European Review for Medical and Pharmacological Sciences 2024; 28: 269-277

An impactful prospective study on pulmonary tuberculosis in geriatric populations besides its clinical outcomes and implications in the Indian subcontinent

K. DHAMOTHARASWAMY[1], H. SELVARAJ[1], K. CHIDAMBARAM[2], M. DHANASEKARAN[3], K. DURAISAMY[4], N.A. KHAN[5], S. THANGAVEL[6]

[1]Faculty of Pharmacy, Karpagam Academy of Higher Education, Coimbatore, India
[2]Department of Pharmacology and Toxicology, College of Pharmacy, King Khalid University, Abha, Saudi Arabia
[3]Department of Drug Discovery and Development, Harrison College of Pharmacy, University of Auburn, Alabama, USA
[4]District TB Centre, Erode, India
[5]Department of Clinical Pharmacy, College of Pharmacy, King Khalid University, Abha, Saudi Arabia
[6]Department of Pharmacy Practice, Nandha College of Pharmacy, Erode, Tamilnadu, India

Abstract. – OBJECTIVE: Geriatric populations are most at risk for the tuberculosis pandemic, and as people age, the rate of infection rises steadily and drastically. Geriatric individuals frequently experience diagnostic challenges with a wide range of comorbidities, but employing all available standard and novel methods to diagnose any infection is crucial. The prophylactic and therapeutic management for the geriatric population presents a significant difficulty and challenge in assessing an appropriate and effective therapeutic outcome due to prolonged drug therapy and adverse drug reactions. The present study aims to determine the prevalence of tuberculosis in the geriatric population in the Indian subcontinent, its risk factors, clinical outcomes, and adherence to the medication.

PATIENTS AND METHODS: A prospective observational investigation was conducted in a tertiary care Hospital in Erode, Tamil Nadu, India, from April 2021 to September 2022. A total of 1,014 patients were screened, and 176 participants were selected. The participants were then subjected to medication adherence evaluation, and clinical data was collected. The statistical analysis was performed using SPSS version 20.0.

RESULTS: Among 176 participants, 135 (76.70%) were old (65-74 age), 37 (21.02%) were very old (75-84 age) TB patients, and 4 (2.27%) patients were extremely old TB patients (>85). Medication adherence was improved from baseline to the end of the study ($p \leq 0.000$). 110 patients completed the treatment (62.5%). 41 patients were cured in between treatments (23.29%), 13 patients died during the treatment (7.38%), 9 patients lost their follow-up (5.11%), 3 patients failed to respond to the treatment (1.70%).

CONCLUSIONS: The effectiveness of therapy critically depends on the patient's medication adherence to anti-TB therapy. In addition to having a higher likelihood of therapy failure, elderly patients did not appropriately respond to the treatment and completely recovered from the infection even after effective pharmacotherapy.

Key Words:
Tuberculosis, Elderly patients, Treatment Strategies, Geriatrics, Diagnosis, Prevention, Comorbidities, Diabetes mellitus, HIV.

Introduction

The infectious bacterial pathogen *Mycobacterium tuberculosis* is the prime cause of tuberculosis (TB), which is among the most common infectious illnesses worldwide. Nevertheless, the diagnosis, prophylactic, and effective therapeutic management of TB remains a lethal concern for public health globally[1]. Geriatrics is a specialization that focuses on many elements of the physiologic condition, such as exploratory, curative, supporting, and social implications of diseases and providing care for the unique health needs of the elderly[2]. Geriatric TB accounts for most of these cases, which are frequently overlooked due

Corresponding Author: Hemalatha Selvaraj, MD; e-mail: hema.mpharm@gmail.com

to accompanying comorbidities and repetitive clinical manifestations[3]. The frequency of TB in the geriatric population fluctuates significantly between developing and developed countries[4]. By 2026, India's geriatric population is expected to exceed 12.6% of the overall population. According to the India TB study, a massive difference in demographic breakdown among TB occurrence cases is predicted to prevail across the country by 2020[5].

Detecting TB in high-risk populations through periodic monitoring is logistically and financially a stigma for lower-middle-income countries like India. Simultaneously, failing to detect and engage this alarmingly increasing problem of geriatric TB could pose a substantial barrier to the National TB Elimination Programme's (NTEP) continual efforts to reach the country's targeted end-TB goals in 2025[6]. To implement this substantially valuable healthcare goal, it is critical to identify specific clinical information and demographic details of subgroups that may be highly susceptible to poor therapeutic outcomes and, if required, to give them additional healthcare. According to the current literature and previous research[7-11] available from Asia (India, Hong Kong), and Africa, specifically in Ethiopia, TB patients of 60 years of age and older belong to a sub-category with deprived treatment effectiveness. The ineffective ATT efficacy and higher mortality rate may be due to poor medication adherence, drug intolerance, and existing acute and/or chronic co-morbidities.

