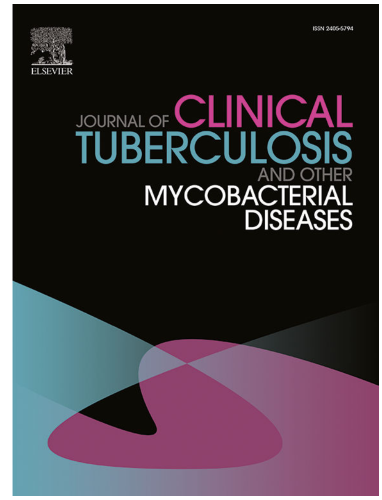
Journal Pre-proofs



Case Report

Relationship of family caregivers' associated factors with medication adherence among elderly with tuberculosis in Iran

Somayeh Hassani, Farahnaz Mohammadi Shahboulagi, Mahshid Foroughan, Payam Tabarsi, Gholamreza Ghaedamini Harouni, Hamidreza Jamaati, Mohammad Varahram, Seyed Mohammad Seyedmehdi, Seyed Alireza Nadji

PII: S2405-5794(24)00075-5
DOI: https://doi.org/10.1016/j.jctube.2024.100488
Reference: JCTUBE 100488

To appear in: *Journal of Clinical Tuberculosis and Other Mycobacterial Diseases*

Please cite this article as: S. Hassani, F. Mohammadi Shahboulagi, M. Foroughan, P. Tabarsi, G. Ghaedamini Harouni, H. Jamaati, M. Varahram, S. Mohammad Seyedmehdi, S. Alireza Nadji, Relationship of family caregivers' associated factors with medication adherence among elderly with tuberculosis in Iran, *Journal of Clinical Tuberculosis and Other Mycobacterial Diseases* (2024), doi: https://doi.org/10.1016/j.jctube.2024.100488

Relationship of family caregivers' associated factors with medication adherence among elderly with tuberculosis in Iran

Somayeh Hassani[1], Farahnaz Mohammadi Shahboulagi [2]*, Mahshid Foroughan[2], Payam Tabarsi[3], Gholamreza Ghaedamini Harouni[4], Hamidreza Jamaati[1], Mohammad Varahram[5], Seyed Mohammad Seyedmehdi[1], Seyed Alireza Nadji[6]

1 Choronic Respiratory Disease Research Center, National Research Institute of Tuberculosis and Lung Diseases (NRITLD), Shahid Beheshti University of Medical Sciences, Tehran, Iran

2 Iranian Research Center on Aging, University of Social Welfare and Rehabilitation Sciences, Tehran, Iran

3 Clinical Tuberculosis and Epidemiology Research Center, National Research Institute of Tuberculosis and Lung Diseases (NRITLD), Shahid Beheshti University of Medical Sciences, Tehran, Iran

4 Social Welfare management Research Center, University of Social Welfare and Rehabilitation Sciences, Tehran, Iran

5 Mycobacteriology Research Center, National Research Institute of Tuberculosis and Lung Diseases (NRITLD), Shahid Beheshti University of Medical Sciences, Tehran, Iran

6 Virology Research Center, National Research Institute of Tuberculosis and Lung Diseases (NRITLD), Shahid Beheshti University of Medical Sciences, Tehran, Iran

*Corresponding author: Farahnaz Mohammadi Shahboulagi

ABSTRACT

Background and Objective. The global incidence rate of tuberculosis and related death among the elderly are 3 times and 6 times more than that of non-elderly, respectively. Therefore, the successful treatment of tuberculosis in the elderly affects all national tuberculosis control programs. Given the fact that "medication adherence" is the main key to effective treatment, it is essential to identify the factors related to medication adherence in the elderly with tuberculosis and provide appropriate interventions. Family caregivers play a pivot role in the elderly care and treatment, and their characteristics can influence the medication adherence of the elderly with tuberculosis. The objective of present study was determining the medication adherence of the elderly with tuberculosis and the factors related to their family caregivers in Iran.

Method. The present study was carried out through descriptive-analytical method and convenience sampling. 305 elderly patients with tuberculosis as well as their family caregivers who met the inclusion criteria were selected from those who referred to infectious diseases clinic of Masih Deneshvari Hospital in Tehran. Demographic and background data, 12-item standard general health questionnaire, Zarit Scale of Caregiver Burden questionnaire and Morisky Green Levine Medication Adherence questionnaire were used for the elderly with tuberculosis. The significance level for statistical tests was considered 0.05. Data analysis of the study was done using SPSS-25 software. Independent t-test, One-way ANOVA, Tukey's test, Spearman's correlation test and ordinal logistic regression model were also used for the analytical statistics.

Findings. Out of the elderly with tuberculosis, 44.92% had low medication adherence, 27.54% had moderate medication adherence, and 27.54% had full medication adherence. Medication adherence of married elderly was significantly better than single, widowed or lonely elderly ($p<0.001$ and $F=53.192$). The medication adherence was significantly better among the elderly whose caregivers had better general health ($p>0.001$ and $r=0.776$) and no burden or low burden according to Zarit scale ($p>0.001$ and $F = 357/96$). In addition, there was a significant relationship between general characteristics of the caregivers (age, gender, marital status, number of children, education, knowledge about tuberculosis, sources of information, relativity to the patient, number of caregivers, employment status, and affordability) and the medication adherence of the elderly with tuberculosis. The results of simultaneous regression test of ordinal logistic regression showed that variables predict medication adherence behavior to a very acceptable level. The coefficient of determination values obtained from McFadden (0.4), Nagelkerke (0.747) and Cox-Snell (0.714) statistics demonstrated high explanatory power of the model by predictor variables.

Conclusion. The results of the present study suggested that the characteristics of family caregivers were associated with the medication adherence of the elderly patients. Therefore, policy making, providing treatment protocols emphasizing on the family role, investigating the characteristics of caregivers during patient visits and performing appropriate interventions will play vital roles in improving medication adherence of the elderly and controlling tuberculosis.

Keywords: elderly, tuberculosis, medication adherence, family caregivers.

