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Research Article

The Prevalence of Multidrug Resistant Tuberculosis (MDR-TB) in Different Age Groups Keeping Gene-Xpert MTB/RIF as A Gold Standard Technique

Nazeeha Waseem[1*], Umair Waqas[2], Mubasher Rauf[3], Munazza Zaka Bhatti[4], Khushbakhat Maqbool[5], Muhammad Ahmad Naeem[6]

[1]Medical Imaging Doctor, University of Lahore, Gujrat, Pakistan
[2]Lecturer, University of Lahore, Gujrat, Pakistan
[3]Assistant Professor, Cholistan University of Veterinary and Animal Sciences, Bahawalpur
[4,5]Microbiologist, Government College University, Faisalabad, Pakistan
[6]Lecturer, University of Lahore, Gujrat, Pakistan

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Abstract: ***Background:*** Tuberculosis (TB) is an infectious disease caused by a bacterium called *Mycobacterium tuberculosis*, which affects the lungs most of all. Multidrug-resistant tuberculosis (MDR-TB) shows resistance to Isoniazid and Rifampicin both of which are the first-line anti-TB drugs. This is one of the critical health concerns all over the world and MDR-TB represents a major threat to control of the disease worldwide because of its high mortality and limited treatment therapy. ***Methodology****:* The present study was designed to determine the spread of MDR-TB in Gujrat, Punjab Pakistan. A total of 300 sputum samples were collected from suspected patients at Aziz Bhatti Shaheed Teaching Hospital, Gujrat. All the information regarding patients and their previous history of infection was collected through a predesigned questionnaire. After collection all the sputum samples were directly screened for acid fast bacilli through Z-N and Fluorescent staining. Molecular confirmation of MDR-TB was done by Gene-Xpert MTB/RIF assay. ***Results:*** Out of 300 samples 167(55.7%) were male and 133(44.3%) were females among those 149 were new patients and 49 were previously treated patients. ZN staining reveled 153 (51.0%) positive cases and mostly (n=60; 39.2%) were found in 21-40 years age. Moreover, 199 (66.3%) cases were positive for MTB by fluorescent staining and mostly (n=76; 38%) were observed in 21-40years age group. However, 214 (71.3%) MTB cases were identified by Gene-Xpert and among these, 25 (8.3%) were MDR-TB. Out of 25 cases 18 (72%) were females and 07 (28%) were male patients. ***Conclusion:*** There was high prevalence of MTB (71.3%) and MDR-TB (8.3%) in clinical setting of Gujrat. Therefore, it is the need of the hour to conduct surveillance study to overcome this problem.

Keywords: Tuberculosis, MDR-TB, Gene-Xpert.

INTRODUCTION

Tuberculosis (TB) is an airborne irresistible infection caused by *Mycobacterium tuberculosis* (MTB). This bacterial infection is caused by different strains of *Mycobacterium*, generally MTB. This bacterium for the most part assaults the lungs (Pulmonary TB) however MTB can cause disease in any organ of the body, called Extra-Pulmonary Tuberculosis (EPTB) [1] As per World health Organization (WHO) 2018, TB is a leading public health issue in entire world [12]. The prevalence of disease is more in developing countries due to poor hygiene maintenance. China, India, Russia and Indonesia together are creating half of the global economic burden due to TB [2] Pakistan ranks 5th with 179.2 million people among 22 highest TB burdened countries and holds for 63% TB cases in Eastern Mediterranean region. National TB Control Program (NTP) Pakistan indicated that almost 413,450 TB cases arise every year in the country. Predominance of TB in Pakistan is 630,000 cases with mortality rate of 60,000 [3] It is a growing international health concern focusing as one of the arising infectious causes of death in the world today [2]. The differentiation of Non-Tuberculosis Mycobacterium is significant, since some of these species are impervious to vast of the first line antibiotics utilized in tuberculosis treatment therapy [4].

