Tuberculosis in geriatric patients: a cross-sectional study from tertiary care hospital in Maharashtra

Pooja Shah[1], Sae Pol[2], Vaishali Gaikwad[3], Jyoti[4], Rajesh Karyakarte[5]*

[1]Assistant Professor, Department of Microbiology, BJ GMC Pune
[2]Associate Professor, Department of Microbiology, BJ GMC Pune
[3]Associate Professor, Department of Microbiology, GMC Satara
[4]Junior Resident, Department of Microbiology, BJ GMC Pune
[5]Professor and HOD, Department of Microbiology, BJ GMC Pune

***Corresponding Author:**
Rajesh Karyakarte, Professor and HOD, Department of Microbiology, BJ GMC Pune
E-MAIL: karyakarte@hotmail.com

ABSTRACT

Background- By the year 2031, an anticipated 194 million Indian population will be aged 60 years or above. They are more prone to various infections due to lowered immunity and Tuberculosis (TB) is one of them. The use of various diagnostic methods for TB needs to be investigated in the geriatric population. **Material and methods:** A cross-sectional study was conducted from 1st January 2022 to 31st December 2022. All TB patients of 60 years and above were enrolled. Their sputum samples were subjected to CBNAAT and positive samples were tested by LPA for detection of isoniazid resistance and resistance to second-line drugs. **Results:** In our study, most positive cases were from the age group of 60-65 years (50.82%). Infected males were 65.57% and females were 34.43%. M. CBNAAT detected tuberculosis in 18.43%. 90.16% were rifampicin sensitive, and resistant were 8.20%. By LPA, isoniazid monoresistant was seen in 4.92%, rifampicin monoresistant in 1.64%. **Conclusion :** As per our study, geriatric patients in the age group of 60-65 years were mainly positive for tuberculosis. This age group though immunocompromised but still active can spread the infection in the community. So, this age group should be closely observed in the mission of NTEP.

KEYWORDS: CBNAAAT, M. tuberculosis, Geriatric, TAT

INTRODUCTION

Tuberculosis (TB) is a major health problem in India and it is estimated that in 2016, there were 10.4 million new cases of TB worldwide and among them, 2.8 million cases were from India. [1] This makes India carry one-fourth of the burden of tuberculosis cases. TB which is mainly presumed to be a disease of the young population, is increasing to an extent in the elderly age group. [2–4] The Geriatric age group is susceptible to many opportunistic infections because of their low immunity and tuberculosis is one of them. With increasing age, there is a decrease in T lymphocytes, an increase in proliferative responses and synthesis of gamma interferon. [5, 6] Multi-drug resistant Tuberculosis (MDR-TB) is a public health crisis and a major threat to health security. According to WHO, 484000 new cases of resistance to rifampicin (RIF) were seen which accounts for 78% of MDR-TB cases. [7] Though Lowenstein Jensen (LJ) culture is the gold standard, it takes a longer time for growth and delays the treatment. Microscopic examination by Ziehl-Neelsen (ZN) staining is less sensitive though it's cheap and has high specificity. [8] WHO recommended CBNAAT in December 2010 for laboratory diagnosis of tuberculosis, it employs five distinct molecular beacons each labelled with differently coloured fluorophore and responds to the specific nucleic acid sequence within the rpoB gene of Mycobacterium tuberculosis (M. Tuberculosis). It takes around two hours and hence helps in rapid and early treatment of patients, and this also limits the spread of disease in the community. However, resistance to isoniazid is not confirmed by CBNAAT. Also, the status of resistance to second-line drugs cannot be known by CBNAAT. Line Probe Assay, which is a qualitative test, can be used to confirm isoniazid resistance and resistance to second-line drugs. Our Aims of study are to study the occurrence of tuberculosis, the detection of rifampicin resistance by CBNAAT and the isoniazid resistance and resistance to second-line drugs by Line probe assay in CBNAAT-positive patients.

MATERIAL AND METHODS

A cross-sectional study was conducted at the National Tuberculosis Elimination Programme (NTEP) centre, Byra-

mjee Jeejeebhoy (BJ) Government Medical College, Pune, Maharashtra from 1st January 2022 to 31st December 2022. All suspected TB patients (Pulmonary and Extrapulmonary) aged 60 years and above based on clinical features were enrolled in the study. CBNAAT and LPA investigations were done as per NTEP guidelines after obtaining informed consent from patients.