Introduction

Tuberculosis (TB) is one of the world's deadliest infectious diseases (1, 2). Globally, the frequency of TB among the elderly is three times higher (3, 4), and TB-related mortality is six times higher than in non-elderly adults (5). Factors that contribute to the occurrence of TB or may reactivate latent tuberculosis in the elderly (1) include biological changes associated with aging, loss of defense barriers, decreased cellular immune response, acute and chronic diseases, malnutrition (1, 3, 6), poverty, reduced access to health systems (3), and hospitalization in care centers. Reports indicate an increase in the world's elderly population, especially in developing countries with an estimated population of elderly individuals over 60 years old reaching 2 billion people in 2050 from 600 million in 2000 (3). It is expected that the incidence of TB in this age group will increase following demographic changes and the growing elderly population (3). According to the latest report of the World Health Organization in 2019, the TB epidemic in the Eastern Mediterranean, Southeast Asia, and Western Pacific regions has shifted significantly towards the elderly (7). As a result, TB in the elderly may impact all TB control programs in a country (4, 8), necessitating the efficiency of TB control programs in both developed and developing countries (4).

Medication adherence and successful treatment are crucial in controlling tuberculosis (9-15). Therefore, an accurate understanding of the barriers and facilitators of medication adherence is essential for interventions, improving drug compliance and achieving better treatment outcomes for TB patients (16). Most TB patients are treated on an outpatient basis under the supervision of family caregivers (17, 18). As TB patients age, their ability to care for themselves decreases, and they increasingly rely on family caregivers due to comorbidities and reduced physical ability (17-20). The communicability of tuberculosis, the stigma associated with its diagnosis, the necessity for strict adherence to specific antibiotic treatment regimens, and the unique psychosocial and physical vulnerabilities of the elderly make medication adherence in tuberculosis a more complex issue compared to other chronic conditions in the elderly. Consequently, the role of family caregivers in ensuring medication adherence for elderly tuberculosis patients is particularly critical. A qualitative study conducted by the authors of this article aimed to investigate the factors affecting medication adherence among elderly individuals with tuberculosis in Iran, revealing that caregivers' characteristics are significant factors influencing medication adherence in this population(16). Other studies have explored the impact of family caregivers' characteristics on medication adherence (21-27), for example, Laghari investigated the effect of family caregivers' characteristics on the medication adherence of children with TB. The findings of his study suggested that male gender, age over 45 years and lack of formal education for the caregivers, as well as financial barriers and lack of training from healthcare workers had a significant relationship with non-adherence to medication among children with TB (26). In Ansari's study in India, low family income and extremely low social level of the family were related to non-adherence to medication of TB patients (27). However, up to the present moment, the factors related to family caregivers such as the ability of caregivers to adapt to the caring role, self-efficacy, belief in the ability to provide care, and their role in medication adherence of the elderly (28), especially the elderly with TB, have received less attention. On the other hand, the role of family caregivers' characteristics in influencing the treatment adherence of TB patients is impacted by the cultural context of different societies (29). In Iranian society, major cultural characteristics include the necessity of family-centered care and the challenging responsibility of caring for the elderly by family caregivers (30), these can affect the relationship between factors associated with family caregivers and the medication adherence in elderly individuals with tuberculosis. Given the significance of identifying factors affecting medication adherence in elderly individuals with tuberculosis, and the lack of studies in this field in Iran, this study aims to determine the medication adherence of the elderly with tuberculosis and the factors related to their family caregivers. By investigating the relationship between these factors and medication adherence, appropriate interventions can be implemented to improve medication adherence, TB prevention strategies (31), and help policy makers, health care providers, society and patients to address problems caused by TB (2).

Materials and Method

Study design, sample size and data collection

The present study is a descriptive-analytical study and a part of a more extensive study to design and test the structural equation modeling (SEM), which was conducted in two qualitative and quantitative phases in 2023. In order to collect data, a researcher-made tool was used, which was derived from selected variables of the qualitative phase (based on the interview with family caregivers, using the Delphi method and polling the experts in TB and elderly health) (16). The researcher-made tool included questions focusing on evaluation of demographic and background information of caregivers, such as age, sex, marital status, number of children, education, employment status, affordability, relativity to the patient, knowledge about TB and its treatment, sources to get information about TB, and the importance of treating elderly from the caregiver's perspective. In addition, 12-item standard general health questionnaire (GHQ-12), Zarit Caregiver Burden Interview (ZBI) and Morisky Green Levine Medication Adherence questionnaire were used for the elderly with TB.

GHQ-12 was first designed by Goldberg in 1972 (32). This test has 12 items and has two subscales of positive mental health symptoms and mental disorder symptoms (32). There are several scoring methods for this questionnaire. The most common scoring methods which were used in this study include the conventional scoring method and Likert scoring method. Psychometrics of GHQ-12 among Iranian youth was conducted by Ebadi et al. in 2013. The questionnaire had adequate validity and its Cronbach's alpha coefficient was reported 0.87 (33).

ZBI was designed in 1980 by Zarit et al. to determine the level of caring burden. This interview includes 22 items about personal, social, emotional and economic caring strains imposed on the caregiver in caring role. Items are measured on a 5-point Likert scale from 0 (never) to 4 (always). The score range of the questionnaire is from 0 to 88, and an increase in the score means an increase in the caring burden (34). In 2008, Navidian et al. examined the validity of this questionnaire through content validity and reported a positive and high correlation by Hamilton Anxiety Questionnaire (r=0.67) and Beck Depression Questionnaire (r=0.89). Besides, the reliability of ZBI was reported 0.94 using the test-retest method (35).

Morisky Green Levine (MGL) adherence scale was designed by Morisky, Green and Levin in 1986, which includes 4 items to evaluate the patient's attitude towards treatment. The answer to the questions is “yes” or “no”. The results of this scale range from 0 to 4, and the developers have proposed three levels of medication adherence: high, medium and low adherence with 0, 1-2 and 3-4 points, respectively (36). Cronbach's alpha coefficient for this questionnaire regarding blood pressure control is 0.61 and it has concurrent and predictive validity (36). This questionnaire has been used as a useful tool to assess medication adherence in many studies on chronic diseases (37), including diabetes, blood pressure (38) and TB (38-43). In 2017, Jafari et al. determined the validity and reliability of this questionnaire for the elderly with high blood pressure; Cronbach's alpha coefficient was 0.86 and its retest reliability was 0.92 (44).

The sample size in the present study, considering 43 observed variables and 12 latent variables obtained from the qualitative phase (16) and the sample size formula of SEM studies by Soper (45), was estimated to be 305 subjects.

