

AN INSIGHT INTO THE DEMOGRAPHICS OF RIFAMPICIN RESISTANCE IN A TERTIARY CARE SETTING OF KARACHI

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ABSTRACT

Background: Multidrug resistant tuberculosis (MDR-TB) is a public health issue in Pakistan. The objective of this study was to describe the demographics of rifampicin resistant TB patients in the largest TB associated tertiary care setting in Karachi, Pakistan, which can later be used for active case finding and targeted diagnostic approaches.

Methods: A Cross sectional data based study was performed on the demographics of patients labelled as rifampicin resistant using Genexpert® from the period of January 2014 to June 2015 at the Provincial TB reference Laboratory, Dow University of Health Sciences. The records of the patients diagnosed as rifampicin resistant by Genexpert® were tabulated using Microsoft Excel® with anonymization and analyzed using online statistical software.

Results: Among the 252 patients labeled as rifampicin resistant using Genexpert®, 133(52.7%) were males, while 119 (47.22%) were females. The mean age for males at diagnosis (32.824 years) was slightly higher than that for females (29.45 years). Mann-Whitney U test, showed that the distribution of age was significantly different in the two groups ($p < 0.05$). After stratification, several differences were observed among different age groups and a higher proportion of rifampicin resistance in the females of the young age groups was observed. Male patients tended to have a higher age at the time of diagnosis within a group, except in the oldest group of patients.

Conclusions: Few demographic differences exist in rifampicin resistant patients, which can be used for targeting specific population for active case finding and MDR diagnosis.

Key words: Multidrug Resistant Tuberculosis; Rifampicin Resistance; Demographics; Tuberculosis; Karachi

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INTRODUCTION

Drug resistant tuberculosis (TB) is one of the major causes of fatality in TB patients because of difficult and long treatment. It is mainly treated using second line expensive antimycobacterial drugs, which include capreomycin, kanamycin, amikacin and fluoroquinolones. This treatment is effective, but can have a number of side-effects that may cause patient incomppliance leading to irregularity and interruption of therapy, which may result in serious public health consequences. Mycobacteria have a remarkable power to develop drug resistance, and they commonly develop resistance against Rifampicin and isoniazid used as first line therapeutic agents.

Resistance to Rifampicin is the most commonly occurring drug resistance in TB, which is mostly caused by mutations in rpoB gene. It may or may not be accompanied by resistance to isoniazid. It has been reported that 3.5% of new and 20.5% of previously treated TB cases developed MDR-TB in 2013, of which approximately 9.0% of patients with MDR-TB developed extensively drug resistant TB (XDR-TB) that is almost untreatable. In Pakistan only, there were more than 4000 registered MDR-TB patients by the end of 2014.

Worldwide, the male to female ratio is mostly high for TB and more males are diagnosed with TB than females. Our previous study with TB patients also

showed a higher male:female ratio of 1.42:1 among suspects though males were less likely to be tested smear positive (odds ratio 0.77, p-value <0.01). There are several reasons for this gender disparity, which include barriers that limit access to care takers, self-medication, and treatment from other health care systems, differences in exposure, risk of infection, progression from infection to disease. Some biological factors such as hormonal changes, physiology and life style are also considered to be the causes of this gender disparity in TB.

Data are however limited regarding the existence of this gender disparity in the MDR patients or if conversion to MDR is similar across all age groups in males and females, though some studies have reported that females are at higher risk of developing tuberculosis. Though demographics for conventional TB had been reported from Pakistan, data about drug resistance demographics are still deficient. The objective of this study was to explain the demographics of rifampicin resistance in Karachi, which was carried out using laboratory records of Provincial Tuberculosis Reference Laboratory at Ojha Institute of Chest Diseases.

MATERIALS AND METHODS

Data from rifampicin resistant patients diagnosed using MTB-RIF Assay on Genexpert® from eighteen-month period of January 2016 to June 2016 were tabulated and retrospectively analyzed from the Provincial Tuberculosis Reference Laboratory at Ojha Institute of Chest Diseases, Dow University of Health Sciences, Karachi. Data were collected without

noting down patients' particulars and were anonymously recorded. Institutional approval for ethical concerns was obtained to analyze and report data. Tabulations were performed on Microsoft Excel®, while statistical analyses were carried out using online statistical resources, Microsoft Excel® and SPSS Version 22®.