Procedure:

An early morning deeply expectorated sample was collected from all clinically suspected cases of Tuberculosis who were more than 60 years of age in a sterile wide-mouth container., Extrapulmonary samples were collected depending on the site. The samples were subjected to testing with the GeneXpert MTB/RIF system manufactured by Cepheid, France, for detection of M. tuberculosis and rifampicin resistance. It is a cartridge-based nucleic acid amplification technique which includes semi-quantitative nested real-time PCR. Mutations in the rpoB gene are for the detection of rifampicin resistance. As per the manufacturer's guidelines, two millilitres of sample reagent are added to one millilitre of each fresh sample directly in the collection container. The lid was placed on the container, and it was shaken vigorously 10-20 times. It was then incubated at room temperature. After 10 minutes of incubation, again the container was shaken vigorously 10-20 times. This was followed by incubation for five minutes. The sample must be fluid before being processed with no more clumps of sputum. If it is still viscous, the sample is kept for 5-10 minutes more before processing it in the cartridge. At least two millilitres of processed samples were taken with a plastic transfer pipette from the collection container to a single-use disposable, self-contained GeneXpert cartridge. Then it was subjected to GeneXpert MTB/RIF to create a test. After scanning the cartridge barcode, loading was done on the blinking module. The results were visualized on an attached computer and interpreted using software. CBNAAT was repeated on the second sample if it has shown indeterminate susceptibility to rifampicin. Samples which were positive by CBNAAT for M. tuberculosis were sent for line probe assay.

RESULTS

Patient Demographics and Sample Types: The study enrolled 331 patients suspected of having tuberculosis. The majority of patients were male (64.05%) and belonged to the 60-65 years age group (49.24%). The oldest participant was 97 years old. Table 1

A total of 331 samples were collected from these patients. Of these, 253 (76.44%) were sputum samples, while 78 (23.56%) were extrapulmonary samples. Among the extrapulmonary samples, ascitic fluid was the most common sample type, representing 7.85% of all samples.Table 2

CBNAAT Positivity and Bacterial Load: CBNAAT detected M. tuberculosis in 61 patients (18.43%). The bacterial load varied among the positive samples. Nine samples (14.75%)

AGE (YEARS)	MALE No. (%)	FEMALE No. (%)	TOTAL No. (%)
60-65	99 (29.91)	64 (19.34)	163 (49.24)
65-70	48 (14.50)	21 (6.34)	69 (20.85)
70-75	34 (10.27)	21 (6.34)	55 (16.61)
75-80	18 (5.44)	05 (1.51)	23 (6.95)
80-85	09 (2.71)	06 (1.81)	15 (4.53)
86-90	02 (0.60)	02 (0.60)	04 (1.21)
90-95	00 (00)	00 (00)	00 (00)
95-100	02 (0.60)	00 (00)	02 (0.60)
Total	**212 (64.05)**	**119 (35.95)**	**331 (100)**

Table 1: Age and gender distribution of suspected cases of Tuberculosis

had very high bacterial load, 32 (52.46%) had low bacterial load, 10 (16.39%) had very low bacterial load, and 10 (16.39%) had medium bacterial load.

Type of Sample	No. of Samples No. (%)	Samples Positive for M. tuberculosis by CBNAAT (Row wise %)
Pulmonary: Sputum	253 (76.44)	54 (21.34)
Extrapulmonary	78 (23.56)	7 (8.97)
Ascitic fluid	26 (7.85)	2 (7.69)
CSF	21 (6.34)	1 (4.76)
Pus	13 (3.93)	3 (23.08)
Urine	04 (1.21)	0
Lymph node aspirate	02 (0.60)	0
Biopsy material	07 (2.11)	1 (14.28)
Pericardial fluid	04 (1.21)	0
Drain fluid	01 (0.30)	0
Total (Pulmonary + Extra Pulmonary)	331 (100)	61 (18.43)

Table 2: Type of Sample and CBNAAT Positivity in Geriatric Patients for TB

Out of 253 Sputum samples, 54 (21.34%) samples tested positive for M. tuberculosis by CBNAAT. Extra-pulmonary samples constituted 23.56% of all samples. Overall, 18.43%

of all samples tested positive for M. tuberculosis by CBNAAT.

