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Original Article

Prevalence of MDR-TB in Patients of Pulmonary Tuberculosis at a DHQ Hospital

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Abstract

Objective: The objective of this study was to determine the prevalence of MDR-TB in patients clinically diagnosed as pulmonary tuberculosis.
Study type, settings & duration: This descriptive cross-sectional study was conducted at tuberculosis clinic, Chest Medicine Department at DHQ Hospital Khanewal in collaboration with Department of Microbiology, Government College University Faisalabad from February 2020 to October 2020.
Methodology: After taking informed consent, 200 clinically diagnosed pulmonary tuberculosis patients were included. Demographic data was recorded and 3 early morning sputum samples were obtained from each patient to be assessed by GeneXpert-PCR. For statistical analysis, SPSS Version 20 was used. For quantitative variables, mean ± SD were calculated. For qualitative variables, percentages and frequencies were calculated. Effect modifiers and confounders were controlled through stratification and chi square test applied with *p*-value ≤0.05 significant.
Results: Mean age was 46±11.3 years with 104 (52.0%) males. Seventy-three (36.5%) were urban residents while 127 (63.5%) belonged to rural areas. Regarding sample consistency, 107 (53.5%) were mucopurulent, 34 (17.0%) purulent and 59 (29.5%) salivary consistency. Using GeneXpert-PCR, 80 (40.0%) patients were positive for tuberculosis. Rifampicin resistance was seen in 9 (4.5%) patients.
Conclusion: More than two-third patients (40.0%) tested positive for tuberculosis using GeneXpert-PCR and rifampicin resistance was seen in 4.5%. It is important to diagnose such infections timely and to check anti-mycobacterium drug statuses for its treatment to prevent excessive use of drugs and to reduce disease morbidity and mortality.
Key words: Multidrug resistant tuberculosis, pulmonary tuberculosis, GeneXpert-PCR.

Introduction

Tuberculosis remains a main reason of morbidity and mortality globally because of its higher incidence rates in the developing nations. Conferring to World Health Organization (WHO) tuberculosis report[1] of 2017 there were nearly 1.3 million HIV-negative and 0.3 million HIV-positive TB casualties with approximately 10 million new cases with 66% from eight countries: Indonesia, India, Philippines, China, Pakistan, Nigeria, Bangladesh and South Africa. Pakistan positions 6th comprehensively among the 22 high-TB burdened nations and contributes an expected 43 percent of the infection towards the Eastern Mediterranean district.[2] Yearly around 430,000 individuals including 15,000 youngsters contract tuberculosis in Pakistan[3] and consistently 70,000 passing on can be ascribed to the disease in the nation. Pakistan is likewise assessed to have the fourth most astounding pervasiveness of multi drug resistance tuberculosis all inclusive. Over 500 laboratories established in 70 middle and poor countries were able to carry out Line Probe Assay[4] for diagnosing resistance against main antibiotics used for TB which are Rifampicin and Isoniazid in few days at the end of 2015. Though molecular testing is the favored diagnostic approach for quicker cognition of multi-drug as well

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Authors Contribution

AIB & MAZ conceptualized the project. AIB & MAZ & SA did the data collection. NIB, FA, & MQT did the literature search. NIB & SA performed the statistical analysis. Drafting, revision & writing of manuscript were done by all authors.

as extensive drug resistance TB,[5] standard smear and culture is vital to check response of the treatments used. Whilst quickly distinguishing patients qualified for MDR-TB treatment, the GeneXpert-PCR[6] test is constrained to the discovery of rifampicin restriction. Most of the rifampicin resistant strains are also resistant to isoniazid, so it also can be used as a marker for multi-drug resistant Mycobacterium tuberculosis.[7] Notwithstanding the GeneXpert-PCR case, the WHO supported the utilization of the tests used for Hain line.[8]

Timely diagnostic and curative measures for MDR strains as per standard protocol of WHO guideline is the basic and successful strategies to control multi drug resistant TB. Local figures[9] of the drug susceptibility model of MDR in hospital settings oppose to establish a proper therapeutic measure, to minimize therapeutics ineffectiveness and control secondary infections of MDR TB cases. Many patients take their treatment from local unauthorized practitioners[10] and clinicians who lead to delay the detection of causative agents[11] prolong the treatment as well as failure to achieve the target. In the study by Adejumo et al.[12] Total cases (2497) were screened for MTB and RR-TB using CBNAAT Genexpert and 37.7% were found to be positive for MTB while 23.4% were found to be positive for RR-TB. As the prevalence of tuberculosis is increasing day by day and the antibiotic resistance rate is also getting high, this is at alarming levels in many districts of Punjab. Keeping in view the importance and of the issue, the present study was conducted among the population of district Khanewal Punjab to determine the prevalence of MDR-TB in patients diagnosed as pulmonary tuberculosis clinically.

