Correspondence

DOI: 10.5582/bst.2023.01243

Call for special attention to the caregiver burden of patients with drug-resistant tuberculosis in low- and middle-income countries

Shuqi Wu[1,§], Hailin Zhang[1,§], Yi Wang[1], Jin Wang[1], Peize Zhang[1], Tetsuya Asakawa[2,*], Yi Lin[1,*]

[1] Department of Pulmonary Medicine and Tuberculosis, National Clinical Research Center for Infectious Diseases, the Third People's Hospital of Shenzhen, Shenzhen, Guangdong, China;
[2] Institute of Neurology, National Clinical Research Center for Infectious Diseases, the Third People's Hospital of Shenzhen, Shenzhen, Guangdong, China.

SUMMARY The tuberculosis (TB)-related caregiver burden (CB), and particularly the multidrug and extensively drug-resistant tuberculosis (M/XDR-TB)-related CB, is not rare in caregivers caring for TB patients, especially when a family member is the caregiver. However, the existing studies on this topic are insufficient. This study briefly summarized the risk factors for the imposition of a TB-related CB and reasons why caregivers for patients with M/XDR-TB are more susceptible to a CB. We propose that special measures should be implemented to alleviate the TB-related CB based on our clinical experience and insights from China. This may improve the situation of caregivers for TB patients and ultimately improve the quality of life of TB patients.

Keywords tuberculosis, caregiver burden, multidrug and extensively drug-resistant tuberculosis, caregiver, quality of life

For a long time, tuberculosis (TB) has been regarded as a global public concern, particularly in low- and middle-income countries. Drug-resistant TB (DR-TB) is highlighted because most cases of DR-TB are refractory and often have a poor clinical outcome. Nonetheless, DR-TB has never been rigorously defined thus far. According to a report from the World Health Organization (WHO) (*1*), such cases are conventionally classified into multidrug-resistant TB (MDR-TB) and extensively drug-resistant TB (XDR-TB). They are sometimes grouped together as multidrug and extensively drug-resistant tuberculosis (M/XDR-TB). MDR-TB is a TB infection that is resistant to the most effective anti-TB drugs (such as isoniazid and rifampicin), whereas XDR-TB is MDR-TB plus resistance to fluoroquinolone as well as at least one second-line injectable agent, such as amikacin, kanamycin and/or capreomycin (*1*). According to a later expert consultation issued by the WHO, the definition of XDR-TB was updated, and pre-XDR-TB was suggested. Briefly, pre-XDR-TB is MDR-TB plus resistance to fluoroquinolone, whereas XDR-TB is MDR-TB plus resistance to fluoroquinolone and at least one additional Group A drug (*2*). Here, we have used the conventional definition of M/XDR-TB. Cases of M/XDR-TB are clinically problematic (Figure 1). Patients often undergo long-term anti-TB treatment that does not have satisfactory efficacy; targeted organs deteriorate, TB is a persistent airborne illness, and there are severe adverse reactions to long-term repeated therapy. According to the WHO's 2022 Global Tuberculosis Report, the number of people newly diagnosed with TB totaled approximately 6.4 million worldwide, 450,000 of whom were rifampicin-resistant TB (RR-TB). Among the patients with RR-TB and MDR-TB, only 1/3 underwent regular treatment during the COVID-19 pandemic, resulting in up to 1.6 million people dying from TB (3). Among patients with MDR-TB undergoing regular treatment, the disease was satisfactory controlled in only 59% (3), and the remaining patients may develop XDR-TB. The refractory nature of M/XDR-TB and the long duration of illness may impose a substantial burden on patients, their family, medical insurance, and needless to say, their caregivers.