The current healthcare system should anticipate a drastic increase in geriatric TB patients, and consequently, this may offer challenges with diagnosis, clinical presentation, and disease spectrum[12-15]. Underlying medical conditions such as chronic alcohol consumption, malnourishment, comorbidities such as diabetes mellitus, HIV infection, atherosclerosis, hypertension, cardiovascular issues (stroke, myocardial infarction), renal diseases, neurological disorders, and physiological changes associated with aging can all affect the inherent defense mechanisms, impede microbial clearance systems, and promotes a predicted age-related decrease in cellular immune function to microorganisms like *Mycobacterium tuberculosis*[16]. The outcome of therapeutic management of TB in elderly patients is challenging because of the difficulty in diagnosing TB, increased incidences of ADR, hypersensitivity reactions, allergic manifestations, comorbidities, and complications of the patients in adherence to the regimen[16]. Hence, this study focuses on assessing the prevalence, risk factors, drug-related adverse effects, and adherence to anti-TB drug regimens in pulmonary tuberculosis in elderly patients.

Patients and Methods

Study Design, Period, and Site

This prospective observational investigation was performed in a Tertiary Care Hospital in Erode district, Tamilnadu, among the patients who visited the Directly Observed Therapy (DOT) centre under NTEP program. The study was conducted from April 2021 to September 2022. The out-patient Department screened for pulmonary TB in patients aged 65 years and older who had one or more chest symptoms (fever, chills, chest pain, pain with breathing or coughing, cough, coughing up blood or mucus). The current study analyzed the sociodemographic characteristics and adverse drug reactions encountered in patients administered with ATT in geriatric patients. Furthermore, the current study also analyzed the results of TB care and medication adherence to ATT (ATT-rifampin, isoniazid, pyrazinamide, and ethambutol). The results achieved in this vulnerable group will determine how effectively the National TB Elimination Programme of India might manage the condition.

Data Source and Variables

A medication history interview form was used to gather information about the patient, including demographic data, socioeconomic status, and past medical and medication histories. Mass microscopic radiography and three sputum smears for acid-fast bacilli were employed as a primary screening method. Category-I and Category-II ATT drugs were prescribed to the patients. The socioeconomic status of the patients was measured by using the Kuppusamy Scale in rural as well as urban areas. Kuppuswamy developed this scale in 1976, and it consists of an overall rating that combines the levels of education and profession of the family head, as well as the family's monthly income, yielding an index of 3-29. Based on the score, the socioeconomic status was categorized into different ranges: Class I (upper) with a score of 26-29, Class II (upper-middle) with a score of 16-25, Class III (lower-middle) with a score of 11-15, Class IV (upper-lower) with a score of 5-10, and class V (lower) with a score of 1-4. Pharmaceutical care was given, and med-

ication-related concerns, such as adverse drug reactions, hypersensitivity reactions, and allergic manifestations, were monitored. At the end of the intensive phase and the maintenance phase, patient adherence to medication was evaluated using the Morisky, Green, & Levine (MGL) Medication Adherence Questionnaire. The Morisky, Green, and Levine (MGL) Medication Adherence Questionnaire consists of four items, each of which is given a score of "0" for yes and "1" for no. Scores of "0" indicate complete compliance, "1 or 2" a moderate level, and "3 or 4" a subpar level. Following the fulfillment of the screening criteria, 176 patients were assessed. The following evaluations of the treatment results for research patients were made following the NTEP Technical Guidelines. (1) Cured (Patient who is successfully treated); (2) The cure is complete (Patient who has completed intensive and continuous phase under DOTS); (3) There is a lack of follow-up (Figure 1).

Ethics Considerations

Ethical approval for the current study was obtained from the Institutional Human Ethics Committee of Dhanvantri Multispecialty Hospital, Erode, Tamilnadu (REF: DCC/IEC/025/2021). Also, the written informed consent form was collected from the subjects or bystanders.

Statistical Analysis

The statistical analysis was performed using Statistical Package for Social Sciences (IBM Corp., Armonk, NY, USA), version 20.0. Medication Adherence in elderly patients was evaluated by the Chi-square test and a *p*-value lower than 0.05 was considered statistically significant.

