Scholars Journal of Applied Medical Sciences (SJAMS)
Abbreviated Key Title: Sch. J. App. Med. Sci.
©Scholars Academic and Scientific Publisher
A Unit of Scholars Academic and Scientific Society, India
www.saspublishers.com

ISSN 2320-6691 (Online)
ISSN 2347-954X (Print)

Medicine

To Study the Rifampicin Resistance in Sputum Positive Pulmonary Tuberculosis Patient by CB-NAAT

Dr. Bhimrao Rupsingh Pawar[1], Dr. Anvesh Singh Parmar[2*]
[1]Ex-Resident, Department of Medicine, GR Medical College, Gwalior, India
[2]Senior Resident, Department of Medicine, GR Medical College, Gwalior, India

Original Research Article

***Corresponding author**
Dr. Anvesh Singh Parmar

Article History
Received: 13.04.2018
Accepted: 22.04.2018
Published: 30.04.2018

DOI:
10.36347/sjams.2018.v06i04.028

Abstract: Tuberculosis (TB) burden in India is very high accounting for nearly 20% of the global incidence. India also ranks second in holding multi drug resistant (MDR)-TB cases. To identify rifampicin resistance cases in sputum positive pulmonary tuberculosis patients by history, clinic radiological tools, sputum examination and performing cartridge based nucleic acid amplification test (CB-NAAT) on suspected MDR cases. Hundred sputum- positive tuberculosis patients were studied. Three sputum samples were collected from each patient. The specimens collected, packed at the collection centers and sent to the linked CB-NAAT laboratory. Bacteriological examination was performed. Mean age of study population was 37.5±14.03 years. Males (79%) outnumbered the females. Most of them were farmers (49%). All the patients had productive cough followed by fever (79%) and breathlessness (67%). Diabetes mellitus (6.3% in male and 9.5% in female) was the most common co-morbid condition. Twenty eight percent of the cases were resistant to rifampicin. Maximum (71.4%) of the study subjects resistant to rifampicin were males compared to female (28.6%) (p=0.246).Sputum AFB resistant to rifampicin and sputum AFB sensitive to rifampicin was insignificant in default cases (32.1% vs. 23.6%, p>0.05), but significant in relapse (46.4% vs. 20.8%, p=0.010) and new cases (25.5% vs. 55.6, p=0.002) respectively. About one fourth of our patients were resistant to rifampicin and males were more affected. Diabetes mellitus was the common co-morbid condition. Significant difference was observed in relapse and new cases between rifampicin resistance and sensitivity.

Keywords: Rifampicin resistance, CB-NAAT, multi drug resistance.

INTRODUCTION

The global burden of tuberculosis is still large. Recent data suggest that around 9 million new Mycobacterium tuberculosis and approx 1.7 million global mortality takes place annually [1]. In India 9.4 million patients are living with tuberculosis. India also ranks 2nd in holding multi drug resistant cases [2].

Multi-drug-resistant tuberculosis (MDR-TB) can be defined as the tuberculosis infection caused by bacteria which is resistant to treatment with at least two first line anti-tuberculosis drugs such as isoniazid and rifampicin [3].

Smear microscopy is the foundation for the diagnosis of tuberculosis in resource-limited settings. But it has modest (35-80%) sensitivity and poor positive predictive value [4]. Tuberculosis demand rapid diagnosis and detection of rifampicin resistance in order to manage it effectively. Cartridge Based Nucliec Acid Amplification Test (CB- NAAT) is a novel diagnostic device also called as Gene Xpert MTB/RIF assay for the diagnosis of tuberculosis and rapid detection of rifampicin resistance in clinical specimens.

The present study was performed to identify rifampicin resistance cases in sputum positive pulmonary tuberculosis patients by history, clinic radiological tools, sputum examination and performing CB-NAAT on suspected MDR cases.

MATERIALS AND METHODS

An observational study was performed on 100 sputum- positive tuberculosis patients admitted in the Department of Medicine, G R Medical College and JAH, Gwalior, Madhya Pradesh.

All tuberculosis patients with symptoms of cough with or without expectoration, fever, weight loss and radiological features suggestive of pulmonary tuberculosis (fibrocavitatory lesion) were included in the study.

Patients with chronic liver disease and chronic kidney disorders were excluded from the study. HIV

patients, patients on immunosuppressive therapy, sputum negative pulmonary tuberculosis, extra pulmonary tuberculosis and pediatric age group patients were also excluded from the study.

Bacteriological examination of three sputum specimens were examined (an early morning specimen and two spot specimens). All sputum smear microscopy were performed by Ziehl-Neelsen Stain method and results were reported as positive (Grade 3+; more than 10 AFB per oil immersion field, Grade 2+; 1-10 AFB per oil immersion field and Grade 1+; 10-99 AFB per 100 oil immersion fields), scantly (1-9 AFB per 100 oil immersion fields) and negative (No AFB in 100 oil fields, also termed as Grade 0).