Data collection was from the beginning of October 2022 to the end of February 2023 and sampling was done in convenience method. The participants in this study were elderly patients with TB and their family caregivers with the inclusion criteria as follows: elderly with TB aged 60 years and above, definite diagnosis of pulmonary tuberculosis, diagnosed as a new patient, passing at least one month from the start of treatment, having no cognitive problems based on the short cognitive performance test (46), referring to the Infectious Diseases Clinic of Masih Daneshvari Hospital in Tehran (nerve center for TB treatment in Iran), who gave informed consent to participate in the study. The following patients were excluded from the survey: patients with history of hospitalization in the last month, being infected with human immunodeficiency virus, diagnosis of drug-resistant tuberculosis and previous history of TB treatment for less than 4 weeks. These patients and their family caregivers had the experience of previous TB treatment, which could cause bias in the present study. Patients with smear-negative pulmonary tuberculosis, who had received antibiotics before TB treatment due to differential diagnoses, were also excluded from the study. The family caregivers of the patients who were responsible for partial or full care of the patient for at least 6 months and were willing to participate in the study, were talked to simultaneously and individually, and informed consent was obtained from them. Then the family caregivers filled out the caregivers' questionnaires.

Ethical Considerations

The present research is a part of the PhD course. The thesis has been approved by the ethics committee of the University of Welfare and Rehabilitation Sciences with the ethical code IR.USWR.REC.1399.254. Necessary permits to conduct this survey were obtained from the university's research vice-chancellor. The objectives of the research were explained to the research participants and written informed consent was obtained. All subjects were free to participate or leave the study. Patients were informed that their non-cooperation in the study would not affect their treatment process. Additionally, confidentiality of the participants' information was maintained at all stages of the project.

Data Analysis

In the present study, 305 data related to the elderly with TB and 305 data related to their family caregivers were analyzed. A significance level of 0.05 was considered for statistical tests. The data analysis of the study was done using SPSS-25 software. In the analytical statistics section, independent t-test, one-way ANOVA, Tukey's test, Spearman's correlation test and ordinal logistic regression model were used.

Findings

The mean age of the elderly was 72.39 (±8.95) years and 52.5% of the patients (160 cases) were men. The mean (standard deviation) score of medication adherence in the elderly with TB was 2.02 (SD=1.56). 44.92% of the elderly with TB had low medication adherence, 27.54% had moderate medication adherence, and 27.54% had full medication adherence. The mean age of family caregivers was 50.55 (±12.43) years. 57.7% of caregivers were female and 84.6% were married. The mean number of caregivers' children was 2.79 (±1.60). According to the self-report questionnaire, 74.8% of the caregivers had financial hardship.

The findings resulting from the comparison of the mean medication adherence score of the elderly with TB based on factors related to family caregivers are demonstrated in Table 1.

Spearman's correlation coefficient exhibited that the general health score of the caregivers had a direct and significant relationship with the medication adherence score of the elderly, so that as the health condition of the caregivers worsened, the medication adherence of the elderly decreased significantly ($r=0.776$ and $p<0.001$). The results are not shown in the table. Moreover, there was a direct and significant relationship between the number of caregivers' children and the mean medication adherence score of the elderly with TB. Although the intensity of the association was weak, but with the increase in the number of caregivers' children, the medication adherence of the elderly decreased significantly ($r=0.164$ and $p=0.004$). These results are not shown in the table.

In addition, following variables were tested separately and simultaneously in the ordinal logistic regression model: general health score, marital status, adequacy of family income, curability of TB from the caregivers perspective, relativity to the patient, responsibility for caring the patient lonely, the need to take full TB medication from caregivers perspective, data obtained from the nurse that the assumptions of multicollinearity and proportional odds were valid for them (Table 2). The results of simultaneous ordinal logistic regression depicted that the variables (except the obtained data from the nurse) predicted a very acceptable medication adherence behavior. The coefficient determination analysis results of McFadden (0.4), Nagelkerke (0.747) and Cox-Snell (0.714) indicated the high explanatory power of the model by the predictor variables.

Discussion

The present study was conducted for the first time in Iran with the aim of determining the medication adherence of the elderly with TB and the factors related to their family caregivers. The results of this study revealed that family caregivers play a pivot role in medication adherence of the elderly with TB. Other studies have also emphasized the substantial role of family caregivers in medication adherence of TB patients (20) and the elderly with other diseases (24, 25, 47).

Regarding the factors related to supportive family, married elderly and the elderly who lived with their spouses had better medication adherence. Elderly patients who provided their own medicines had better medication adherence than the elderly whose medicines were provided by family caregivers, professional caregivers or others. Besides, the elderly whose family caregivers provided their medicines had better medication adherence than the elderly who were provided medication by others (professional caregivers, friends, neighbors, etc.). The findings of other studies also accentuated the prominent role of family caregivers on medication adherence of the elderly (24, 25, 47). Studies have found that the elderly with chronic diseases who were married followed doctor's instructions better and had better medication adherence (48-51). Marital status was considered as a criterion for the elderly to have social networks (51, 52) and it also indicated the importance of the spouse's role as a family caregiver in facilitating the treatment and medication adherence of the elderly (53).

On the other hand, some studies suggested that the reduction or shortage of medicines at home was another hurdle in TB medication adherence (54). In Roy et al.'s study, the elderly who found it difficult to supply medicine tried to keep the medicine for a longer period of time by skipping some of their doses (55). Elderly patient's inability to provide medicine as well as lack of family support (56) and necessary knowledge about the exact dose and timing of each medication could affect the non-adherence of elderly patients with TB. The findings of the present study showed the effect of caregiver's relatedness degree on medication adherence of the elderly with TB. The findings of other studies also demonstrated that a first-degree relative was a better caregiver and played a more effective role in the patient's medication adherence (57).