Results

A prospective observational study was carried out on 1,014 patients. Among the 1,014 patients, 176 patients fell under the geriatric patients category and were selected for the study. Out of the 176 TB patients, 135 (76.7%) were the youngest old, 37 (21.02%) were middle-old TB patients, and 4 (2.27%) patients were the oldest old TB patients (Table I). Among 176 patients, 136 (77.2%) were male TB patients, and 40 (22.8%) were female TB patients. Of 176 patients, 2 (1.1%) had reactive HIV status, and 174 (98.9%) had non-reactive HIV status. In this study, among 176 patients, 28 (15.90%) patients were hyperglycaemic (TB patients with diabetes mellitus), and 147 (83.52%) patients did not show any signs of hyperglycemia. Concerning the socio-economic status, 3 (1.7%) patients were class-I (Upper class), 18 (10.2%) patients were class-II (Up-

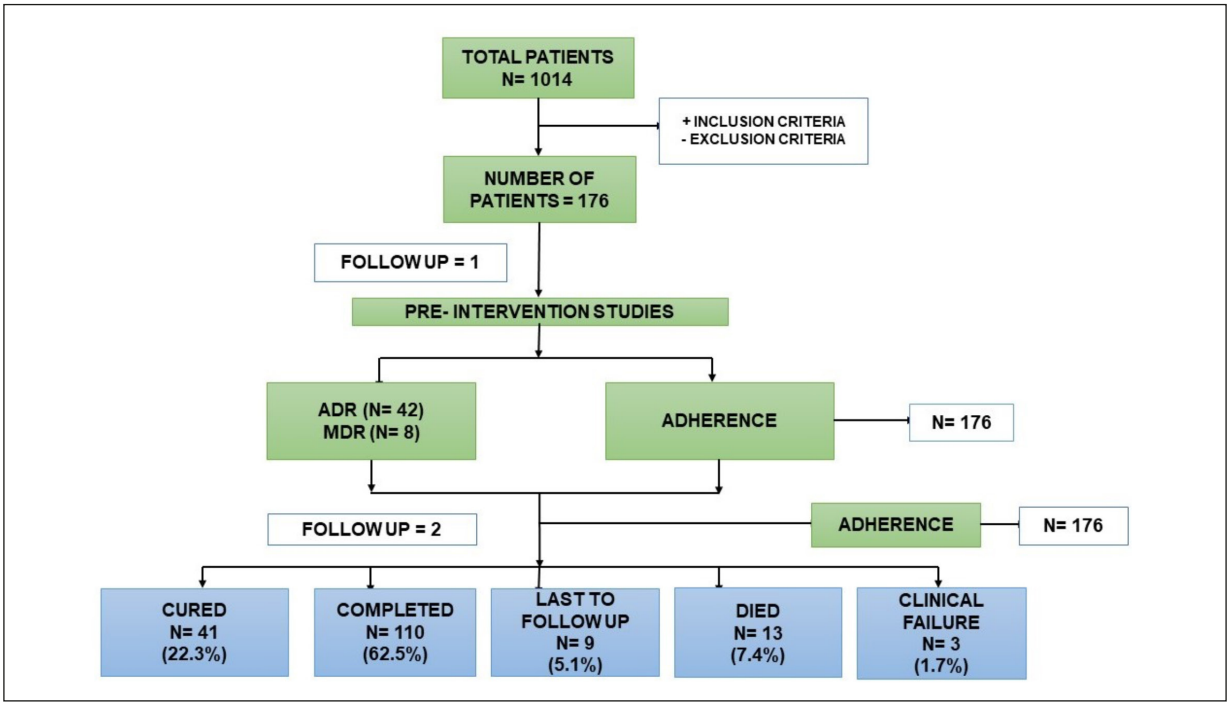

Figure 1. Depicts the overview of the research of participants into various phases throughout the study's follow-up.

Table I. Demographic details of the patients (n=176).

Variables	Gender		Total	*p*
	Male	Female		
Age				
Old (65-74)	99 (73.3%)	36 (26.7%)	135	0.010*
Very old (75-84)	35 (94.6%)	2 (5.4%)	37	
Extremely old (> 85)	2 (50.0%)	2 (50.0%)	4	
HIV				
Reactive	0	2 (100.0%)	2	0.009*
Non-reactive	136 (78.2%)	38 (21.8%)	174	
Diabetic mellitus				
Diabetic mellitus	22 (75.9%)	7 (24.1%)	29	0.843^{NS}
Non-diabetic	114 (77.6%)	33 (22.4%)	147	
Socio-economic status				
Class I (Upper class)	1 (33.3%)	2 (66.7%)	3	0.288^{NS}
Class II (Upper-Middle)	13 (72.2%)	5 (27.8%)	18	
Class III (Lower-Middle)	25 (86.2%)	4 (13.8%)	29	
Class IV (Upper-Lower)	70 (77.8%)	20 (22.2%)	90	
Class V (Lower)	27 (75.0%)	9 (25.0%)	36	
Type of TB case				
New	116 (76.8%)	35 (23.2%)	151	0.817^{NS}
MDR	6 (75.0%)	2 (25.0%)	8	
Recurrent	11 (78.6%)	3 (21.4%)	14	
Default	3 (100.0)	0	3	
Type of regimen				
Category I	129 (78.7%)	35 (21.3%)	164	0.040*
Category II	1 (25.0%)	3 (75.0%)	4	
MDR short	6 (75.0%)	2 (25.0%)	8	