The Mycobacterial cell wall contains a high extent of lipids content mycolic acid. Some major mycolic acid containing molecules such as trehalose-6, 6'- dimycolate causes characteristics appearance and acts as a virulence factor and could play a crucial role in the adaptation of Mycobacterium to intracellular growth and survival, immune modulation and drug resistance

***Corresponding Author:** Nazeeha Waseem

[5] MTB are dispatched from individual to individual through aerosol droplet nuclei containing the microorganism and is spread by coughing, sneezing, spitting, speaking which produces irresistible vaporized droplets 1.0 to 5.0 micrometer in distance across, each of the one droplet can transmit the disease. When a person sneezed, he released up to 40,000 droplets [6]. TB infection begins when the Mycobacteria reach the pulmonary alveoli, where they attack and initiate with in alveolar macrophages [7, 9]. The definitive symptoms of dynamic TB disease are chronic cough that lasts for 3 weeks or more with blood-tinged sputum, fever, chills, night sweats, fatigue, loss of appetite and loss of weight [8]. The essential site of infections in the lungs is generally either the upper part of the lower lobe or the lower part of the upper lobe [10] Anti-microbial is generally required to be taken for a moderately lengthy time span. The standard period of time for a course of TB anti-microbial is around a half year [11].

MDR-TB clarifies abnormal state of protection from Rifampicin and Isoniazid by organism. Resistance to isoniazid is caused by mutations at one of the two main sites, in either the *katG* or *inhA* genes [13]. Since 2006, even more resistant strain of MTB has emerged labeled as Extensively Drug Resistant (XDR-MTB). Additionally, being MDR these strains also show resistant to any flouroquinolones and any of the injectable 2nd-line drugs i.e. capreomycin, amikacin and kanamycin. Moreover, recently one more alarming situation has occurred showing strains which are found resistant to all the available anti-TB drugs labeled as Total Drug Resistant (TDR-MTB) [14].

MATERIALS AND METHODS

It was a cross-sectional and observational study. The data collection was done by a performa and the information was recorded on pre-coded questionnaires after taking informed consent.

A total of 300 sputum samples were collected from suspected TB patients from Aziz Bhatti Shaheed Teaching Hospital, Gujrat Pakistan during February 2020 - July 2020.

All consenting new and previously treated patients suspected of pulmonary TB of any age and gender visiting the hospital was included in this study and all the extra-pulmonary TB patients were excluded from this study. Ziehl-Neelsen staining, Fluorescent and Gene-Xpert MTB/RIF assay techniques were used for the confirmation of Multidrug resistance tuberculosis. The data is expressed in the form of tables and graphs by using MS Excel 365 and Endnote X7.

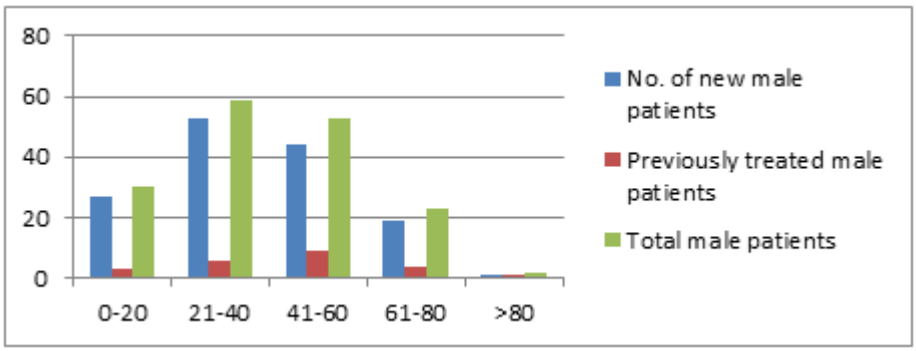
RESULTS

Out of 300 sputum samples 167 (55.7%) were male patients while 133(44.3%) were females. Out of these 144 were new male patients and 23 were previously treated male patients while 105 were new female patients and 26 were previously treated female patients.

