim Yar Khan City & four surrounding Union Councils for treatment of TB under DOTS program.

Being a tertiary care facility, department also serves as a referral center for patients all over the District Rahim Yar Khan, as well as from the adjacent districts of Punjab, Sindh & Baluchistan. However, in this study, only the patients from the population mentioned above i.e., patients residing in the area allocated for the TB DOTS diagnostic center of Department of Pulmonology, Sheikh Zayed Medical College / Hospital, Rahim Yar Khan, Pakistan were included and patients referred from other DOTS catchment areas were excluded.

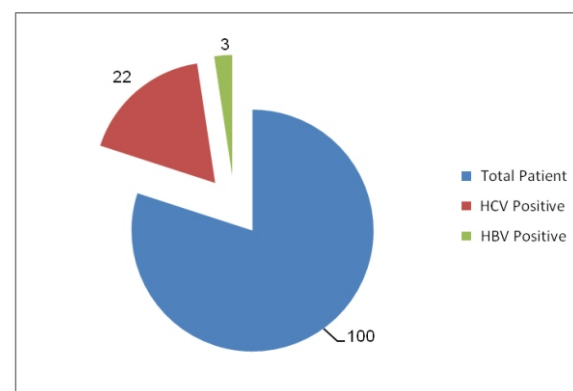
Consent was taken from the patients for inclusion in this study & drawing of blood sample for HCV & HBV testing. Demographic data of each patient was collected on a structured performa. Collected samples were tested for anti HCV antibodies & HBsAg at the Department of Pathology, Sheikh

Zayed Medical College & Hospital, Rahim Yar Khan, Pakistan by a rapid chromatographic immunoassay in serum / plasma using Hepatitis C virus one step test device and Hepatitis B surface Antigen (HBsAg) test device manufactured by ACON laboratories, Inc. USA. ACON HCV has a reported sensitivity of 99.8%, specificity of 99.9% and accuracy of 99.9%. Positive & doubtful results were confirmed by ELISA using the kits provided by Bio-Tech Co., Ltd. USA. Results were analyzed by age, gender, educational & socioeconomic status by SPSS version 15.0.

RESULTS

Figure I represent the overall prevalence of HBV (3%) and HCV (22%). Table I shows the sociodemographic data of subjects of this study as well as the prevalence of HCV in relation with sex, residential status, educational status, marital status, history of travel abroad and history of blood transfusion. Majority of these patients (66%) were young between the ages of 15 - 49 years. Most of subjects of this study belonged to poor socioeconomic class, 41% were earning less than 5000 rupees/month and 76% less than 10,000 rupees/month. None of the patients admitted any use of illicit drugs.

Figure I: Overall prevalence of HCV and HBV



Only 3 out of 100 patients were infected with HBV. Male: female ratio was 2:1. All 3 were living in urban areas. None of them had blood transfusion or travelled abroad. Two were unmarried and one married. None of the TB patients in this study had dual infection with both HBV & HCV. The median age of subjects of this study was 32.5 years. The TB patients co infected with HBV had a lower median

age of 24 years & mean age of 22 years when compared with the patients infected with HCV (median and mean age 41.5 years).

Table I: Sociodemographic characteristics & prevalence of HCV

	Total Patients	HCV Positive	% of total	P Value
	100	22	22%	
AGE (Years)				
Range	09 to 90	15 to 90	---	---
Median	32.50	41.50	---	---
Mean	35.90	41.55	---	--
SEX				
Male	56	16	28%	0.07
Female	44	06	13%	
RESIDENCE				
Urban	79	16	20%	0.41
Rural	21	06	28%	
EDUCATION				
Uneducated	51	12	23.5%	0.7
Educated	49	09	18.3%	
MARITAL STATUS				
Never Married	32	03	9.81%	0.03
Married	68	19	27.9%	
History of Travel Abroad				
Yes	04	02	50%	0.16
No	96	20	20.9%	
History of Blood Transfusion				
Yes	08	05	62.5%	0.004

DISCUSSION

In our study, 3% and 22% pulmonary TB cases were found to be infected with HBV & HCV, respectively. The prevalence of HBV in this study is comparable to the other studies reported from Pakistan.^{12,14} However, HCV seroprevalence is alarmingly high when compared with the figures reported in recent studies from various parts of Pakistan.^{14,17,18} Two recent systemic reviews have revealed that 4.7% of adult population of Pakistan had HCV infection.^{5,12} In PMRC study¹⁴ the prevalence of HBV at Rahim Yar Khan was 4.7% & HVC was 6.6%. Despite the fact that none of our patients admitted use of any illicit drug (I/V oral or inhalation) and only small number (8%) admitted blood transfusion, the prevalence of HCV in TB patients in our study is very high (4 - 6 folds higher than reported prevalence in adult population of Pakistan).