Chi Square Test : * - $p < 0.05$; NS (Not Significant) - $p > 0.05$.

per-Middle class), 29 (16.5%) patients were class-III (Lower-Middle class), 90 (51.1%) patients were class-IV (Upper-Lower class), 36 (20.5%) patients were class-V (Lower class). The current study also analyzed the onset and type of TB and ruled out that, among 176 patients, 151 (85.8%) were newly diagnosed with TB, 8 (4.5%) were known to have MDR TB, 14 (8%) were showed recurrent TB symptoms, and 3 (1.7%) were defaulted TB patients. Of the 176 study participants following the treatment regimen, 164 (93.2%) patients took category I ATT drugs, 4 (2.3%) patients took category II ATT drugs, and 8 (4.5%) patients took MDR short drugs (Table I). Association of demographic profile with gender distribution showed statically significant (p-value<0.05) in age-wise distribution (p-value<0.010*), HIV status (p-value<0.009*), and type of regimen received (p-value<0.040*). The following risk factors were observed in the geriatric TB patients: 3 (1.7%) patients were alcoholic; 3 (1.7%) patients had been in contact with known TB patients; 3 (1.7%) patients had diabetes mellitus as a comorbid condition; 3 (1.7%) patients had a history of smoking, alcohol consumption, malnutrition, HIV; 4 (2.3%) patients were found to be malnourished; 132 (75 %) patients were non-smoker and alcoholic; 6 (3.4%) patients were tobacco users; 3 (1.7%) patients were from urban slums; and 19 (10.8%) patients were affected by other factors (Table II).

The current study depicts the following ADR observed in the elderly TB patients, namely, 10 (23.8%) patients had GI disturbances, 3 (7.1%)

Table II. Risk factors of tuberculosis in elderly patients (n=176).

Risk factors	Number of patients	Percentage
Alcoholic	3	1.7
Contact of known TB patients	3	1.7
Diabetes mellitus	3	1.7
Smoker, alcoholic, malnutrition, HIV	3	1.7
Malnutrition	4	2.3
Non-smoker, Non-alcoholic	132	75.0
Tobacco	6	3.4
Urban slum	3	1.7
Other	19	10.8

patients had arthritis, burning sensation of eyes, cutaneous reactions, flu syndrome, hepatotoxicity, and visual disturbances in 2 (4.8%) patients each, 4 (9.5%) patients had dizziness/vertigo, peripheral neuropathy, ototoxicity, and nephrotoxicity in 1 (2.4%) patient, 6 (14.3%) patients had hypersensitivity reaction, gout, and respiratory syndrome in 3 (7.1%) patients (Table III).

The medication non-adherence of ATT drugs using the MGL scale was analyzed, and the comparison of scores of medications non-adherence of ATT Drugs using the MGL Scale by Chi-square test was further performed. Out of 176 patients, in the baseline period, 42 (23.9%) patients had low adherence, 125 (71%) patients had medium adherence, and 9 (5.1%) patients had high adherence. Eventually, by the end of the study period, the medication non-adherence was increased to 11 (6.3%), 30 (17.04%) patients had medium adherence, and 135 (76.70%) patients had high adherence. Overall, the statistical inference was significant (Table IV).

This study was performed using the comparison of scores of the MGL scale-paired sample *t*-test (Table V). As per the study, the mean adherence was 1.56±1.040, and the end score mean value was 2.84±1.147. The statistical inference ultimately was found to be statistically significant.

Among 176 patients, 110 patients completed the treatment, and the treatment completion percentage was 62.5%. 41 patients were cured in between treatments (23.29%), 13 patients died during the treatment (7.38%), 9 patients lost their follow-up (5.11%), and 3 patients failed to respond to the treatment (1.70%) (Figure 2).

Table III. Drug-related side effects of ATT drugs in elderly patients.