All the patients were divided into 5 age groups such as 0-20 years of age, 21-40 years, 41-60 years, 61-80 years and above 80 years of age. In male category there were 30 (10.0%) patients in 0-20 years group, 59 (19.6%) in 21-40 years, 53 (17.6%) in 41-60, 23 (7.66%) in 61-80 and 02(0.66%) in >80 years of age (Table1)

Table-1: Age distribution of male patients

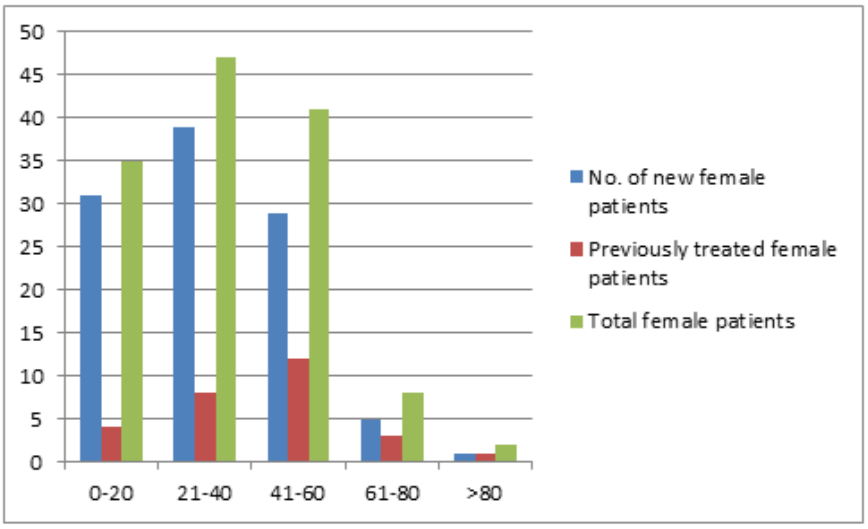
Age group in years	No. of new male patients	Previously treated male patients	Total male patients
0-20	27	03	30
21-40	53	06	59
41-60	44	09	53
61-80	19	04	23
>80	01	01	02
Total	144	23	167



In female patient's category there were 35 (11.6%) patients in 0-20 yrs group, 47 (15.6%) in 21-40 yrs, 41 (13.6%) in 41-60, 08 (2.66%) in 61-80 and 02 (0.66%) in >80 years of age (Table 2).

Table-2: Age distribution of female patients

Age group in years	No. of new female patients	Previously treated female patients	Total female patients
0-20	31	04	35
21-40	39	08	47
41-60	29	12	41
61-80	05	03	08
>80	01	01	02
Total	105	28	133



Z-N staining was performed on all the samples as a screening test and the results were found as 153 (51.0%) positive for MTB and 147 (49.0%) negative for MTB infection. The highest positivity rate by Z-N staining diagnostic technique was found in age group 21-40 years which was 60 positive cases. Among these, 6 were graded as scanty, 26 as 1+, 16 as 2+ and 12 as 3+. Moreover 41 positive cases were found in age group 41-60 years of which 10 were scanty, 17 were 1+, 11 were 2+ and 12 were 3+ (Figure1).

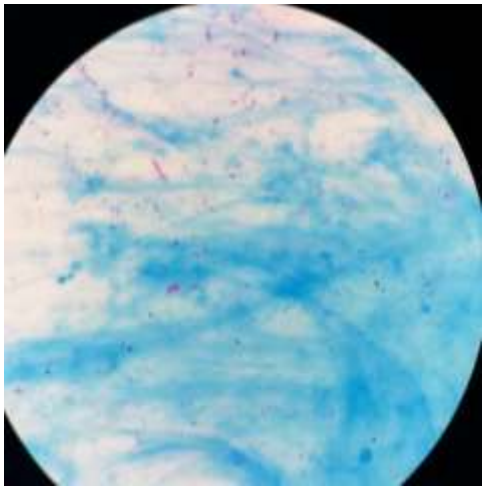


Fig-1: MTB positive slides stained with Z-N staining technique showing Acid Fast Bacilli (3+)

Fluorescent staining technique was applied on all the samples for further confirmation of MTB after Z-N stain. Total 199 (66.3%) patients were found positive for MTB by this technique and 101 (33.7%) were negative. The highest positivity rate by fluorescent staining was found in age group 21-40 years which was 76 positive cases. Among them 6 were graded as scanty, 28 as 1+, 24 as 2+ and 18 as 3+ grading following 53 positive cases in age group 41-60 years out of which 10 were scanty, 24 were 1+, 12 were 2+ and 07 were 3+ (Figure2).