RESULTS

Altogether 252 patients were diagnosed as rifampicin resistant using MTB-RIF Assay on Genexpert® during the 18 month period from January 2014 to June 2015, out of which 133(52.7%) were males, while 119 (47.22%) were females. Ages of ten of these patients were missing from the records, due to which they were excluded from all analyses and data were analyzed only for 125 males and 117 females. The mean for males (32.824 years) was slightly higher than mean age for females (29.45 years) (Table 1), Distribution of data was non-parametric as confirmed by a Kolmogorov-Smirnov test on patient ages using SPSS Version 22®, D(242)=0.151, p= 0.000. Mann-Whitney U test, showed that the distribution of ages was significantly different in the two groups (p < 0.05).

Data were stratified according to different age groups (Figure 1) and tabulated for different age groups in Microsoft Excel®. A scatter plot showed male patients as a group had higher ages at the time of diagnosis within a group as compared to females in younger and middle age groups, though in the older age group, ages of female patients were on the higher side (Figure 2).

Table 1: Mean age of the two groups of RIFAMPICIN resistant patients.

	Mean	SD
Males	32.824	13.79169
Females	29.45	13.56625

Table 2. Age-based stratified data for the two age groups of RIFAMPICIN Resistant patients.

	<18	18-45	>45
Males	3(2.34%)	100(78.13%)	25(19.53)
Females	20(17.09%)	82(70.08%)	15(12.82%)

Figure 1: Stratified age distribution of RIFAMPICIN Resistant patients

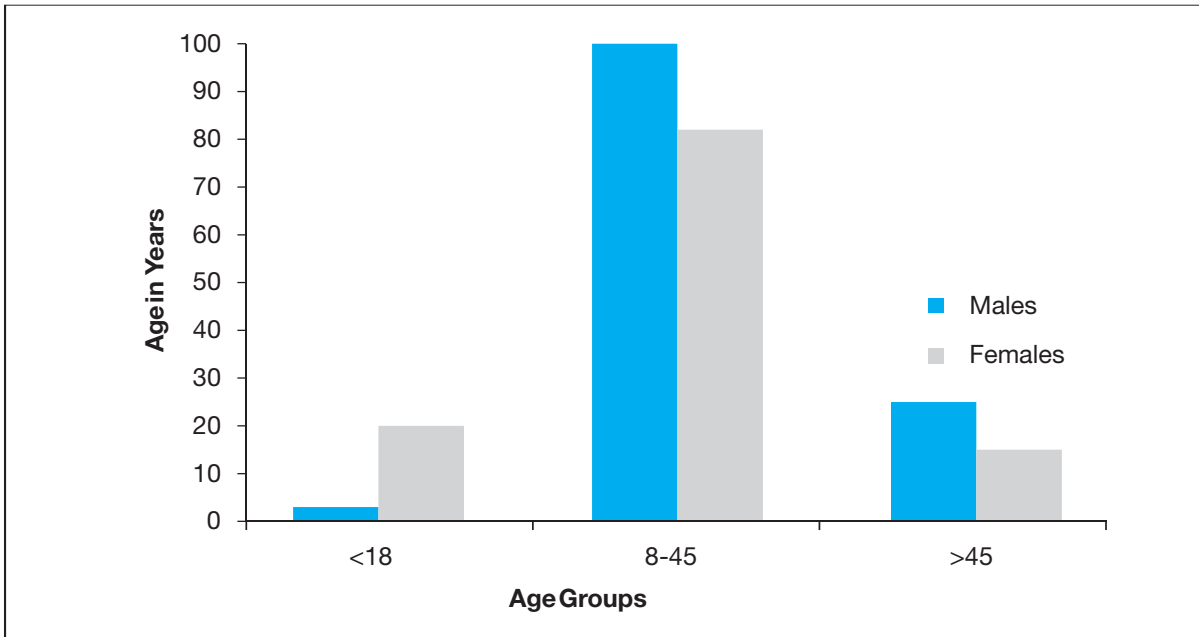
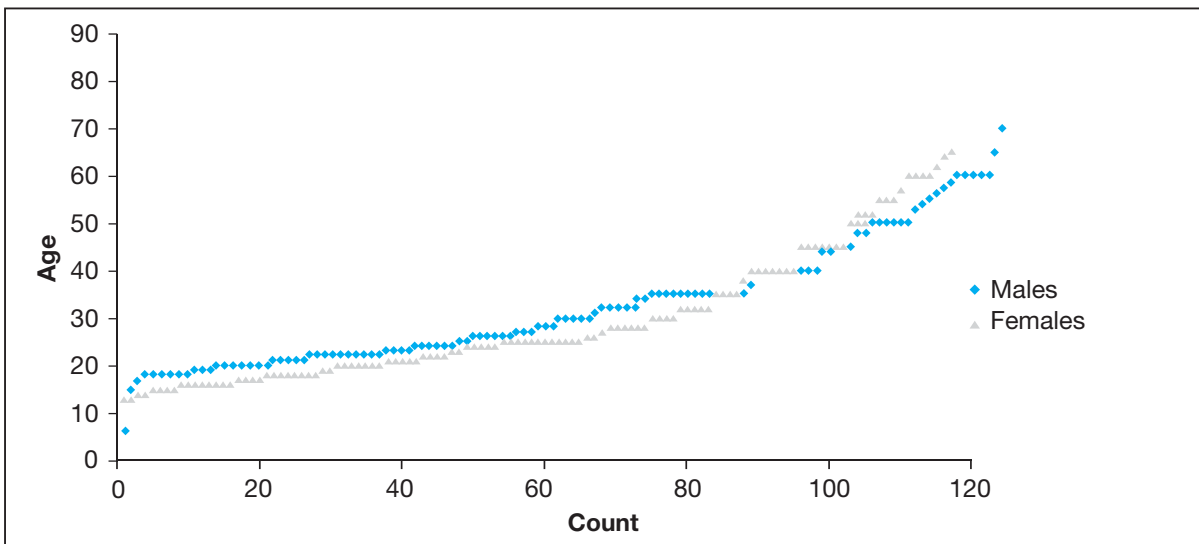