ADRs	Frequency (n = 42)	Percentage
GI disturbances	10	23.8
Arthritis	3	7.1
Burning sensation of eyes	2	4.8
Cutaneous reaction	2	4.8
Dizziness/vertigo	4	9.5
Flu syndrome	2	4.8
Gout	3	7.1
Hepatotoxicity	2	4.8
Peripheral neuropathy	1	2.4
Hypersensitivity reaction	6	14.3
Visual disturbances	2	4.8
Ototoxicity	1	2.4
Nephrotoxicity	1	2.4
Respiratory symptoms	3	7.1

Discussion

Geriatric TB is a significant public health concern globally since it severely escalates morbidity and mortality[17]. The current study was performed in a specific district in the State of Tamil Nadu, India. Since this state had an increased incidence of TB, the study focused on the geriatric population with or without comorbidities (diabetes mellitus and HIV) and patients with varying lifestyles (alcohol consumption and smoking).

Table IV. Comparison of scores of medications non-adherence of ATT drugs using MGL scale.

	End				
Adherence	High	Medium	Low	Total	Statistical inference
High	7 (5.2%)	2 (6.7%)	0	9 (5.1%)	0.003***
Medium	94 (69.6%)	21 (70%)	10 (90.9%)	125 (71%)	
Low	34 (25.2%)	7 (23.3%)	1 (9.1%)	42 (23.9%)	
Baseline	**135**	**30**	**11**	**176**	

Chi-square test: ***The difference between groups was statistically significant at the 99.9% confidence interval ($p < 0.001$).

Table V. Comparison of scores of medications non-adherence of ATT drugs using MGL Scale.

Pair	Mean	N	S.D.	Mean	S.D.	*t*	df	Statistical inference
Adherence total	1.56	176	1.040	1.27	1.569	10.760	175	0.000***
End score	2.84	176	1.147					

Paired *t*-test: ***The difference between groups was statistically significant at the 99.9% confidence interval ($p < 0.001$).

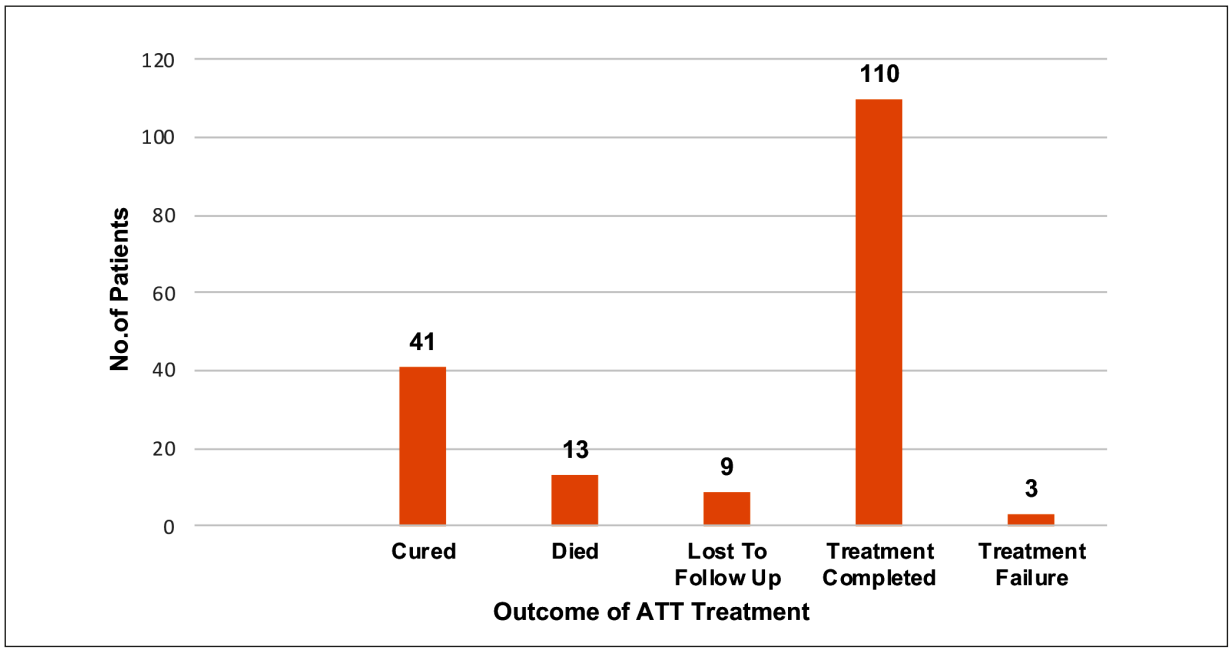

Figure 2. Outcome of treatment of pulmonary tuberculosis in elderly patients.