In terms of general characteristics of family caregivers, the following were associated with better medication adherence among the elderly TB patients: age below 40 years, being female, being single, having fewer children, less number of caregivers, being unemployed, caregiver's affordability, low or no care burden, improved general health, higher education, having knowledge about the contagiousness and curability of TB, knowledge about the importance of taking the full course of TB treatment and getting information from reliable sources. Aged caregivers were affected by a wide range of issues, including comorbidity, polypharmacy, reduced physical strength and vision, thus they were not efficient in caring the elderly patients (58); however, young caregivers had less comorbidity, less physical problems and ability, and had fewer impediments to provide adequate care to elderly patients; as a result, it could be expected that their patients had better medication adherence. The findings of our study imparted that medication adherence was better in the elderly whose caregivers were female. Other studies also exposed that when the responsibility of caring the elderly was on women or female children, the patient's medication adherence was better. These findings might be due to the greater sense of dedication and influence in women (57, 59). Meanwhile, some studies demonstrated that the caregiver's gender did not affect the patient's medication adherence (60, 61). In Iran, women make up the majority of family caregivers due to popular and traditional beliefs and values (30, 62). Additionally, in countries like Iran, men traditionally bear the majority of job responsibilities and provide financial support for their families. This economic role for men can sometimes lead to a decrease in their involvement in caring for the elderly. Therefore, it is important to note that due to this cultural belief, women experience a greater burden from caregiving, physical strain and psychological distress compared to men (63). The increased physical and mental burden on family caregivers ultimately diminishes their health (64), which can impact the quality of care provided to elderly patients, potentially leading to patient neglect (65). Therefore, healthcare providers should actively monitor the physical and mental well-being of family caregivers (66). Being single, having no children, and being unemployed bring about more time to caregivers for caring the elderly with TB. Besides, less number of caregivers leads to a more precise division of caring responsibilities among caregivers and prevents caring negligence caused by multiple caregivers. In Iranian culture, strong family bond makes people extremely committed to family members. Therefore, when a family member is experiencing illness, the concerns of other family members increase (67). The findings of Negarandeh et al.'s study in Iran represented that most of the family caregivers who were responsible for caring the elderly with heart disease neglected their health. Caregivers' health affected the quality of providing patient care (27). Due to taking care of the patient, health of the caregivers is neglected and related problems prevent caregivers from fulfilling their caring role. Therefore, healthcare provider should always pay attention to the caregivers' health and follow up on their health issues (27).

Regarding the knowledge of family caregivers, the findings of the present study suggested that caregivers' education, knowledge about the contagiousness and curability of TB, knowledge about the importance of taking the full course of TB treatment and getting information from reliable scientific sources played a dominant role in the medication adherence of the elderly with TB. Other studies likewise showed that insufficient knowledge of family caregivers about TB and its treatment was associated with non-adherence to medication (68-70). Caregivers who considered illness as an integral part of the aging process did not accompany the elderly for visits and treatment (59, 71). However, the family caregivers' knowledge about TB prevented the isolation of the patient and brought about more family support for the patient (49). In addition, the health culture of a TB patient is affected by the information received from family members (72); hence, improving the knowledge and awareness of family caregivers about TB and its treatment should be a vital part of TB treatment policies (49). In Iran and many other countries, it is common for a family member, friend, or neighbor to be responsible for monitoring a tuberculosis patient's drug consumption after diagnosis. However, healthcare centers do not provide family caregivers with follow-up, supervision and guidance. Policies and protocols for tuberculosis treatment, especially for elderly patients, should prioritize consistent communication, thorough training and monitoring the family caregivers. Healthcare providers should offer comprehensive training to family caregivers before starting the treatment, as well as throughout the entire process, and providing them with appropriate interventions when necessary.

One limitation in this study is conducting the study in just one center: Dr. Masih Daneshvari Hospital. However, as this hospital serves as the primary center for tuberculosis treatment in Iran, patients from all over the country come there for treatment. Therefore, the findings of the study were not significantly disputed by considering just a single institution. Nevertheless, it is recommended further researches at a national level to ensure more precise results. In the present study, we excluded a group of patients who had a history of previous tuberculosis disease and treatment-resistant tuberculosis, because we believed that these factors could potentially affect medication adherence in elderly patients with tuberculosis and family caregivers' understanding of the condition. As a result, it may lead to bias in our findings. To further explore the impact of these variables on our research findings, we recommend that separate studies be conducted and the results should be compared.

Conclusion

Despite numerous efforts, many TB patients, especially the elderly, do not have full medication adherence. Therefore, knowing the factors related to medication adherence and providing appropriate interventions are significant steps towards maintaining and improving the health of the elderly with TB and other members of community. The findings of the present study exhibited that factors related to family caregivers (including supportive family, general characteristics of family caregivers, and knowledge of family caregivers) affected the medication adherence of the elderly with TB. Therefore, policymaking, providing treatment protocols emphasizing the family role, investigating the characteristics of caregivers during patient visits and providing appropriate interventions to empower caregivers during treatment will play an indispensable role in improving the medication adherence of the elderly and controlling TB.

Acknowledgments

We are extremely grateful to all the professors, physicians and nurses in Masih Daneshvari Hospital for their sincere cooperation in conducting this project.

Data Availability

The data is available and there is no restriction on additional information.

Conflict of Interest

The authors have no conflict of interest in this study.

References

1. Shaik KU, Dattu S, Krishnamurthy S, Revanasiddappa H, Reddy Y. A prospective study of pulmonary tuberculosis in rural geriatric population of South India. J Clin Sci Res. 2016;5:28-32.

2. Boru CG, Shimels T, Bilal AI. Factors contributing to non-adherence with treatment among TB patients in Sodo Woreda, Gurage Zone, Southern Ethiopia: A qualitative study. Journal of infection and public health. 2017;10(5):527-33.

3. Oshi DC, Oshi SN, Alobu I, Ukwaja KN. Profile and treatment outcomes of tuberculosis in the elderly in southeastern Nigeria, 2011–2012. PLoS One. 2014;9(11):e111910.

4. Li J, Chung P-H, Leung CL, Nishikiori N, Chan EY, Yeoh E-K. The strategic framework of tuberculosis control and prevention in the elderly: a scoping review towards End TB targets. Infectious diseases of poverty. 2017;6(1):70.

5. Hussein MT, Yousef LM, Abusedera MA. Pattern of pulmonary tuberculosis in elderly patients in Sohag Governorate: hospital based study. Egyptian Journal of Chest Diseases and Tuberculosis. 2013;62(2):269-74.

6. Schaaf HS, Collins A, Bekker A, DAVIES PD. Tuberculosis at extremes of age. Respirology. 2010;15(5):747-63.

7. Organization WH. World Health Organization Global Tuberculosis Report 2013. World Health Organization: Geneva, Switzerland. 2019.

