

Frequency of Hepatitis C Virus in Diagnosed Tuberculosis Cases

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ABSTRACT

Background: The frequency of hepatitis C virus infection along with tuberculosis has not been widely investigated and very low statistics on rates of hepatitis C virus co-infection in tuberculosis patients. Hepatotoxicity is the major side effect of anti-tuberculosis therapy hepatitis HCV liver disease elevates the chances of hepatotoxicity up-to five folds.

Aim: To see the frequency of Hepatitis C virus infection amongst people with diagnosed Tuberculosis using gene Xpert technique. To evaluate the factors associated with HCV infection in patients with MTB tuberculosis and to determine sensitivity and specificity of the tests.

Study design: Comparative analytical study.

Place and duration of study: Pathology Department, Civil Hospital Mirpur Khas Sindh from 1st January 2017 to 31st December 2018.

Methodology: Three hundred and thirteen patients of tuberculosis diagnosed by Genexpert included while testing hepatitis C virus using immunochromatography rapid test technique, enzyme linked immunosorbent assay method and polymerase chain reaction test for confirmation.

Results: Higher frequency of tuberculosis infection in males 57.8%, 42.5% between 20-39 years and 22% of hepatitis C virus infection in tuberculosis patients. Sensitivity of rapid test and enzyme-linked immunosorbent assay was 79% and 96% respectively while the specificity of rapid test and enzyme-linked immunosorbent assay was 91% and 99% respectively.

Conclusion: The high frequency of hepatitis C virus co-infection was found among tuberculosis cases in Mirpur Khas Division Sindh. Enzyme-linked immunosorbent assay method is more accurate, reliable as compared to rapid immunochromatography test for hepatitis C virus and polymerase chain reaction is still gold standard.

Keywords: TB, Hepatitis C virus, Mycobacterium tuberculosis, PCR, Genexpert, Rapid test

INTRODUCTION

Tuberculosis is an infective disorder caused by members of the genus *Mycobacterium*. Nine classes in the (genus) are related to as (MTBC) Mycobacterium tuberculosis complex. In the MTBC, Mycobacterium tuberculosis (MTB), M. *Africanus* and M. *Canetti* are the common biological agents of tuberculosis¹. The principal causative agent of the disease i.e. *Mycobacterium tuberculosis* mostly damage the lungs but can also deteriorate the other organs of the body. Tuberculosis continues a main health problem in both low socioeconomic developing and economically developed countries². World health organization estimated the prevalence of TB in Pakistan as extreme. Pakistan occupies sixth position in the world's 22 largest TB burden countries. According to WHO findings it is theorized that 410000 incident cases occur in Pakistan every year with 69000 yearly deaths with TB³. Another study conducted at Islamabad revealed that diagnosed patients of TB are rising in Pakistan with approximately 27,000 new cases per year⁴. At the Department of Pulmonology in Civil Hospital Hyderabad, Khanet al⁵ performed an observational study and showed the increased prevalence of multi-drug resistance tuberculosis (MDR-TB) in Sindh province of Pakistan. The Governmental TB Control Program in

Pakistan is now operating to improve the treatment success rate and reduce it to 91%. The World Health Organization (WHO) evaluates that there were 8.6 million new cases of Tuberculosis worldwide in 2012 and 1.3 million people demise⁶. Tuberculosis is a communicable disease which shows variable clinical manifestations. Its causative agent MTB is an obligate lung pathogen. Its large amount can be found in lungs cavities from where it can be easily transmitted to others through aerosol particles⁷. The beginning of infection takes place with the admission of MTB into the human pulmonary airspace. Secondary tuberculosis in adults usually occur by the reactivation of the latent primary infection after months or years of the primary infection. Secondary tuberculosis is characterized by productive typed necrosis of the primary minor lesions⁸. Throughout the world the diagnosis of TB is the difficult task⁹. Number of methods is used to diagnose TB included culture, acid-fast microscopy. The sputum having smear-positive acid-fast bacilli (AFB) is generally a preliminary indication in the diagnosis of lung tuberculosis, but the test is not tuberculosis-specific¹⁰. The contemporary treatment strategies suggest that isolation of *Mycobacterium tuberculosis* from a sputum culture is quiet unavoidable to confirm the diagnosis of lung TB¹¹. With the progress of new molecular diagnostics, a swift and sensitive test has been developed to diagnose TB, together with MDR-TB (multidrug resistant-TB). The *Xpert MTB/RIF* assay is a molecular-based speedy test which has technologize the