This impactful prospective clinical study on geriatric TB patients identifies the type of individuals at high risk for TB, comorbidities that can increase the risk, TB-induced comorbidities, the rate of occurrence of TB in a specific population, appropriate preventative and therapeutic regimen, and iatrogenesis associated with the ATT medications. Based on the above data obtained regarding vulnerable individuals (geriatric population), healthcare professionals can assimilate the key etiopathological aspects underlying the occurrence of health problems. They can propose effective diagnostic, prophylactic, and therapeutic strategies to prevent and control diseases in a specific population or community. Thus, in our study, by assessing the individual at risk, explicitly the geriatric population, healthcare professionals can steer their effective ATT health outcome strategies at this specific group. TB is one of the most universal infectious pathologies around the globe. Regardless of the current improved diagnosis, superior pharmacological interventions, and patient education, approximately two billion individuals (approximately) are infected with TB. Furthermore, ten million individuals develop TB pathologies in addition to nearly two million deaths/year[18].

The national program will be significantly impacted in several ways by the findings from the current study. The 4:1 ratio of male to female geriatric individuals with TB is a major concern for contemporary and future healthcare. Additionally, there is a major concern about underreporting of TB in females. By conforming to the epidemiological configuration of TB in this geographic location, our findings also confirmed the incidence surveys carried out in Tamil Nadu[19-22].

The MGL questionnaire was used to determine the patient's medication adherence behavior both at the baseline and end of the study. The study demonstrated a statistically significant change in medication adherence behaviors during the intervention. Besides, the investigators faced certain issues during the study period regarding the lengthy treatment period, the need for combination medicine, unwanted adverse drug reactions, and adherence. Moreover, patients who repeatedly experience fast improvement in their symptoms may cover up the significance of sticking to extensive pharmacological therapy that may be viewed as unneeded. Patient adherence to treatment appears to be significantly influenced by support from family members, which can include collecting the drugs, monetary support, and emotional support as well[23].

Thus, truly, TB is the primary and leading source of mortality related to any type of infection around the globe. Globally, TB is associated

with the highest mortality in human immunodeficiency virus (HIV) patients, causing nearly 40% mortality in the HIV populace. The United Nations Sustainable Development Goals and the World Health Organization's (WHO's) End TB Strategy have designed definite, determined goals for 2020-2035, comprising a 35% decrease in the out-and-out number of TB-related mortalities and a twenty percent decrease reduction in the incidence of TB[24]. According to WHO, the rate of TB occurrence was highly prevalent in Southeast Asia and Africa regions, and a significant number of cases were seen in HIV patients. Another crucial therapeutic issue is multidrug-resistant (MDR) or Rifampicin-resistant (RR) (resistance to at least both isoniazid and rifampicin), which resulted in an increased number of TB[25]. Interestingly, iatrogenesis (drug-induced pathologies) can significantly increase the risk for cardiovascular events, neurotoxicity, nephrotoxicity, hepatotoxicity, gastrointestinal (GI) issues, and pulmonary complications[26].

Geriatrics is a clinical science that specifically engages in offering supportive prophylactic and therapeutic interventions to drastically improve healthcare for the distinctive health requirements of elderly adults[27]. During the physiological aging process, there is a major decline in cellular functions, eventually resulting in decreased tissue and organ functions. Thus, this notably increases the risk for inflammation, mitochondrial dysfunction, excitotoxicity, oxidative stress, apoptosis, necrosis, and infection[28]. There is a severe immunosenescence (remodeling of immune changes that occurs in the elderly/geriatric individual) which results in malfunction of the immune system due to decreased role of the primary (bone marrow, thymus) and secondary immune organs (lymph nodes, spleen and tissues within the different mucous membrane linings in mammals) ensuing in the alterations of the immune system of an elderly individual, that is meticulously associated to the increased rate of infections, autoimmune pathologies, and cancer/malignant tumors[29]. The notable geriatric pathologies include cognitive impairment, arthritic conditions, cancer, asthma, chronic renal disease, persistent obstructive pulmonary disease, dementia, diabetes mellitus, infections, mental disorders, movement disorders (Parkinson's disease), muscular weakness, osteoporosis, and stroke. The new clinical concept of "Geriatric syndromes" was coined in the modern scientific world to understand the major clinical pathologies to improve health outcomes in elderly patients. The geriatric syndromes comprise bone fractures (spontaneous), dementia, delirium, depression, failure to thrive, falls, functional decline, incontinence (lack of voluntary control over defecation and/or urination), vertigo, neglect, and abuse of an elderly individual. Thus, geriatrics occurs due to the cumulative and aggregated erosion of the various physiological systems[28]. One of the major systems reflecting an anatomical and functional decline is the immune system, which is precisely unified and connected to the body as immune cells are present in all organ systems and recirculate in the blood and lymph. The targeted specific immune response to pathogens in geriatric patients has significantly declined. Therefore, the present study focussed on the pathology of TB in a geriatric population.