8. Velayutham BRV, Nair D, Chandrasekaran V, Raman B, Sekar G, Watson B, et al. Profile and response to anti-tuberculosis treatment among elderly tuberculosis patients treated under the TB Control programme in South India. PloS one. 2014;9(3):e88045.

9. Tola HH, Karimi M, Yekaninejad MS. Effects of sociodemographic characteristics and patients' health beliefs on tuberculosis treatment adherence in Ethiopia: a structural equation modelling approach. Infectious diseases of poverty. 2017;6(1):167.

10. McDonnell M, Turner J, Weaver MT. Antecedents of adherence to antituberculosis therapy. Public Health Nursing. 2001;18(6):392-400.

11. Khalili H, Dashti-Khavidaki S, Sajadi S, Hajiabolbaghi M. Assessment of adherence to tuberculosis drug regimen. DARU Journal of Pharmaceutical Sciences. 2008;16(1):47-50.

12. Azizi N, Karimy M, Salahshour VN. Determinants of adherence to tuberculosis treatment in Iranian patients: application of health belief model. The Journal of Infection in Developing Countries. 2018;12(09):706-11.

13. Adane AA, Alene KA, Koye DN, Zeleke BM. Non-adherence to anti-tuberculosis treatment and determinant factors among patients with tuberculosis in northwest Ethiopia. PloS one. 2013;8(11):e78791.

14. Freire ILS, dos Santos FR, de Menezes LCC, de Medeiros AB, de Lima RF, da Silva BCO. Adherence of Elderly People to Tuberculosis Treatment/Adesão dos Idosos às Formas de Administração do Tratamento da Tuberculose. Revista de Pesquisa: Cuidado é Fundamental Online. 2019;11(3):555-9.

15. Mok J, An D, Kim S, Lee M, Kim C, Son H. Treatment outcomes and factors affecting treatment outcomes of new patients with tuberculosis in Busan, South Korea: a retrospective study of a citywide registry, 2014–2015. BMC infectious diseases. 2018;18(1):655.

16. Hassani S, Mohammadi Shahboulagi F, Foroughan M, Nadji SA, Tabarsi P, Ghaedamini Harouni G. Factors Associated with Medication Adherence in Elderly Individuals with Tuberculosis: A Qualitative Study. Canadian Journal of Infectious Diseases and Medical Microbiology. 2023;2023.

17. Martin LR, Williams SL, Haskard KB, DiMatteo MR. The challenge of patient adherence. Therapeutics and clinical risk management. 2005;1(3):189-99.

18. Andreasyan D, Bazarchyan A, Manukyan S, Muradyan G, Torosyan A, Chamanyan A, et al. Health system performance assessment. Yerevan (Armenia): National Institute of Health. 2016.

19. Tonoyan T, Muradyan L. Health inequalities in Armenia-analysis of survey results. International journal for equity in health. 2012;11(1):1-12.

20. Gebremariam MK, Bjune GA, Frich JC. Barriers and facilitators of adherence to TB treatment in patients on concomitant TB and HIV treatment: a qualitative study. BMC public health. 2010;10:1-9.

21. Liefooghe R, Muynck A. The dynamics of tuberculosis treatment adherence. Journal-pakistan medical association. 2001;51(1):3-9.

22. Seetha M, Srikantaramu N, Aneja K, Singh H. Influence of motivation of patients and their family members on the drug collection by patients. Indian J Tuberc. 1981;28:182-90.

23. Grigoryan Z, McPherson R, Harutyunyan T, Truzyan N, Sahakyan S. Factors Influencing Treatment Adherence Among Drug-Sensitive Tuberculosis (DS-TB) Patients in Armenia: A Qualitative Study. Patient preference and adherence. 2022:2399-408.

24. Paz-Soldán VA, Alban RE, Jones CD, Oberhelman RA. The provision of and need for social support among adult and pediatric patients with tuberculosis in Lima, Peru: a qualitative study. BMC health services research. 2013;13(1):1-12.

25. Kaulagekar-Nagarkar A, Dhake D, Jha P. Perspective of tuberculosis patients on family support and care in rural Maharashtra. The Indian journal of tuberculosis. 2012;59(4):224-30.

26. Laghari M, Talpur BA, Sulaiman SAS, Khan AH, Bhatti Z. Assessment of adherence to anti-tuberculosis treatment and predictors for non-adherence among the caregivers of children with tuberculosis. Transactions of the Royal Society of Tropical Medicine and Hygiene. 2021;115(8):904-13.

27. Ansari MS, Khayyam KU, Sharma M, Imam F, Behera D. The role of socio-economic factors responsible for non-compliance of directly observed treatment short-course among tuberculosis patients. วารสาร การ แพทย์ และ วิทยาศาสตร์ สุขภาพ (Journal of Medicine and Health Science). 2011;18(2):78-86.

28. El-Saifi N, Moyle W, Jones C, Alston-Knox C. Determinants of medication adherence in older people with dementia from the caregivers' perspective. International psychogeriatrics. 2019;31(3):331-9.

29. Samal J. Family perspectives in the care and support of tuberculosis patients: An Indian context. The Journal of Association of Chest Physicians. 2017;5(2):67-9.

30. Shamsikhani S, Ahmadi F, Kazemnejad A, Vaismoradi M. Typology of family support in home care for Iranian older people: a qualitative study. International Journal of Environmental Research and Public Health. 2021;18(12):6361.

31. Culqui DR, Grijalva CG, Cayla JA, Horna-Campos O, Ch KA. Factors associated with the non-completion of conventional anti-tuberculosis treatment in Peru. Archivos de Bronconeumología (English Edition). 2012;48(5):150-5.

32. Goldberg DP. User's guide to the General Health Questionnaire. Windsor. 1988.

33. Montazeri A, Harirchi AM, Shariati M, Garmaroudi G, Ebadi M, Fateh A. The 12-item General Health Questionnaire (GHQ-12): translation and validation study of the Iranian version. Health and quality of life outcomes. 2003;1:1-4.

34. Zarit SH, Reever KE, Bach-Peterson J. Relatives of the impaired elderly: correlates of feelings of burden. The gerontologist. 1980;20(6):649-55.

35. Navidian A, Bahari F. Burden experienced by family caregivers of patients with mental disorders. Pakistan Journal of Psychological Research. 2008;23(1-2):19-29.