All the suspected drug resistant cases (on the basis of history, clinic radiological and bacteriological assessment) were included. Sputum sample collected adequately and sent to labs where sputum AFB and culture/sensitivity was carried out as per guidelines of World Health Organization (WHO)**.**

Complete history was taken with emphasis on history of anti-tubercular therapy, general physical and systemic examination of the cardiovascular, respiratory, and abdominal and central nervous system was performed. Necessary investigations were carried out to diagnose the cases that fit into inclusion criteria.

All sputum specimens were collected in pre-sterilized falcon tubes and packed using standard three layer packing system. The specimen was transported in cold chain through the locally feasible transport system like courier, speed post, human carrier etc. The specimens collected and packed at the collection centers were sent to the linked CB-NAAT laboratory preferably in cold chain on the same day along with correctly filled request for culture and drug sensitivity testing (C-DST) form from the referring facilities. On the receipt of the specimen, the lab technician was required to process the specimen. The results were available within 1 hour and 45 minutes. The results of all cases detected with MTB positive and rifampicin resistance were communicated to the District TB Officer with copy to the linked drug resistant tuberculosis (DR-TB) centre and the consultant concerned.

All the data was analysed using IBM SPSS ver. 20 software. Categorical variable were expressed in percentage. Mean was obtained for numerical data and expressed as mean ± standard deviation (SD). P value of <0.05 was considered as significant.

RESULTS

Mean age of study population was 37.5±14.03 years. Most of the patients (30%) were in their third decade of life. Out of 100 sputum- positive tuberculosis patients, 79% were male and 21% were female. Maximum (49%) study participants were farmers by profession followed by 18% students.

Symptomatology revealed that all the patients had productive cough followed by fever (79%) and breathlessness (67%). Weight loss and loss of appetite was observed in 39% and 29% patients respectively.

The most common co-morbid condition among study population was diabetes mellitus (6.3% in male and 9.5% in female). None of the female patients had history of alcohol and smoking addiction, but 16 (20.3%) and 6 (7.6%) male patients were reported to be addicted with smoking and alcohol respectively.

Pallor was the most common sign of complication seen (29%) followed by icterus, which was seen in 3% of the study population.

Analysis of sensitivity to rifampicin revealed that 28% of the cases were resistant to rifampicin. Majority of the cases were new sputum positive (46%) followed by 28% and 26% of relapse and default cases respectively.

Among rifampicin resistant cases, 71.4% were males whereas females were 28.6% (p=0.246). Association of different variables such as age, sex, occupation, presence of diabetes mellitus, HIV status, smoking, alcohol and history of contact was insignificant (p>0.05; in relation to the sensitivity to rifampicin).

Table-1: Distribution of cases according to the type of case and their association with their rifampicin sensitivity

Type of case	Sputum AFB resistant to rifampicin	Sputum AFB sensitive to rifampicin	P value
Default	9(32.1)	17(23.6)	NS
Relapse	13(46.4)	15(20.8)	0.010
New	6(25.5)	40(55.6)	0.002

Data is expressed as number of patients (%), NS; not significant, AFB; acid fast bacillus, P value< 0.05 is considered as significant

DISCUSSION

CB-NAAT is a new fully automated plateform endorsed by WHO in 2010 which permits rapid detection (< 2 hr) and requires minimal health care worker's skill. NAAT detects mutation in rpoB gene which code for resistance for rifampicin, as this most often coincides with isoniazide resistance; serve as surrogate marker for MDR [5].

Male predominance was observed in present study which coincides with Pandhi *et al*. where 72% of the patients were male [1]. A cross-sectional study performed by Bhatt *et al*. in Ahmedabad on 81 Multi Drug Resistant Tuberculosis patients also reported male dominance and majority of the patients were in age group of 16-45 years which is in accordance with the present study finding [6]. The reasons for male dominance can be multifactorial; one being gender base inequality, where female are involved in poor health seeking behavior and obtaining health care services. Second, because male are the most commonly involved in occupation they are more susceptible to tuberculosis.

An observational retrospective cohort study done by Kurniawati *et al*. on 653 tuberculosis patients reported that 47.9% were smoker and only 12.1% were on alcohol use but in present study none of the female had history of alcohol use and smoking, but males were addicted to both alcohol and smoking which is comparable to Kurniawati *et al*.[7] Kurniawati *et al*. also reported that 26% of the patients had diabetes mellitus as co-morbidity which is higher than what is reported by the present study (7%) but is similar to the Saugat *et al*. [7, 8].

In present study, 28% cases were resistant to Rifampicin, out of that 28.6% were females and 71.4% were males. Saugat *et al*. in their study of 100 sputum smear AFB positive patients reported no significant association between age and gender with drug resistance [8]. A report by WHO on MDR from different countries has also not recorded any significant association between drug resistance and gender of the patient which is in accordance with the present study[9]. But a population-based study in Georgia by Lomtadze *et al*. on 1314 patients with AFB smear and culture positive pulmonary TB reported that previous TB treatment and female gender were independent risk factors for the presence of MDR-TB [10]. Dewan *et al*. studied 100 tuberculosis patients and reported that 25% of the patients were refampicin resistance which is in accordance to present study data [5].