This study implicated the outcome of treatment, such as cure, loss of follow-up, and mortality of patients after ATT therapy. Major predictors of mortality after ATT include socioeconomic characteristics that apply to geriatric individuals, such as social exclusion, and malnutrition. Our study analysis has shown a positive result towards the outcome of ATT treatment. These findings indicated the efforts taken by healthcare professionals (physicians, pharmacists, nurses, and DOTS providers) to make geriatric TB patients adherent to the treatment regimen in reducing morbidity and mortality and thus significantly improving healthcare in geriatric patients with TB.

Conclusions

Tuberculosis treatment among the elderly is challenging due to the initial limits of respiratory deprivation and contact assessment, which are routinely used in long-term care institutions, as well as the ongoing provision of ATT. This study insisted that there is a need for a multidisciplinary healthcare team, including geriatricians, to improve therapeutic progression in the group of elderly patients.

Conflict of Interest

The authors declare that they have no conflict of interests.

Acknowledgements

The authors extend their appreciation to the Deanship of Scientific Research at King Khalid University for supporting through Large Groups (RGP 2/131/1444).

Ethics Approval
The research was approved by the Institutional Human Ethics Committee of Dhanvantri Multispecialty Hospital, Erode, Tamilnadu (REF: DCC/IEC/025/2021).

Informed Consent
Informed consent was obtained from all the participants in written format.

Data Availability
The data that support the findings of this study are available from the corresponding author (Dr. Hemalatha Selvaraj), upon reasonable request.

Funding
The authors extend their appreciation to the Deanship of Scientific Research at King Khalid University for supporting through Large Groups (RGP.2/131/1444).

Authors' Contribution
Hemalatha Selvaraj contributed to data collection, data analysis, data interpretation, manuscript writing, literature review, and revision; Kumudha Dhamotharaswamy contributed to the study of Conceptualization. Kanagaraj Duraisamy contributed to data acquisition. Kumarappan Chidambaram and N.A.Khan narrated the article. Muralikrishnan Dhanasekaran revised and proofed the manuscript. Sivakumar Thangavel crtically revised manuscript. All authors read and approved the final version of the manuscript.

ORCID ID
K. Chidambaram: 0000-0002-7981-4562
K. Dhamotharaswamy: 0000-0001-9928-9091
H. Selvaraj: 0000-0001-6698-8179
M. Dhanasekaran: 0000-0001-8986-3440