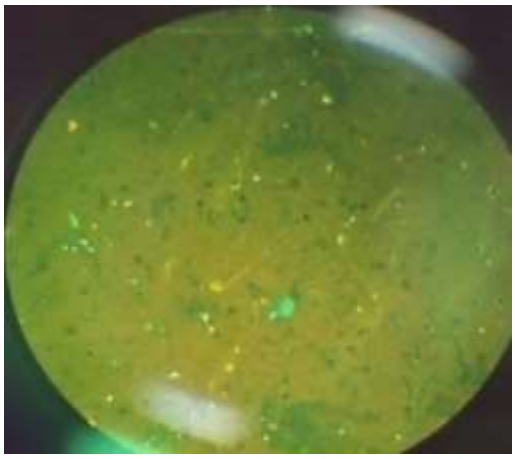


Fig-2: MTB positive slides stained with fluorescent staining technique showing Acid Fast Bacilli (2+)

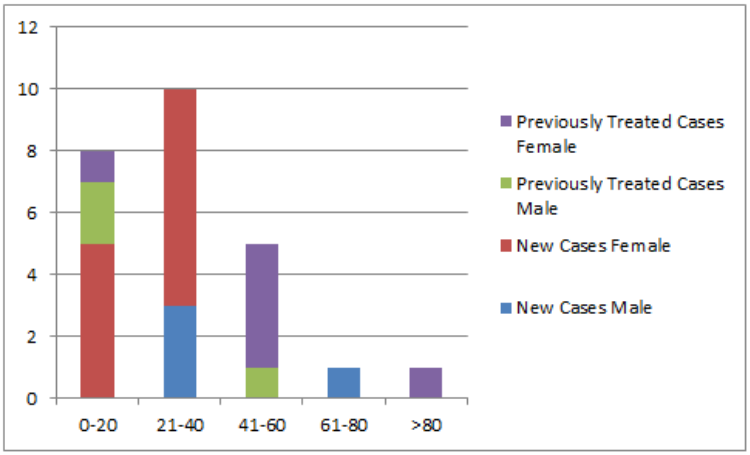
Gene-Xpert MTB/RIF Assay was performed on all the samples to confirm the MTB positivity on molecular basis and the findings were as 214 (71.3%) Positive for MTB and 86 (28.7%) negative for MTB. We have found 153 (51%) positive patients by Z-N staining technique and 199 (66.3%) positive for MTB by fluorescent staining technique while 214 (71.3%) were detected positive for MTB.

A total of 25 MDR-TB cases were detected out of which highest resistance rate was found in age group 21-40 years in male patients which was 03. While in female patients 07 were found to be resistant in age group 21-40 years and 06 in 0-20 years of age group.

Among 25 MDR-TB cases 07 were male patients while 18 were females making a percentage of 28% and 72% respectively.

Table-3: Age distribution of MDR-TB Cases

Age group in years	New Cases		Previously Treated Cases	
	Male	Female	Male	Female
0-20	0	5	2	1
21-40	3	7	0	0
41-60	0	0	1	4
61-80	1	0	0	0
>80	0	0	0	1
Total	4	12	3	6
	16		09	