For those patients with severe illness, caregivers usually have to play a key role in maintaining the patients' activities of daily living (ADL), such as making meals, performing household chores, running errands, and even assisting them financially (*4*). The psychological, physical, and financial burden on caregivers, referred to as the "caregiver burden (CB)", has garnered a great deal of attention in the last decade. The CB is a multidimensional response to perceived

stress and negative assessments involving objective and subjective feelings (*5*). It is reportedly associated with the financial status, social role, and educational level of the caregivers, the severity of the patient's disease, and long-term care (*6-9*). Most of the previous studies on the CB mainly focused on non-communicable diseases such as cancer (*7*), stroke (*9*), and Alzheimer's disease (*6*). Few studies have investigated the CB of M/XDR-TB. However, the M/XDR-TB-related CB cannot be ignored since M/XDR-TB is communicable and often long in duration. China is the second leading country suffering from a high burden of M/XDR-TB. Here, we have briefly summarized our clinical experience and insights regarding the M/XDR-TB-related CB. This information could help to control and prevent the TB-related CB.

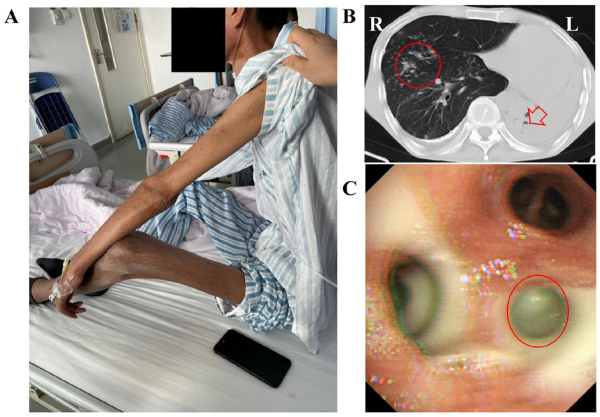

Figure 1. Images from a typical patient with M/XDR-TB. A 49-year-old man with a 10-year history of XDR-TB. Six months later, he died from respiratory failure. (A). The general appearance of the patient. He is suffering from malnutrition, dyscrasia, and chronic respiratory failure. He has almost lost the ability for self-care and he depends on a caregiver for his daily activities. (B). Chest CT findings suggest that the left lung is destroyed (red arrow) and that disseminated TB is present in the right lung (red ring). (C). Findings from tracheobronchoscopy. White purulent exudate and phlegm were visible, even in the bronchus (red circle). CT: computerized tomography; TB: tuberculosis; XDR-TB: extensively drug-resistant tuberculosis.

Risks factors for the imposition of a TB-related CB

In general, risk factors for a CB among caregivers mainly include the physical burden, financial burden, and psychological and social burden. Examples are concerns of being infected due to living with patients, anxiety, depression, social isolation, and a long duration of caring for the patient (Figure 2) (*10*). If these factors are not properly controlled, they may impose a CB on caregivers, influence the quality of care, and ultimately worsen the clinical outcome for TB patients.

i) Physical burden

Patients with M/XDR-TB are commonly suffering from deterioration of pulmonary function caused by airway stenosis, destruction of the pulmonary parenchyma, and other structural damage to the lungs (Figure 1). The decreased tolerance for activity due to a poor vital capacity always causes a marked reduction in ADL and quality of life (QOL) (*11*). Accordingly, patients have to depend more on caregivers for their daily lives. Stressed patients might make exorbitant demands while receiving care. Moreover, the stress in patients might be "transmitted" to caregivers and induce a stressful state in caregivers. Choi *et al*. reported that approximately 43–53% of caregivers developed clinically significant fatigue in the intensive care unit. They had worse scores in terms of a depression assessment, health risk behaviors, and sleep quality that were believed to be caused by the burden of patient care and long-term hospitalization (*12*). In addition, most caregivers for M/XDR-TB patients are family members who were never