36. Morisky DE, Green LW, Levine DM. Concurrent and predictive validity of a self-reported measure of medication adherence. Medical care. 1986:67-74.

37. Fernandez-Lazaro CI, García-González JM, Adams DP, Fernandez-Lazaro D, Mielgo-Ayuso J, Caballero-Garcia A, et al. Adherence to treatment and related factors among patients with chronic conditions in primary care: a cross-sectional study. BMC family practice. 2019;20(1):132.

38. Fagundez G, Perez-Freixo H, Eyene J, Momo JC, Biyé L, Esono T, et al. Treatment adherence of tuberculosis patients attending two reference units in Equatorial Guinea. PloS one. 2016;11(9):e0161995.

39. Shiratani KN. Psychological changes and associated factors among patients with tuberculosis who received directly observed treatment short-course in metropolitan areas of Japan: quantitative and qualitative perspectives. BMC public health. 2019;19(1):1642.

40. Corless IB, Wantland D, Bhengu B, McInerney P, Ncama B, Nicholas PK, et al. HIV and tuberculosis in Durban, South Africa: adherence to two medication regimens. AIDS care. 2009;21(9):1106-13.

41. Huang R, Ren G, Hu J. Bracelet-and self-directed observational therapy for control of tuberculosis: study protocol for a cluster randomized controlled trial. Trials. 2017;18(1):1-10.

42. McInerney PA, Nicholas PK, Wantland D, Corless IB, Ncama B, Bhengu B, et al. Characteristics of anti-tuberculosis medication adherence in South Africa. Applied Nursing Research. 2007;20(4):164-70.

43. Nezenega ZS, Tafere TE. Patient satisfaction on tuberculosis treatment service and adherence to treatment in public health facilities of Sidama zone, South Ethiopia. BMC health services research. 2013;13(1):110.

44. Jafari Oori M MF, K NT. Designing and testing a predictive model for medication adherence in the elderly with high blood pressure. Tehran: university of social welfare and rehabilitation sciences; 2020.

45. Soper DS. A-priori Sample Size Calculator for Multiple Regression [Software]. Available from https://www.danielsoper.com/statcalc 2022.

46. Bakhtiyari F, Foroughan M, Fakhrzadeh H, Nazari N, Najafi B, Alizadeh M, et al. Validation of the persian version of Abbreviated Mental Test (AMT) in elderly residents of Kahrizak charity foundation. Iranian journal of Diabetes and Metabolism. 2014;13(6):487-94.

47. Tekle B, Mariam D H, Ali A. Defaulting from DOTS and its determinants in three districts of Arsi Zone in Ethiopia. The International Journal of Tuberculosis and Lung Disease. 2002;6(7):573-9.

48. Truzyan N, Crape B, Harutyunyan T, Petrosyan V. Family-based tuberculosis counseling supports directly observed therapy in Armenia: a pilot project. Journal of Tuberculosis Research. 2018;6(02):113.

49. Lewis CP, Newell JN. Improving tuberculosis care in low income countries–a qualitative study of patients' understanding of" patient support" in Nepal. BMC public health. 2009;9:1-8.

50. Wu J-R, Lennie TA, Chung ML, Frazier SK, Dekker RL, Biddle MJ, et al. Medication adherence mediates the relationship between marital status and cardiac event-free survival in patients with heart failure. Heart & Lung. 2012;41(2):107-14.

51. Trivedi RB, Ayotte B, Edelman D, Bosworth HB. The association of emotional well-being and marital status with treatment adherence among patients with hypertension. Journal of behavioral medicine. 2008;31:489-97.

52. Caldwell JR, Theisen V, Kaunisto CA, Reddy PJ, Smythe PS, Smith DW. Psychosocial factors influence control of moderate and severe hypertension. Social science & medicine. 1983;17(12):773-82.

53. Kulkarni SP, Alexander KP, Lytle B, Heiss G, Peterson ED. Long-term adherence with cardiovascular drug regimens. American heart journal. 2006;151(1):185-91.

54. Courtwright A, Turner AN. Tuberculosis and stigmatization: pathways and interventions. Public health reports. 2010;125(4_suppl):34-42.

55. Roy NT, Sajith M, Bansode MP. Assessment of Factors Associated with Low Adherence to Pharmacotherapy in Elderly Patients. Journal of Young Pharmacists. 2017;9(2).

56. Sagbakken M, Frich JC, Bjune G. Barriers and enablers in the management of tuberculosis treatment in Addis Ababa, Ethiopia: a qualitative study. BMC public health. 2008;8(1):1-11.

57. Yee D, Valiquette C, Pelletier M, Parisien I, Rocher I, Menzies D. Incidence of serious side effects from first-line antituberculosis drugs among patients treated for active tuberculosis. American journal of respiratory and critical care medicine. 2003;167(11):1472-7.

58. Axelsson M, Brink E, Lundgren J, Lötvall J. The influence of personality traits on reported adherence to medication in individuals with chronic disease: an epidemiological study in West Sweden. PloS one. 2011;6(3):e18241.

59. Linkievicz NM, Sgnaolin V, Engroff P, Behr Gomes Jardim G, Cataldo Neto A. Association between Big Five personality factors and medication adherence in the elderly. Trends in Psychiatry and Psychotherapy. 2022;44.

60. Hazrati-Meimaneh Z, Amini-Tehrani M, Pourabbasi A, Gharlipour Z, Rahimi F, Ranjbar-Shams P, et al. The impact of personality traits on medication adherence and self-care in patients with type 2 diabetes mellitus: The moderating role of gender and age. Journal of Psychosomatic Research. 2020;136:110178.

61. Aflakseir A, Nikroo F, Mollazade J. Predicting Medication Adherence Based on Personality Characteristics in Individuals with Type 2 Diabetes Mellitus. Iranian journal of diabetes and obesity. 2020.

62. Farahnaz Mohammady S, Fatemeh D, Mansure Yadavar M. [Facilitator and barrier factors in family caregiving process of Iranian frail elderly: a qualitative study. 2008.

63. Sharma N, Chakrabarti S, Grover S. Gender differences in caregiving among family-caregivers of people with mental illnesses. World journal of psychiatry. 2016;6(1):7.