It is important to note that 5 out of 8 subjects

(62.5%) who had history of blood transfusion were screened positive for HCV infection against 17 out of 92 patients (18.5%) who did not receive any blood product and difference is statistically significant (p value 0.004). This finding reflects unsafe blood transfusion practices (both lack of appropriate screening of blood and unnecessary transfusions) in the country. According to the WHO office in Pakistan about 1.2 to 1.5 million transfusions are carried out annually in Pakistan.^{18,19}

A higher prevalence of HCV infection in the married TB patients in this study (25.7% vs. 9.8%) is another important statistically significant finding with p value of 0.03 considering its spread by sexual route. These patients might infect their spouses or they might have been infected by them. However, spouses of these patients were not screened.

In this study, 16 out of 56 male patients (28%) were tested positive for HCV against 6 out of 44 female patients (13%) however, this was not found to be statistically significant (p value 0.07). There was no statistically significant difference of prevalence among the uneducated patients (23.5%) and educated (18%) in this study (p value 0.7). Similarly, difference of prevalence of HCV infection in rural & urban residents was not found to be statistically significant (p value 0.41).

Although, prevalence of HCV infection has been studied in various high risk groups, only few studied prevalence in specific diseases. In one such study in the depressed population,²⁰ the prevalence of hepatitis C was 23%. Such study in pulmonary TB patients has an added importance as the presence of any significant liver dysfunction may force the treating physician to amend the treatment which can adversely affect the treatment outcome. In this contest, this high prevalence in our study is alarming. Considering the small number of the patients in this study, it might be justified to conduct larger study to determine the prevalence of HCV and HBV and if the results are replicated, then efforts should be made to determine factors responsible for that.

In addition to the smaller number of subjects in this study, there are few limitations. For example, details of injectables other than drug abuse or blood transfusion have not been determined. It is important as general population of Pakistan believes that treatment by injections is more effective than oral medication²¹ and these chronically ill patients might have received such treatment prior to the

actual diagnosis of TB. Similarly, additional risk factors present in Pakistani society like ear piercing, non-sterile surgical and dental practices of unqualified health care workers (quacks)²² and daily face and armpit shaving at community barber shops by traditional long-handled razor²³ have not been addressed in this study.

It is important to note that in this study 25% of Pulmonary TB patients living in the area of this study are infected with either HCV (22%) or HBV (03%). This is a very large infectious pool in any society. There is an urgent need to address this issue. Considering the fact that both especially HCV infection has the potential to chronically infect people, these people will be present in society for very long time. Due to number of risk factors present in Pakistani society, this infectious pool is likely to expand further. Secondly, in due course of time, many of these patients are likely to develop complication of chronic liver disease which will make diagnosis and treatment of TB difficult. The most of the first line drugs Rifampicin (R), Isoniazid (H) and Pyrazinamide (Z) are hepatotoxic. In presence of moderate to advance liver disease treating physicians will be forced to exclude / withhold one, two or all three agents from regimen resulting in a compromised treatment. These patients will likely to remain infectious for longer period of time & more likely to have unfavorable outcomes like relapse & treatment failure. This will adversely affect the TB control efforts. At present, there is no effective vaccine against HCV and its treatment is very costly & not uniformly effective. In this situation, it is very important to go all out for preventive measures. Considering the seriousness of this global public health threat, the Sixty-third World Health Assembly asked the member states to observe 28th July each year as World Hepatitis Day to raise awareness.²⁴ First World Hepatitis Day was observed on 28 July 2011. The theme was "This is hepatitis.... Know it. Confront it. Hepatitis affects everyone, everywhere". WHO is arguing the governments to strengthen efforts to fight viral hepatitis. To provide a global vision for the prevention and control of viral hepatitis, World Health Organization has launched a Framework for Global Action to prevent and Control Viral Hepatitis Infection²⁵ on the occasion of World Hepatitis Day 2012. The theme for the campaign

was "This is hepatitis.... it's closer than you think". There is an urgent need to increase awareness among public to adopt the preventive measures & enforce health authorities to take active steps for control of this potential disaster.

CONCLUSION

There is an alarmingly high prevalence of HCV infection in pulmonary TB cases. Larger study is needed to confirm it and its causative factors for proper preventive and corrective measures.

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