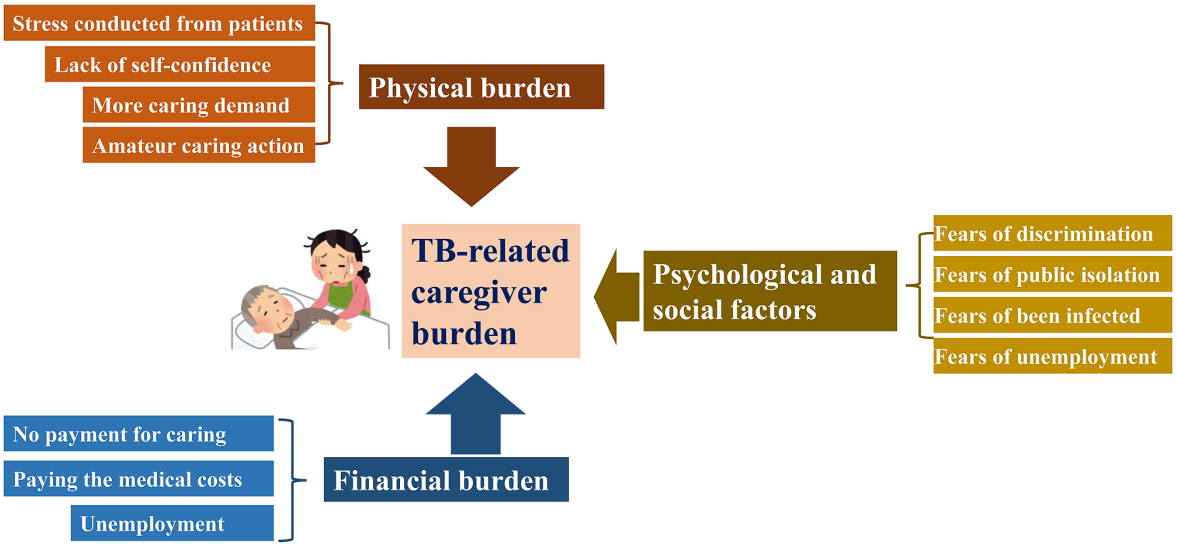

Figure 2. Risk factors for a TB-related caregiver burden.

trained in nursing, let alone nursing in a TB scenario, instead of professional caregivers. Mollica *et al*. reported that approximately 56.6% of caregivers had never been trained for all of the tasks they were performing (*13*). Such a "lack of training" may increase the physical burden (care by a layman). Moreover, lack of self-confidence might also contribute to the development of stress in these untrained caregivers (*13*).

ii) Financial burden

Costs of medical care might be a factor causing stress. According to a WHO report, 47% of TB patients and their families on average have to face TB-related catastrophic costs in 25 countries (*14*). Moreover, patients with M/XDR-TB have to face much-higher medical costs and develop stress more easily, which might be associated with longer hospitalization and more severe illness (*15*). A China-based study found that patients with M/XDR-TB had a 68.3% longer duration of therapy and an 87.0% higher hospitalization rate in comparison to patients with common TB (*16,17*). In addition, patients with M/XDR-TB are more susceptible to income loss and/or unemployment. In China, approximately 48% of TB patients had an average out-of-pocket spending of over 300 USD per month for their M/XDR-TB treatment (*18*). All of these factors worsen the financial situation of patients with M/XDR-TB, preventing caregivers, and particularly caregivers who are family members, from receiving full payment. Conversely, as a family member, the caregiver commonly has to pay the treatment costs together with the patient. In addition, unemployment due to caregiving is not rare. Pucciarelli *et al*. found that more than half (46%) of caregivers for stroke patients experienced at least one change in their employment due to caregiving (*19*). This heavy financial burden may cause stress both in patients and their caregivers.

iii) Psychological and social factors

Psychological problems in caregivers have been gradually recognized and garnered attention. Thana *et al*. found that anxiety and depression in caregivers were closely associated with lower caregiver self-esteem, a higher perceived health burden, and lack of family support (*20*). Hu *et al*. reported that of 117 caregivers, 43.9% had mild depression, 26.5% had moderate depression, and 27.4% had severe depression (*21*). The psychological problems originate from the following misgivings: *i*) Fears of discrimination and public isolation (*22*); *ii*) Worrying about unemployment; and iii) Worrying about been infected. Indeed, caregivers per se also have a higher risk of TB infection. The prevalence of a latent TB infection is reported to potentially increase with prolonged exposure, with an incremental increase in prevalence of 8.2% per 250 hours of exposure (*23*). Although prophylactic treatment has been proved to be effective in preventing caregivers from developing active TB, it cannot completely eliminate the risk of TB developing. This situation differs markedly from caring for patients with non-communicable diseases (cancer, Alzheimer's disease, diabetes, stroke, *etc*.). Hence, worrying about the risk of infection may further exacerbate the psychological burden in caregivers for TB patients.