Rifampicin Sensitivity	No. (%)
Sensitive	55 (90.2)
Resistant	5 (8.2)
Intermediate	1 (1.6)

Table 3: Rifampicin Sensitivity of M. tuberculosis by CBNAAT

Drug Susceptibility Testing: Line probe assay (LPA) was performed on 44 (72.13%) CBNAAT-positive samples. All isolates were sensitive to second-line drugs. Among the 61 CBNAAT-positive samples, 5 (8.20%) were resistant to rifampicin, 3 (4.92%) were resistant to isoniazid, and 1 (1.64%) was resistant to both drugs, making it multidrug-resistant tuberculosis (MDR-TB).

LPA Findings in CBNAAT-Positive Patients	No. (% out of 61)
Negative	16 (26.22%)
Rifampicin Sensitive, Isoniazid Sensitive	19 (31.15%)
Rifampicin Monoresistant	5 (8.20%)
Rifampicin Sensitive, Isoniazid Resistant (High Level)	2 (3.28%)
Rifampicin Sensitive, Isoniazid Resistant (Low Level)	1 (1.64%)
Rifampicin Resistant, Isoniazid Resistant	1 (1.64%)
Total	44 (72.13%)

Table 4: Line Probe Assay findings in CBNAAT-positive patients.

Ten samples were subjected to MGIT. Out of them, 4 were contaminated and 6 were negative. We sent positive samples to IRL Pune. Microscopy is repeated there. Microscopy negative samples are subjected to MGIT and positive samples to LPA.

DISCUSSION

Tuberculosis (TB) is a major global health problem, particularly in developing countries like India. While most studies on TB focus on the adult population, geriatric patients are particularly vulnerable due to weakened immunity. This study aimed to investigate the occurrence of TB and drug sensitivity patterns in elderly individuals.

Our findings indicate that the age group of 60-65 years was most suspected of tuberculosis (TB), with males representing 64.05% of suspected cases and females accounting for 35.95%. This distribution is consistent with the study by Gennaro et al. (2020), where males were also more clinically suspected than females, specifically constituting 49% of all suspected cases below the age of 75. [9]

Among confirmed TB cases identified by CBNAAT in our study, males comprised 65.57% and females 34.43%. Notably, 50.82% of confirmed cases belonged to the 60-65 age group. These findings align with the study by Rahman N et al. (2021), which reported a mean age of 65 years for confirmed TB patients, with males (51%) being more affected than females. [10]

In the study of Sharma R K et al. 72% of males were affected and, in the study, conducted by Anantkrishnan R et al., 76% were in the age group of 60-69 years, 22% were in 70-79 years and only 2% were in 80-89 years. [11, 12] This correlates with our study. Life expectancy in India is 68 years, hence, the more commonly suspected age group was 60-65 years. Males were more affected in our study as males are more exposed to outside environments for work purposes. In developing countries like India, females in rural areas are still not allowed to work; therefore, their exposure to the outside environment is much less.

The most commonly received sample was sputum (76.44%), and amongst extrapulmonary samples, ascitic fluid was most commonly received (7.85%) followed by CSF (6.34%) and pus (3.93%). Urine, lymph node aspirate, biopsy material, and drain fluid were received in a few cases. In the study of Rahman N et al, sputum samples were 56.2%, CSF were 17.1% and pleural fluid was 12.5%. [10] In a study conducted by Kwon et al. which was done on extrapulmonary samples of geriatric patients, lymph node aspirate was most common followed by skeletal tuberculosis, and pericardial and miliary tuberculosis were the next. [13]

In our study, Mycobacterium tuberculosis was detected in 18.43% by CBNAAT. In the study done by Sharma R K et al. in geriatric patients, 19.68% pulmonary and 11.57% extrapulmonary samples were positive which correlates with our study. [11] In the study conducted by Di Gennaro F et al. [9] 63% were culture positive in geriatric patients while in the study of Hase et al. 60% were positive. [14] Their percentages are very high compared to our study. The reason could be lowered immunity, lack of isolation facilities for family members diagnosed with tuberculosis positives, and lack of care for elderly patients.

In our study, Rifampicin sensitivity was 90.16%, 8.20% were resistant and 1.64% were intermediate. In the study by Sharma R K et al., 87.09% were Rifampicin sensitive and 12.90% were resistant. This correlates to our study. [11] Considerably lower resistance was found in our study which could be due to proper adherence to treatment, regular follow-ups, and instructions given to positive patients to keep their diet healthy.