Methodology

The descriptive cross-sectional study enrolled patients of clinically diagnosed pulmonary tuberculosis visiting TB clinic/Chest Medicine Department at DHQ Hospital Khanewal in collaboration with the Department of Microbiology, Government College University Faisalabad from February 2020 to October 2020. For confidence interval of 95% with confidence limit 6%, sample size required was 200 (using anticipated frequency 23.2%).[12] MDR-TB was defined as rifampicin resistance on GeneXpert-PCR testing. After taking informed consent, 200 clinically diagnosed pulmonary tuberculosis patients were included in the study. Patients with extra-pulmonary tuberculosis and with other lung diseases such as asthma were excluded. Demographic data including age, gender, residential status along with medical history for previous tuberculosis, AFB staining results and treatment history was recorded. Early morning sputum sample was obtained from each patient in sterile containers to avoid contamination, according to standard guidelines and precautions to be used for molecular identification by GeneXpert-PCR to find the presence of Mycobacterium Tuberculosis complex as well as rifampicin resistance. The data was recorded in a predesigned questionnaire. For statistical analysis, SPSS version 20 was used. For quantitative variables, mean $\pm$ SD was calculated. For qualitative variables, percentages and frequencies were calculated. Effect modifiers and confounders were controlled through stratification and Chi Square test applied with p-value ≤0.05 significant.

The Ethical approval was obtained from Institutional Review Board of Government College University Faisalabad, Faisalabad.

Results

Two hundred patients were enrolled at DHQ hospital Khanewal out of which 100 (50.0%) had previously been treated for tuberculosis. Mean age of the patients was 46$\pm$11.3 years with 104 (52.0%) males and 96 (48.0%) females.

Table 1: Demographic characteristics of patients and rifampicin resistance.

Demographic Characteristics	*Rifampicin Resistance*		*p-value*
	Present N (%)	*Absent N (%)*	
Sex:			
Male	4 (3.8)	100 (96.2)	0.323
Female	5 (5.2)	91 (94.8)	
Age:			
<25 years	4 (6.6)	56 (93.3)	0.490
26-50 years	2 (2.1)	91 (97.9)	
>51 years	3 (6.3)	44 (93.6)	
Residential Status:			
Rural	6 (4.7)	121 (95.3)	0.251
Urban	3 (4.1)	70 (95.9)	
Patients Category:			
New	4 (40.0)	96 (96.0)	0.132
Relapse	5 (50.0)	95 (95.0)	
Sputum Consistency:			
Mucopurulent	9 (8.4)	98 (91.6)	0.007
Purulent	0 (0.0)	34 (100.0)	
Saliva	0 (0.0)	59 (100.0)	
AFB Microscopy:			
Negative	0 (0.0)	55 (100.0)	0.008
Positive	7 (10.9)	57 (89.1)	
Not available	2 (2.4)	80 (97.6)	

On further distribution, 93 (46.5%) were aged 26-50 years, 60 (30.0%) were younger than 26 years whereas 47 (23.5%) were older than 50 years. Seventy-three (36.5%) were urban residents

while 127 (63.5%) belonged to rural areas. Regarding sample consistency, 107 (53.5%) were mucopurulent, 34 (17.0%) were purulent and 59 (29.5%) were of salivary consistency. Using GeneXpert-PCR, 80 (40.0%) patients were positive for tuberculosis and Rifampicin Resistance was seen in 9 (4.5%) patients. On review of prior data, 64 (32.0%) patients were positive for ZN stain AFB microscopy, 54 (27.0%) were negative while report was not available/not done in 82 (41.0%). Comparison of demographic characteristics and Rifampicin Resistance is shown in Table.