Solutions: What can we do next?

Other than TB patients per se, the burden on caregivers for TB patients, and particularly the M/XDR-TB-related CB, cannot be ignored. Nevertheless, studies on this topic remain insufficient, so further information is not available. Other than scientific research, several measures should be considered to alleviate the TB-related CB. This may improve the situation of caregivers for TB patients and ultimately improve the QOL of TB patients.

i) In terms of the physical burden, professional training in nursing for family caregivers should be provided to improve the efficiency of care in order to reduce the mental and physical exhaustion and enhance the self-confidence of caregivers for TB patients.

ii) In terms of the financial burden, the government should pay attention to this population. Measures should be taken to alleviate the financial burden on TB patients and their caregivers, such as the establishment of a special insurance system to assist patients with refractory M/XDR-TB and their caregivers, reducing or exempting them from taxes, and providing a special allowance to them.

iii) In terms of the psychological and social factors, regular psychological care such as psychological counseling and therapy are highly recommended to ameliorate the depression and anxiety in patients and their caregivers.

The TB-related CB, and the refractory M/XDR-TB-related CB in particular, should not be ignored especially in low- and middle-income countries. On the basis of our clinical experience, we therefore propose that special attention should be paid to the CB of TB, and particularly the refractory M/XDR-TB-related CB.

Funding: This work was supported by the Shenzhen Science and Technological Foundation (grant nos. JSGG20220301090005007 and JSGG20220606141001003), the Third People's Hospital of Shenzhen Foundation (grant nos. G2021027 and G2022062), and the Shenzhen High-level Hospital Construction Fund (grant no.23274G1001).

Conflict of Interest: The authors have no conflicts of interest to disclose.