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TB diagnosis.¹² *Xpert MTB/RIF*® (or *Xpert*) can concurrently identify MTB complex DNA and mutations related to rifampicin (RIF) resistance (a reliable proxy for MDR-TB) straight from sputum specimens not more than 2 hours, and it lessens the chance of biosafety danger to staff.¹³ Hepatitis is caused by hepatitis C virus (HCV). At global level HCV is a major burden on human health. Recently an estimate suggest that there are more than 186 million people having interminable HCV which causes over 0.3 million deaths every year. As this disease virus is borne in blood that directly affects the cells of liver, due to high infection this will damage liver and causes cancer. The most usual means of infection is blood to blood contact which may be transmitted by unsterilized injection practices, unsafe health care, non-screened blood transfusions and blood products.¹⁴ It is also found to be transferred from mother to her infant.¹⁵ For the identification of HCV the RNA plays an important role to diagnose HCV.¹⁶ The typical investigative measures are First, to do a simple blood test to see for HCV antibodies in the blood. A reactive test means that the person has had exposure to the virus than the person will be put through a second blood test called a hepatitis C RNA test. Viral genotype and subtype tests, afterwards, valuation of resistance-associated substitutions.¹⁴ HCV core antigen (HCV-cAg) acts as an alternative to HCV-RNA testing to confirm current HCV infection for early diagnosis of HCV.¹⁷ In 2019, 88% of existing tuberculosis cases happened in the high TB problem nations. Eight countries responsible for two thirds of the current Tuberculosis cases: India, China, Indonesia, Pakistan, Nigeria. Globally, high counts of co-contamination beside tuberculosis and hepatitis C infection happen.¹⁸ Worldwide, the incidence of HCV infection in TB patients has not been comprehensively studied, and statistics on the count of HCV co-infection among patients with TB is very limited.

MATERIALS AND METHODS

This research report was organized at Pathology Department in Civil Hospital Mirpur Khas. Suspected cases of Tuberculosis done through OPD route for the definitive diagnosis of Tuberculosis cases. Male and female were carefully chosen above 15 years aged. This report's objective was a distinguish cases of tuberculosis using Genexpert while testing HCV by immunohromotography (ICT) rapid test, ELISA and PCR. Sputum sample was taken in small plastic container with tight lid in polythene bags as the criteria set by WHO. The blood sample was used in gel tube. The data was entered and analyzed through SPSS-20.

RESULTS

Sixty nine (22%) cases of positive hepatitis C (HCV) was significant ($P < 0.05$). Among them, 44 (63.7%) were males and 25 (36.3%) were females (Tables 1-2).

One hundred and eighty one (57.8%) were males and 132 (42.2%) were females. Patients belonging to age group under 20 years 32 (10.2%) belonging age group 20-29 years, 133 (42.5%) belonged to 40-59 years, 108 (34.5%) and 40 (12.8%) were from age group of 60 and above. One hundred (31.9%) belonged fair status only 29 (9.3%) belonged good status and 184 (58.8%) belonged poor

status. Two hundred and sixty three (84%) patients had positive from sputum AFB, 34 (10.9%) had negative sputum AFB and only 2 (0.6%) patients were produced contaminated sputum samples (Table 3).

Sixty nine (22%) patients were positive from PCR, 91 (29.1%) from ICT and 72 (23%) patients were positive from ELISA. The sensitivity of rapid test (ICT) was 79% and specificity was 91% while the sensitivity of ELISA was 96% with 99% specificity (Table 4).