Discussion

Tuberculosis caused by bacteria Mycobacterium tuberculosis is one of the deadliest infectious diseases. Conferring to World Health Organization (WHO) tuberculosis report[1] of 2017 there were nearly 1.3 million HIV-negative and 0.3 million HIV-positive TB casualties with approximately 10 million new cases with 66% from eight countries: Indonesia, India, Philippines, China, Pakistan, Nigeria, Bangladesh and South Africa. Yearly around 430,000 individuals including 15,000 youngsters contract tuberculosis in Pakistan[3]. Multidrug-resistant tuberculosis (MDR-TB), in which there is drug resistance to TB treatment, poses more risk to the survival of TB patients. Tuberculosis (TB) is a main morbidity and mortality worldwide than other contagious diseases because of its higher incidence rates in the developing nations. Its elimination is quite difficult because of death, increase in population and infection through human immunodeficiency virus. Mycobacterium tuberculosis has potential to retain its activity in the tissues of a strong person for a large period of time. Mycobacterium tuberculosis infection changes into tireless and extended progression and transmit into host. Tubercular disease can create infection in an individual following quite a while of torpidity. The present descriptive cross-sectional study was designed for observing diagnostic frequency of pulmonary TB and rifampicin resistant using GeneXpert-PCR among the clinically diagnosed pulmonary tuberculosis patients visiting DHQ Hospital Khanewal. Sputum samples collected from 200 patients showed 40.0% were positive for tuberculosis and Rifampicin Resistance was seen in 4.5%. In the study conducted in Jamshoro by Khan et al.[13] 40.2% had MDR-TB out of the 169 smear-positive patients enrolled. Ali et al.[14] showed 4.9% positivity for MDR-TB in 5759 presumptive tuberculosis cases in Khyber Pakhtunkhwa and 10.4% positivity in patients who had been previous history of tuberculosis treatment. Ullah et al.[11] showed prevalence of MDR-TB as 11.5% in Islamabad. Aftab et al.[15] did DNA sequence analysis of 156 MDR-Mycobacterium tuberculosis samples to show that majority of mutations occur in the 81-bp RRDR of *rpoB* and RRDR at codons 531, 526, and 516 were most frequent.

Tuberculosis is one of the real general medical issues in the underdeveloped nations with around evaluated 60% of the grown-up populace being affected with TB. In Nepal, about 45% of the populace selected with TB.[16] Consistently 40,000 individuals create dynamic TB among them 20,000 have irresistible aspiratory infection. Nepal, by evaluated cases number, is positioned at 27 internationally. In spite of the development and execution of a much-enhanced National Tuberculosis Program (NTP) through DOTS Strategy all through the country, 6000 to 7000 individuals still die from TB every year in Nepal.[17] Among the 385 participants of study 225 were sensitive and 130 showed resistance against INH.[18] This finding was concordant with comparative investigations in different nations. A study from Italy demonstrated 82.2% males and of 17.8% of the females among 90 TB cases.[19]

In our study showed 50.0% had previously been treated for tuberculosis and out of these 55.5% had MDR-TB. Ali et al.[14] demonstrated that MDR-TB was significantly higher in previously treated patients as compared to untreated patients (10.4% Vs 3.2% respectively). Ullah et al.[20] reported drug resistance in 56% relapse patient's ad compared to 12.8% in new cases. Khan et al.[13] reported 82.2% patients were taking their medications regularly, thus providing a link between poor treatment compliance and risk of MDR-TB. Ali et al.[14] observed that 25–34 years aged group was more likely infected with TB (40%), however MDR-TB was most common in 55–64 years age group (6.4%). Age group 10–25 years was the most affected group with MDR-TB in the study by Ullah et al.[20] In the present study 44.5% males and 55.5% females were positive for MDRTB . The study by Khan et al.[13] showed 40.2% cases of MDR-TB. Ali et al.[14] showed tuberculosis to be more frequent in women (39%) as compared to men (29%), however MDR was more frequent in men (62.8%) than women (37.2%). Ullah et al.[20] showed 52.3% female and 47.7% male with 66.2% new cases and 33.8% previously treated patients to report MDR-TB in 10.2%.

In the present study, 40.0% tested positive for tuberculosis using GeneXpert-PCR and rifampicin resistance in 4.5%. On review of prior data in our study, 32.0% patients were positive for ZN stain AFB microscopy, 27.0% were negative while report was not available/not done in 41.0%. In the respiratory samples, GeneXpert-PCR was much more sensitive technique than AFB sputum smear

microscopy. For patients who present high clinical expectancy of pulmonary tuberculosis, GeneXpert-PCR is used as a helpful tool for prompt detection. In case the GeneXpert-PCR result is positive but the culture result is negative, findings should be read attentively and well associated with the history (clinical and cure) of the patient. Beside the benefit of early detection GeneXpert-PCR simultaneously detects Rifampicin resistance in samples and this is useful for MDR-TB patients. Further studies should be carried out in this regard.

It is concluded that drug resistant tuberculosis is a major problem in Pakistan and as well as in the world. More than two-third patients (40.0%) tested positive for tuberculosis using GeneXpert-PCR and rifampicin resistance in 4.5%. It is important to diagnose such kind of infections timely and it is important to check the anti-mycobacterial status of different drugs used for the treatment of tuberculosis in order to prevent the excessive use of anti-mycobacterial. Proper use of drugs is very important to treat such kind of invasive infections timely.

Conflict of interest: None declared.

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