64. Orfila F, Coma-Solé M, Cabanas M, Cegri-Lombardo F, Moleras-Serra A, Pujol-Ribera E. Family caregiver mistreatment of the elderly: prevalence of risk and associated factors. BMC public health. 2018;18:1-14.

65. Beach SR, Schulz R. Family caregiver factors associated with unmet needs for care of older adults. Journal of the American Geriatrics Society. 2017;65(3):560-6.

66. Stensletten K, Bruvik F, Espehaug B, Drageset J. Burden of care, social support, and sense of coherence in elderly caregivers living with individuals with symptoms of dementia. Dementia. 2016;15(6):1422-35.

67. Al-Hajjaj M, Al-Khatim I. High rate of non-compliance with anti-tuberculosis treatment despite a retrieval system: a call for implementation of directly observed therapy in Saudi Arabia. The International Journal of Tuberculosis and Lung Disease. 2000;4(4):345-9.

68. Triasih R, Padmawati R, Duke T, Robertson C, Sawyer S, Graham S. A mixed-methods evaluation of adherence to preventive treatment among child tuberculosis contacts in Indonesia. The International Journal of Tuberculosis and Lung Disease. 2016;20(8):1078-83.

69. Garie KT, Yassin MA, Cuevas LE. Lack of adherence to isoniazid chemoprophylaxis in children in contact with adults with tuberculosis in Southern Ethiopia. PLoS One. 2011;6(11):e26452.

70. Kibirige L, Izudi J, Okoboi S. Discontinuation of tuberculosis treatment among children in the Kampala Capital City Authority health facilities: a mixed-methods study. BMC Infectious Diseases. 2021;21(1):511.

71. Bagchi S, Ambe G, Sathiakumar N. Determinants of poor adherence to anti-tuberculosis treatment in Mumbai, India. International journal of preventive medicine. 2010;1(4):223.

72. Rubel AJ, Garro LC. Social and cultural factors in the successful control of tuberculosis. Public health reports. 1992;107(6):626.

Tables

Table 1. Comparison of the mean score of medication adherence based on factors related to family caregivers

Variable categories	variable groups			Number	mean	SD (standard deviation)	P-Value	Post Hoc Test		
								pairwise	Mean Difference	P-Value
Supportive family	Marital status of the patient	1	married	150	1.21	1.38	F=53.192 P<0.001	1-2	-2.037	0.009
		2	single/divorced	4	3.25	0.50		1-3	-1.575	<0.001
		3	widow	151	2.79	1.32		2-3	0.462	0.777
	Coexistence situation	1	with spouse	51	0.98	1.32	F=36.368 P<0.001	1-2	-1.747	<0.001
		2	with children	88	2.73	1.33		1-3	-0.364	0.443
		3	With spouse and children	98	1.33	1.41		1-4	-1.902	<0.001

		4	alone	68	2.88	1.28		2-3	1.401	<0.001
								2-4	-0.155	0.891
								3-4	-1.556	<0.001
	The person who supply TB medications	1	Patient	86	0.98	1.27	F=36.963 P<0.001	1-2	-1.408	<0.001
		2	Family caregivers	213	2.38	1.47		1-3	-3.023	<0.001
		3	Others	6	4.00	0.00		2-3	-1.615	0.016
general characteristics of the family caregiver	Age group	1	<40	76	1.70	1.35	F=3.860 P=0.010	1-2	-0.766	0.010
		2	41-50	82	2.46	1.42		1-3	-0.349	0.475
								1-4	-0.090	0.987
		3	51-60	86	2.05	1.68		2-3	0.417	0.297
		4	61<	61	1.79	1.70		2-4	0.677	0.048
								3-4	0.260	0.745
	gender	1	Male	129	2.57	1.40	t =5.571 P<0.001	-	-	-
		2	Female	176	1.62	1.56		-	-	-
	Marital status	1	married	258	2.07	1.55	F=3.535 P=0.015	1-2	0.740	0.063
								1-3	0.296	0.942
		2	single	30	1.33	1.49		1-4	-1.051	0.230
								2-3	-0.444	0.873

		3	divorced	9	1.78	1.72		2-4	-1.792	0.019
		4	widow	8	3.13	0.99		3-4	-1.347	0.276
	Relativity to the patient	1	Daughter	82	1.87	1.51	F=32.429 P<0.001	1-2	-0.986	0.007
								1-3	0.907	<0.001
		2	Second-degree relative	27	2.85	1.10		1-4	-1.025	<0.001
								1-5	-1.991	0.001
								2-3	1.893	<0.001
								2-4	-0.039	1.000
		3	Spouse	97	0.96	1.39		2-5	-1.005	0.372
		4	Son	92	2.89	1.12		3-4	-1.933	<0.001
		5	Neighbor	7	3.86	0.38		3-5	-2.898	<0.001
								4-5	-0.966	0.332
	Responsibility for caring the patient lonely	1	Yes	212	1.48	1.50	t =-13.427 P<0.001	-	-	-
		2	No	93	3.26	0.81		-	-	-

Variable categories			**mean**	**SD**		**Post Hoc Test**

	variable groups							**pairwise**	**Mean Difference**	**P-Value**
general characteristics of the family caregiver	Employment status	1	Employed	155	2.43	1.45	F=13.753 P<0.005	1-2	1.426	<0.001
		2	Retired/Disabled	23	1.00	1.51		1-3	0.717	<0.001
		3	Housewife/Unemployed	127	1.71	1.55		2-3	-0.709	0.094
	Affordability	1	Yes	77	0.36	0.71	F=117.672 P<0.001	1-2	-1.701	<0.001
		2	No, sometimes in financial hardship	93	2.06	1.52		1-3	-2.570	<0.001
		3	No, always in financial hardship	135	2.93	.11		2-3	-0.869	<0.001
	Caring burden	1	no burden or low burden	98	0.65	1.02	F=96.357 P<0.001	1-2	-1.847	<0.001
		2	Mild to moderate burden	158	2.50	1.42		1-3	-2.551	<0.001
		3	Moderate burden	49	3.20	0.87		1-4	-	NA*
								2-3	-0.704	0.001
		4	Severe burden	0	-	-		2-4	-	NA
								3-4	-	NA
Family caregiver knowledge	Caregiver's education	1	illiterate	58	2.79	1.22	F=17.582 P<0.001	1-2	0.556	0.062
								1-3	1.657	<0.001
		2	below high school	156	2.24	1.59		1-4	1.623	<0.001