Most of the reports advocate men to be at increased risk for having susceptible TB then females but Cox *et al*. reported that for MDR-TB females appears to be at higher risk [11]. Faustini et al also noted men to be at lower risk than women for having MDR-TB which is in contrast to the present study data [12]. But Tost *et al*. and Marra *et al*. in their similar studies reported that male is a high risk gender on getting tuberculosis while female have less risk which is in accordance to present study findings[13,14].

CONCLUSION

Present study data revealed that male patients were mostly affected with tuberculosis that were in third decade of their age. Diabetes mellitus was the common co-morbid condition associated with tuberculosis. Resistant to rifampicin was mostly observed in male tuberculosis patients. Significant difference was observed in relapse and new cases between rifampicin resistance and sensitivity. However a large randomized clinical trial is need to confirm the results as present study was done with small sample size.

REFERENCES

1. Pandhi N, Kajal NC, Mahajan N, Singh H. Diagnostic utility of cartridge based nucleic acid amplification test (CBNAAT) in detection of rifampicin resistance in multi drug resistant suspects among sputum positive cases of tuberculosis. Sch J App Med Sci 2016; 4(1B):152-71.
2. Kandi S, Reddy PNS, Reddy VCK, Laxmi R, Kopuu D, Vishnu PH. Prevalence of multidrug resistance among retreatment pulmonary tuberculosis cases in a tertiary care hospital, Hyderabad, India. Lung India : Official Organ of Indian Chest Society 2013; 30(4):277-9.
3. Shen X, DeRiemer K, Yuan ZA, Shen M, Xia Z, Gui X, Wang L, Gao Q, Mei J. Drug-resistant tuberculosis in Shanghai, China, 2000–2006: prevalence, trends and risk factors. The International Journal of Tuberculosis and Lung Disease. 2009 Feb 1;13(2):253-9.
4. Mathew P, Kuo YH, Vazirani B, Eng RH, Weinstein MP. Are three sputum acid fast bacillus smears necessary for discontinuing tuberculosis isolation? J ClinMicrobiol 2002; 40: 3482-4.
5. Dewan R, Anuradha S, Khanna A, Garg S, Singla S, Ish P, Agarwal S. Role of cartridge-based nucleic acid amplification test (CBNAAT) for early diagnosis of pulmonary tuberculosis in HIV. Journal, Indian Academy of Clinical Medicine. 2015 Apr;16(2):115.
6. Bhatt G, Vyas S, Trivedil K. An epidemiological study of multi drug resistant tuberculosis cases registered under Revised National Tuberculosis Control Programme of Ahmedabad City. Indian J Tuberc 2012; 59(1):18-27.
7. Kurniawati F, Sulaiman SAS, Gillani SW. Adverse Drug Reactions of Primary Anti-tuberculosis Drugs Among Tuberculosis Patients Treated in Chest Clinic. Int J of Pharm & Life Sci (IJPLS) 2012; 3 (1): 1331-8.
8. Saugat R, Soni G, Chabda M, Mathur BB, Gujrani M, Thakral P, Modi CS, Kapoor A. Study of

Isoniazid and Rifampicin Resistance among New Sputum Smear Positive Pulmonary Tuberculosis Patients by Line Probe Assay in Bikaner. International journal of scientific study. 2015 Feb 1;2(11):90-5.

9. Fleming MF, Krupitsky E, Tsoy M, Zvartau E, Brazhenko N, Jakubowiak W, McCaul ME. Alcohol and drug use disorders, HIV status and drug resistance in a sample of Russian TB patients. The International Journal of Tuberculosis and Lung Disease. 2006 May 1;10(5):565-70.
10. Lomtadze N, Aspindzelashvili R, Janjgava M, Mirtskhulava V, Wright A, Blumberg HM, Salakaia A. Prevalence and risk factors for multidrug-resistant tuberculosis in the Republic of Georgia: a population-based study. The International Journal of Tuberculosis and Lung Disease. 2009 Jan 1;13(1):68-73.
11. Cox HS, Orozco JD, Male R, Ruesch-Gerdes S, Falzon D, Small I, Doshetov D, Kebede Y, Aziz M. Multidrug-resistant tuberculosis in central Asia. Emerging infectious diseases. 2004 May;10(5):865.
12. Faustini A, Hall AJ, Perucci CA. Risk factors for multidrug resistant tuberculosis in Europe: a systematic review. Thorax. 2006 Feb 1;61(2):158-63.
13. Tost JR, Vidal R, Maldonado J, Caylà JA. Effectiveness and tolerance of antituberculosis treatment regimens without isoniazid and rifampicin: Analysis of 85 cases. Archivos de Bronconeumología ((English Edition)). 2008 Jan 1;44(9):478-83.
14. Marra F, Marra CA, Bruchet N, Richardson K, Moadebi S, Elwood RK, FitzGerald JM. Adverse drug reactions associated with first-line anti-tuberculosis drug regimens. The International Journal of Tuberculosis and Lung Disease. 2007 Aug 1;11(8):868-75.