References

1) Wu IL, Chitnis AS, Jaganath D. A narrative review of tuberculosis in the United States among persons aged 65 years and older. J Clin Tuberc Other Mycobact 2022; 100321.
2) Vezmar Kovačević S, Simišić M, Stojkov Rudinski S, Ćulafić M, Vučićević K, Prostran M, Miljković B. Potentially inappropriate prescribing in older primary care patients. PLoS One 2014; 9: e95536.
3) Tiwari S, Kothandapani SK. Tuberculosis in elderly: The Indian perspective. Int J Adv Med 2018; 5: 983-987.
4) Olmo-Fontánez AM, Turner J. Tuberculosis in an Aging World. Pathogens 2022; 11: 1101.
5) Chakaya J, Khan M, Ntoumi F, Aklillu E, Fatima R, Mwaba P, Kapata N, Mfinanga S, Hasnain SE, Katoto PDMC, Bulabula ANH, Sam-Agudu NA, Nachega JB, Tiberi S, McHugh TD, Abubakar I, Zumla A. Global Tuberculosis Report 2020 - Reflections on the Global TB burden, treatment and prevention efforts. Int J Infect Dis 2021; 113 (Suppl 1): S7-S12.
6) Thakur G, Thakur S, Thakur H. Status and challenges for tuberculosis control in India - Stakeholders' perspective. Indian J Tuberc 2021; 68: 334-339.
7) Shivam S, Saha I, Mondal TK, Dasgupta S, Bhattacharyya KD, Roy RN. Comparative analysis of tuberculosis in geriatric and younger age group: An experience from rural West Bengal, India. Sahel Med J 2014; 17: 71.
8) Touré NO, Dia Kane Y, Diatta A, Ba Diop S, Niang A, Ndiaye EM, Thiam K, Mbaye FB, Badiane M, Hane AA. Tuberculose du sujet âgé [Tuberculosis in elderly persons]. Rev Mal Respir 2010; 27: 1062-1068.
9) Pardeshi G, Deshmukh D. Disease characteristics and treatment outcome in elderly tuberculosis patients on DOTS. Indian J Community Med 2007; 32: 292-294.
10) Sood R. The problem of geriatric tuberculosis. J Indian Acad Clin Med 2000; 5: 156-162.
11) Thomas TY, Rajagopalan S. Tuberculosis and ageing: a global health problem. Clin Infect Dis 2001; 33: 1034-1039.
12) Chan-Yeung M, Noertjojo K, Tan J, Chan S L, Tam C M. Tuberculosis in the elderly in Hong Kong. Int J Tuberc Lung Dis 2002; 6: 771-779.
13) Leung CC, Yew WW, Chan CK, Chau CH, Tam CM, Lam CW, Tam WO, Lau KS, Liu WT. Tuberculosis in older people: a retrospective and comparative study from Hong Kong. J Am Geriatr Soc 2002; 50: 1219-1226.
14) Sumathi S. Comparison and Analysis of Clinical Profile and Treatment Outcome in Elderly TB Patients in Urban and Rural Areas of Tamilnadu-Implications in Management. Univ J Med Med Spec 2018; 4.
15) Morris CD. Pulmonary tuberculosis in the elderly: a different disease? Thorax 1990; 45: 912.
16) Rahman N, Yadav R, Sethi S, Saroch A, Behera A, Bhalla A, Garg M, Pannu AK. Clinical spectrum and outcomes of geriatric tuberculosis emergencies in North India. Turk J Emerg Med 2021; 21: 91-97
17) Bonita R, Beaglehole R, Kjellström T. Basic epidemiology. World Health Organization 2006.
18) de Paiva JP, Magalhães MA, Leal TC, da Silva LF, da Silva LG, do Carmo RF, de Souza CD. Time trend, social vulnerability, and identification of risk areas for tuberculosis in Brazil: An ecological study. Plos One 2022 ; 17: e0247894.
19) Mukherjee A, Saha I, Paul B. Tuberculosis in Patients Below and Above 60 years and Their Treat-

ment Outcome Under RNTCP–A study in Rural West Bengal, India. J Indian Acad Geriatr 2008; 4: 60-63.

20) Murali S, Krishnamoorthy Y, Knudsen S, Roy G, Ellner J, Horsburgh CR, Hochberg N, Salgame P, Prakash Babu S, Sarkar S. Comparison of profile and treatment outcomes between elderly and non-elderly tuberculosis patients in Puducherry and Tamil Nadu, South India. Plos One 2021; 16: e0256773.

21) Akgün KM, Crothers K, Pisani M. Epidemiology and Management of Common Pulmonary Diseases in Older Persons. J Gerontol A Biol Sci Med Sci 2012; 67: 276-291.

22) Caraux-Paz P, Diamantis S, de Wazières B, Gallien S. Tuberculosis in the Elderly. J Clin Med 2021; 10: 5888.

23) Nieuwlaat R, Wilczynski N, Navarro T, Hobson N, Jeffery R, Keepanasseril A, Agoritsas T, Mistry N, Iorio A, Jack S, Sivaramalingam B. Interventions for enhancing medication adherence. Cochrane Database Syst Rev 2014; CD000011

24) World Health Organization. Global Tuberculosis Report 2019; 2018. Available at: https://www.who.int/tb/publications/global_report/en/.

25) Lange C, Aarnoutse RE, Alffenaar JW, Bothamley G, Brinkmann F, Costa J, Chesov D, Van Crevel R, Dedicoat M, Dominguez J, Duarte R. Management of patients with multidrug-resistant tuberculosis. Int J Tuberc Lung Dis 2019; 23: 645-662.

26) Giovannini S, Cesari M, Marzetti E, Leeuwenburgh C, Maggio M, Pahor M. Effects of ACE-inhibition on IGF-1 and IGFBP-3 concentrations in older adults with high cardiovascular risk profile. J Nutr Health Aging 2010; 14: 457-460.

27) Shinu C, Dilip C. Impact of pharmaceutical care programme on health outcome of geriatric patients. Clin Epidemiology Glob Health 2020; 8: 894-898.

28) Solana R, Tarazona R, Aiello AE, Akbar AN, Appay V, Beswick M, Bosch J.A., Campos C, Cantisán S, Cicin-Sain L and Derhovanessian E. CMV and Immunosenescence: from basics to clinics. Immune Ageing 2012; 9: 1-9.

29) Montecino-Rodriguez E, Berent-Maoz B, Dorshkind K. Causes, consequences, and reversal of immune system aging. J Clin Invest 2013; 123: 958-965.