			diploma					2-3	1.101	<0.001
		3	high school diploma	44	1.14	1.29		2-4	1.067	<0.001
		4	university degree	47	1.17	1.32		3-4	-0.034	1.000
	Knowledge about the contagiousness of TB	1	Yes	234	1.67	1.55	t =-10.312 P<0.001	-	-	-
		2	No	71	3.18	0.90		-	-	-
	Knowledge about the curability of TB	1	Yes	291	1.95	1.56	t =-7.903 P<0.001	-	-	-
		2	No	14	3.50	0.65		-	-	-
	Knowledge about the importance of taking the full course of TB treatment	1	None/Low	5	4.00	0.00	F=74.772 P<0.001	1-2	0.768	0.509
		2	Moderate	56	3.23	0.89		1-3	2.706	<0.001
								1-4	0.395	0.895
		3	Full	201	1.29	1.36		2-3	1.939	<0.001
		4	Don't know	43	3.60	0.56		2-4	-0.373	0.410
								3-4	-2.311	<0.001
		1	Yes	72	1.90	1.57	t =-	-	-	-

	Getting information from physician	2	No	33	2.97	1.07	5.073 P<0.001	-	-	-
	Getting information from nurse	1	Yes	66	1.02	1.35	t =-6.650 P<0.001	-	-	-
		2	No	239	2.30	1.50		-	-	-
	Getting information from books, internet and television	1	Yes	124	1.37	1.51	t =-6.331 P<0.001	-	-	-
		2	No	181	2.46	1.44		-	-	-

*Not Available

Table 2. The results of ordinal logistic regression analysis to assess medication adherence predictors

Variable /Variable category		Crude					Adjusted				
		B	SE	P-Value	β (IC 95%)		B	SE	P-Value	β (IC 95%)	
					L	U				L	U
General health	-	0.306	0.023	<0.001	0.260	0.351	0.154	0.028	<0.001	0.098	0.209
Marital status	Married	0.390									
	Single	0[a]					0[a]				

Affordability	No (sometimes or always in financial hardship)	3.267	0.321	<0.001	2.637	3.896	1.574	0.371	<0.001	0.848	2.300
	Yes	0[a]					0[a]				
Knowledge about the curability of TB	Yes	-1.767	0.552	0.001	-2.849	-0.684	-1.583	0.647	0.014	-2.852	-0.314
	No	0[a]					0[a]				
Relativity to the patient	Daughter	1.331	0.282	<0.001	0.778	1.885	0.698	0.378	0.065	-0.042	1.438
	Relatives and neighbors	2.785	0.393	<0.001	2.016	3.555	0.930	0.549	0.090	-0.145	2.006
	Son	2.557	0.296	<0.001	1.977	3.138	0.959	0.429	0.025	0.119	1.799
	Spouse	0[a]					0[a]				
Responsibility for caring the patient lonely	Yes	-2.166	0.254	<0.001	-2.663	-1.669	-1.155	0.343	0.001	-1.826	-0.483
	No	0[a]					0[a]				
Knowledge about the importance of taking the full course of TB treatment	Moderate/Low	-0.573	0.400	0.152	-1.356	0.210	0.623	0.468	0.183	-0.294	1.540
	Full	-3.415	0.383	<0.001	-4.166	-2.663	-1.470	0.427	0.001	-2.308	-0.633
	Don't know	0[a]					0[a]				
Getting information from nurse	Yes	-1.561	0.268	<0.001	-2.087	-1.035	-0.312	0.320	0.329	-0.939	0.315
	No	0[a]					0[a]				

Declaration

Ethics approval and consent to participate
All procedures performed in study involving human participants were in accordance with the ethical standards of the institutional and national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards. This article does not contain any studies with animals performed by any of the authors. The present study is a part of Ph.D. thesis and has been approved by the ethics committee of the University of Social Welfare and Rehabilitation Sciences with ethics code IR.USWR.REC.1399.

Availability of data and materials

The data that support the findings of this study are available from the corresponding author upon reasonable request.

Competing interests

The authors declare no competing interests.

Funding

This research received no specific grant from any funding agency in the public, commercial, or not-for-profit sectors.

Authors' contributions

Somayeh Hassani, Farahnaz Mohammadi Shahboulagi, Mahshid Foroughan, Payam Tabarsi, Gholamreza Ghaedamini Harouni, Hamidreza Jamaati, Mohammad Varahram, Seyed Mohammad Conceived and designed the analysis, collected the data, Seyedmehdi, Seyed Alireza Nadji contributes data or analysis tools, performed the analysis and wrote the paper. All authors reviewed the manuscript.

Acknowledgements

We are extremely grateful to all the professors, physicians and nurses in Masih Daneshvari Hospital for their sincere cooperation in conducting this project.

Informed Consent

Informed consent was obtained from all individual participants included in the study.

Authors' information

Somayeh Hassani[1], Farahnaz Mohammadi Shahboulagi [2]*, Mahshid Foroughan[2], Payam Tabarsi[3], Gholamreza Ghaedamini Harouni[4], Hamidreza Jamaati[1], Mohammad Varahram[5], Seyed Mohammad Seyedmehdi[1], Seyed Alireza Nadji[6]

1 Choronic Respiratory Disease Research Center, National Research Institute of Tuberculosis and Lung Diseases (NRITLD), Shahid Beheshti University of Medical Sciences, Tehran, Iran

2 Iranian Research Center on Aging, University of Social Welfare and Rehabilitation Sciences, Tehran, Iran

3 Clinical Tuberculosis and Epidemiology Research Center, National Research Institute of Tuberculosis and Lung Diseases (NRITLD), Shahid Beheshti University of Medical Sciences, Tehran, Iran

4 Social Welfare management Research Center, University of Social Welfare and Rehabilitation Sciences, Tehran, Iran

5 Mycobacteriology Research Center, National Research Institute of Tuberculosis and Lung Diseases (NRITLD), Shahid Beheshti University of Medical Sciences, Tehran, Iran

6 Virology Research Center, National Research Institute of Tuberculosis and Lung Diseases (NRITLD), Shahid Beheshti University of Medical Sciences, Tehran, Iran

*Corresponding author: Farahnaz Mohammadi Shahboulagi