In our study, LPA showed sensitivity to second-line drugs in all the patients. Isoniazid monoresistance was found in three patients, Rifampicin monoresistance was found in one patient, and resistance to both first-line drugs in 1 patient. Samples that were negative by LPA and positive by CBNAAT were 16. So, despite lowered immunity in geriatric patients, a good sensitivity pattern was seen in our study. However, in another study by Singhal R et al., they found a higher prevalence of resistance among the geriatric population where a total of 1055 Mycobacterium tuberculosis (MTB) isolates were identified. [15]Among these, 117 (11.2%) were diagnosed as rifampicin-resistant (RIF-resistant), including 89 (8.5%) cases of multidrug-resistant tuberculosis (MDR-TB). Additionally, 84 (8%) isolates showed resistance to isoniazid (INH).

CONCLUSION

This study showed that geriatric patients in the age group of 60-65 years were mainly positive for tuberculosis. This age group though immunocompromised but still active can spread the infection in the community. So, this age group should be closely observed in the mission of NTEP.

LIMITATIONS

We have done the study only for one year. More studies are needed to see the overall prevalence of TB in the elderly population and the prevalence of resistance to drugs. More studies need to be done on the detection of sensitivity to second-line drugs.

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REFERENCES

1. World Health Organization. Global tuberculosis report ; 2017. Available from: https://www.who.int/publications/i/item/9789241565516.

2. Sood R. The problem of geriatric tuberculosis. J Acad Clin Med. 2000;5:156–62.

3. Davies PD. Tuberculosis in the elderly: an international perspective. Clin Geriatr. 1997;5:15–26.

4. Ministry of Statistics and Programme Implementation Government of India. Elderly in India-Profile and Programmes; 2016. Available from: https://www.mospi.gov.in/sites/default/files/publication_reports/ElderlyinIndia_2016.pdf.

5. Lesourd B, Mazari L. Nutrition and immunity in the elderly. Proc Nut Soc. 1999;58:685–95.

6. Ben-Yehuda A, Weksler ME. Host resistance and the immune system. Clin Geriatr Med. 1994;8:701–712.

7. Garg A, Agarwal L, Mathur R. Role of GeneXpert or CBNAAT in diagnosing tuberculosis: Present scenario. Med J DY Patil Vidyapeeth. 2022;15:14–23.

8. Chang K, Lu W, Wang J, Zhang K, Jia S, Li F. Rapid and effective diagnosis of tuberculosis and rifampicin resistance with Xpert MTB/RIF assay: A meta-analysis. J Infect. 2012;64:580–588.

9. Gennaro FD, Vittozzi P, Gualano G, Musso M, Mosti S, Mencarini P et al. Active pulmonary tuberculosis in elderly patients: a 2016-2019 retrospective analysis from an Italian Referral Hospital. Antibiotics. 2020;9(8):489.

10. Rahman N, Yadav R, Sethi S, Saroch A, Behera A, Bhalla A. Clinical spectrum and outcomes of geriatric tuberculosis emergencies in North India. Turk J Emerg Med. 2021;21:91–98.

11. Sharma RK, Kumari N, Kumar R, Priya P, Kumar S, Shahi SK. Role of XPERT MTB/RIF assay (Gene Xpert) in diagnosing tuberculosis in elderly patients - a hospital based study. JIGIMS. 2019;5(2):126–130.

12. Ananthakrishnan R, Kumar K, Ganesh M, Kumar A, Krishnan N. The Profile and Treatment Outcomes of the Older (Aged 60 Years and Above) Tuberculosis Patients in Tamilnadu, South India. PLoS ONE. 2013;8(7):67288–67288.

13. Kwon YS, Chi SY, Oh IJ, Kim KS, Kim YI, Lim SC et al. Clinical characteristics and treatment outcomes of tuberculosis in the elderly: a case control study. BMC Infectious Diseases. 2013;13(1):1–7.

14. Hase I, Toren KG, Hirano H, Sakurai K, Horne DJ, Saito T. Pulmonary Tuberculosis in Older Adults: Increased Mortality Related to Tuberculosis Within Two Months of Treatment Initiation. Drugs & Aging. 2021;38:807–815.

15. Singhal R, Sah GC, Sethi P, Singh A, Kumar G, Myneedu VP. Detection of multidrug and extensively drug-resistance and mutation pattern in geriatric patients from North Indian referral institute. Indian Journal of Tuberculosis. 2022;69:287–94.