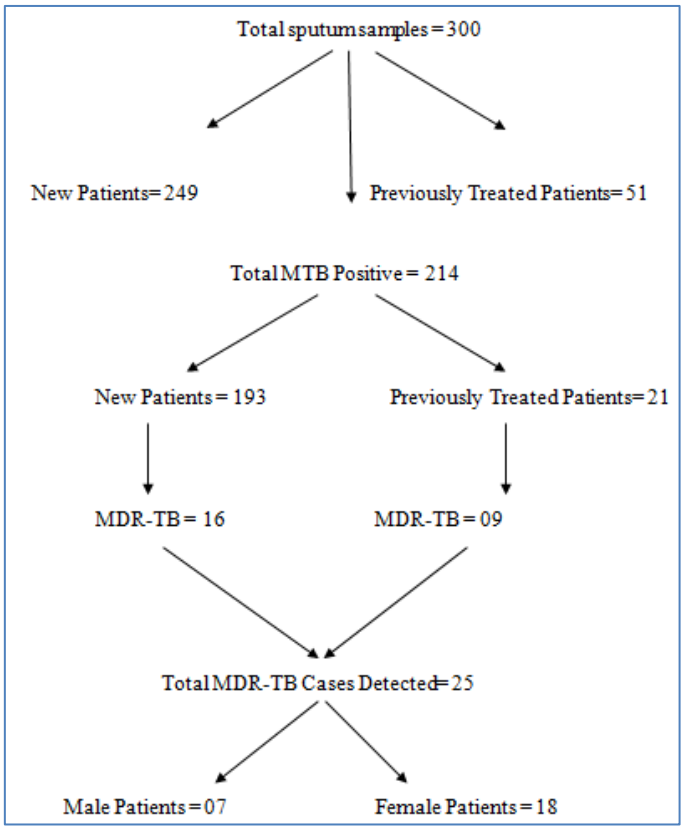


Fig-3: Demographic picture of total samples collected

DISCUSSION

The prevalence of TB in Pakistan is 630,000 cases with mortality rate of 60,000 [3] Drug resistant tuberculosis represents a major threat to TB control worldwide [15] The spread of DR-TB has become the main concern in global TB control nowadays due to its high mortality and confined treatment therapy [16] In the present study, 167 (55.7%) were male and 133 (44.3%) were female patients. These findings are in agreement with study conducted in Nairobi, Kenya reported 54% male and 46% female patients [17]. This study shows that in our population females were particularly at risk for MDR-TB. Our results are in agreement with a previous study in Karachi reporting female as a significant risk factor of MDR-TB [18]. The relationship among females and MDR is prone to be identified with poor access to social insurance in this group: however, this area requires further study [19].

This study report the highest positivity rate of MDR-TB was found in the most productive age group of 21-40 and 41-60 years. A study showed mean age of 32 years prevalent for tuberculosis in Punjab, Pakistan. [20] Another study concluded that pulmonary positive tuberculosis infection in the age group 20-60 and 25% above 60 years [21] According to the Pakistan census 2017, majority of population falls in the age group 25-54 (37.45%) with predominantly males making the age group more vulnerable to the infection. Positive pulmonary TB cases were found to be 214 (71.3%) confirmed by Gene-Xpert assay of which 123 (57%) were males and 91 (42%) were females supported with a similar study also showing overall prevalence of 76.99% pulmonary TB in Kotli, Azad Kashmir, Pakistan [22]. In accordance with our study another study results concluded 53% male and 47% female patients positive for MTB in Khyber Pakhtunkhwa, Pakistan [23]. The associated risk factors for higher infection rate is due to HIV/AIDS, smoking, drinking alcohol, diabetes, socio-economic status, exposure to environment, closed living conditions and lack of education [24]. This study report the prevalence of 8.3% MDR-TB in the population which is consistent with 9.3% depicted by another research and shows an alarming picture [25]. A higher prevalence was analyzed in Morocco which was 12.8% [26]. The difference in prevalence is might be due to difference in population, sample size, socio-economic status. MDR-TB is might be due to lack of rapid diagnosis, non-compliance of treatment, wrong duration of treatment, poor quality of drugs, irrational use of drugs, self-medication and wrong drug dosing lead to emergence of MDR-TB.

CONCLUSION

The High burden of MTB (71.3%) was found in the study area. In this study predominantly the male patients of age group 21-40 years were more affected by Mycobacterium tuberculosis. As far as the concern of Multidrug resistance tuberculosis, females were at higher risk. By using Z-N, Fluorescent and Gene-Xpert techniques the disease was confirmed. The Prevalence of MDR-TB was found to be 8.3% in Gujrat region.

Conflict of interest: None

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