Figure 2: Scatter plot showing the age distribution in two groups of patient



DISCUSSION

Our data shows more male patients being diagnosed as rifampicin resistant, except for the pediatric group, where there was a high number of females. This is in accordance to the reports for conventional tuberculosis, where male gender has been reported to be increasingly associated with the disease in most of the countries, though the case is slightly different in the sub-continent and a few other countries of the Eastern Mediterranean region, where there is almost equal or slightly higher female preponderance in diagnosed TB

patients, which may be due to socio-economic reasons.

On stratification of data, it was observed that age at diagnosis was higher in males as compared to females in young and middle age groups, except for the old age group, where females were getting diagnosed at higher age. This shows that acquisition of MDR infection or conversion to MDR in younger patients is occurring at an earlier stage in females as compared to males. The findings agree with our previous gender-based study on screening and

diagnosis, which showed that females were at higher risk to be diagnosed with tuberculosis among the screened population despite more males seeking medical attention. The difference found in the older age group can be attributed to socio-economic and culture reasons, that older females may be more negligent about their health or are more likely to be ignored for their symptoms. Our findings for the MDR patients are in line with the internationally reported data for the middle and old age groups where more males are screened, diagnosed and receive treatment for tuberculosis and male gender is considered a risk factor for contracting Tuberculosis.

CONCLUSION

Our data about the demographics of MDR conversion/Diagnosis provides an insight for designing an age-based-targeted diagnostic and therapeutic approach so that development and conversion to MDR must be stopped in population at high risk. The older females, who probably ignore their symptoms, or are ignored by the family can be a continuous source of infection for the household. Moreover, efforts need to be directed towards developing literacy and strengthening psychological support for the patients so that they remain motivated throughout their course of therapy. The approach should include not only active case-finding but also active psychological support to the patients so that they continue with their treatment and complete it properly. This can also be brought about by the proper training, motivating and monitoring treatment supporters so that they can help the patients complete their treatment, which will stop the development and spread of MDR TB.

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