References

1. World Health Organization. Multidrug and extensively drug-resistant TB (M/XDR-TB): 2010 global report on surveillance and response. *https://www.who.int/publications/i/item/9789241599191* (accessed October 27, 2022).
2. World Health Organization. Meeting report of the WHO expert consultation on the definition of extensively drug-resistant tuberculosis, 27-29 October 2020. 2021. *https://www.who.int/publications/i/item/9789240018662* (accessed October 27, 2022).
3. World Health Organization. Global tuberculosis report 2022. *https://www.who.int/publications/i/item/9789240061729* (accessed October 27, 2022).
4. Leung DYP, Chan HYL, Chiu PKC, Lo RSK, Lee LLY. Source of Social Support and Caregiving Self-Efficacy on Caregiver Burden and Patient's Quality of Life: A Path Analysis on Patients with Palliative Care Needs and Their Caregivers. Int J Environ Res Public Health. 2020; 17:5457.
5. Bastawrous M. Caregiver burden – A critical discussion. Int J Nurs Stud. 2013; 50:431-441.
6. Pudelewicz A, Talarska D, Baczyk G. Burden of caregivers of patients with Alzheimer's disease. Scand J Caring Sci. 2019; 33:336-341.
7. Seo YJ, Park H. Factors influencing caregiver burden in families of hospitalised patients with lung cancer. J Clin Nurs. 2019; 28:1979-1989.
8. Kimura H, Nishio M, Kukihara H, Koga K, Inoue Y. The role of caregiver burden in the familial functioning, social support, and quality of family life of family caregivers of elders with dementia. J Rural Med. 2019; 14:156-164.
9. Freytes IM, Sullivan M, Schmitzberger M, LeLaurin J, Orozco T, Eliazar-Macke N, Uphold C. Types of stroke-related deficits and their impact on family caregiver's depressive symptoms, burden, and quality of life. Disabil Health J. 2021; 14:101019.
10. Adelman RD, Tmanova LL, Delgado D, Dion S, Lachs MS. Caregiver burden: A clinical review. JAMA. 2014; 311:1052-1060.
11. Singla R, Mallick M, Mrigpuri P, Singla N, Gupta A. Sequelae of pulmonary multidrug-resistant tuberculosis at the completion of treatment. Lung India. 2018; 35:4-8.
12. Choi J, Tate JA, Hoffman LA, Schulz R, Ren D, Donahoe MP, Given BA, Sherwood PR. Fatigue in family caregivers of adult intensive care unit survivors. J Pain Symptom Manage. 2014; 48:353-363.
13. Mollica MA, Litzelman K, Rowland JH, Kent EE. The role of medical/nursing skills training in caregiver confidence and burden: A CanCORS study. Cancer. 2017; 123:4481-4487.
14. World Health Organization. Tuberculosis patient cost surveys: A handbook. Geneva: WHO Press, Geneva, Switzerland; 2017. *https://www.paho.org/en/node/69033* (accessed October 27, 2022).
15. World Health Organization. Global tuberculosis report 2021. *https://www.who.int/publications/i/item/9789240037021* (accessed October 14, 2021).
16. Yang T, Chen T, Che Y, Chen Q, Bo D. Factors associated with catastrophic total costs due to tuberculosis under a designated hospital service model: A cross-sectional study in China. BMC Public Health. 2020; 20:1009.
17. Fang XH, Dan YL, Liu J, Jun L, Zhang ZP, Kan XH, Ma DC, Wu GC. Factors influencing completion of treatment among pulmonary tuberculosis patients. Patient Prefer Adherence. 2019; 13:491-496.
18. Zhang P, Xu G, Song Y, Tan J, Chen T, Deng G. Challenges faced by multidrug-resistant tuberculosis patients in three financially affluent Chinese cities. Risk Manag Healthc Policy. 2020; 13:2387-2394.
19. Pucciarelli G, Ausili D, Galbussera AA, Rebora P, Savini S, Simeone S, Alvaro R, Vellone E. Quality of life, anxiety, depression and burden among stroke caregivers: A longitudinal, observational multicentre study. J Adv Nurs. 2018; doi: 10.1111/jan.13695.
20. Thana K, Sikorskii A, Lehto R, Given C, Wyatt G. Burden and psychological symptoms among caregivers of patients with solid tumor cancers. Eur J Oncol Nurs. 2021; 52:101979.
21. Hu P, Yang Q, Kong L, Hu L, Zeng L. Relationship between the anxiety/depression and care burden of the major caregiver of stroke patients. Medicine (Baltimore). 2018; 97:e12638.
22. Amo-Adjei J. Individual, household and community level factors associated with keeping tuberculosis status secret in Ghana. BMC Public Health. 2016; 16:1196.
23. Reichler MR, Khan A, Yuan Y, Chen B, McAuley J, Mangura B, Sterling TR, Tuberculosis Epidemiologic Studies Consortium Task Order T. Duration of exposure among close contacts of patients with infectious tuberculosis and risk of latent tuberculosis infection. Clin Infect Dis. 2020; 71:1627-1634.

Received September 14, 2023; Revised October 4, 2023; Accepted October 10, 2023.

[§]These authors contributed equally to this work.
**Address correspondence to:*
Tetsuya Asakawa, Institute of Neurology, National Clinical Research Center for Infectious Diseases, the Third People's Hospital of Shenzhen, 29 Bulan Road, Shenzhen 518112, Guangdong, China.
E-mail: asakawat1971@gmail.com

Yi Lin, Department of Pulmonary Medicine and Tuberculosis, National Clinical Research Center for Infectious Diseases, the Third People's Hospital of Shenzhen, 29 Bulan Road, Shenzhen 518112, Guangdong, China.
E-mail: 514195263@qq.com

Released online in J-STAGE as advance publication October 14, 2023.