Table 1: Frequency of diagnosed tuberculosis with gender (n=313)

Diagnosed cases	No.	%
Negative	244	78.0
Positive	69	22.0

Table 2: Comparison of positive cases among gender (n=69)

Gender	No.	%	P value
Male	44	63.7	0.002
Female	25	36.3	

Table 3: General characteristics of diagnose tuberculosis patients by gene x pert (MTB) (n=313)

Myobacterium tuberculosis	No.	%
Gender		
Male	181	57.8
Female	132	42.2
Age (years)		
< 20	32	10.2
20-39	133	42.5
40-59	108	34.5
>60	40	12.8
Socioeconomic status		
Fair	100	31.9
Good	29	9.3
Poor	184	58.8
Sputum AFB		
Positive	263	84.0
Negative	34	10.9
Contaminated	2	0.6
Not done	14	4.5

Table 4: Frequency and comparison of Hepatitis C (HCV) on rapid test device (ICT) and ELISA, with PCR in Mycobacterium tuberculosis (MTB) patients (n=313)

Tuberculosis (MTB) patients (N=313)			
Method	No.	PCR	
		Positive	Negative
ICT			
Positive	91 (29.1%)	69 (75.8%)	22 (24.2%)
Negative	222 (70.9%)	-	222 (100%)
ELISA			
Positive	72 (23%)	69 (95.8%)	3 (4.2%)
Negative	241 (77%)	-	241 (100%)

Sensitivity of ICT = $69/91 \times 100 = 78.8\%$

Specificity of ICT = $222/244 \times 100 = 90.9\%$

Sensitivity of ELISA = $69/72 \times 100 = 95.8\%$

Specificity of ELISA = $24/244 \times 100 = 98.7\%$

DISCUSSION

The frequency of hepatitis C (HCV) positive cases were 22%. In male 44 (24.4%) as compared to female 25 (18.9%) $p < 0.05$. This study is with accordance to another study conducted by Kuniholm et al²⁰ and Richard et al²¹ in Georgia found 22% HCV although various international studies showed frequency rate of HCV in tuberculosis were 7% which documented by Reis et al¹⁹ that is very low

compare with our study. While on the contrary in Thailand a study expressed very high frequency for HCV in tuberculosis which is 31%²². A Pakistani study conducted by Akhtaret al²³ showed frequency of HCV 9.1% by using ELISA technique.

In Tuberculosis patients with liver disease HCV increase the risk of hepatotoxicity than that of tuberculosis patients who do not suffer from liver disease HCV.²⁴ This shows importance of this study. The frequency of males for the disease tuberculosis is 181 whereas females 132. Results showed that males are at higher risk of the disease tuberculosis as compare to female in this region Mirpur Khas division. Literature study reflects same that frequency of tuberculosis among male are significantly higher than female in poor and middle income countries²⁵.

According to WHO the associated factor for the spread for HCV in Pakistan are blood transfusion therapeutic syringes, re use syringes by intravenous drug user, surgery unchanged blade use by barber are the major associate risk factors this study also evaluate the same. The study shows specificity and sensitivity of Rapid test (ICT) 91% and 79% respectively somehow matches with the another study conduct at king Edward medical university Lahore that compare the rapid test with ELISA showed specificity and sensitivity 97% and 95% respectively in our study PCR was the gold standard.²⁶ On ELISA test the detection of HCV showed 99% and 96% specificity and sensitivity respectively which will be accordance with most of the international study.²⁷ This study recommend and suggest that more work to be done on patient taken anti-tuberculosis therapy and infected to HCV get more hepatotoxicity than non-infected HCV.

CONCLUSION

The high frequency of HCV co-infection was detected amongst TB cases in MirpurKhas division Sindh. This suggested to pay more attention on continuous surveillance by the authority to minimize the transmission. Gene Xpert technique is accurate and time saving test for tuberculosis, ELISA method is more accurate, reliable as compared to rapid ICT test for HCV and PCR is still gold standard.

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