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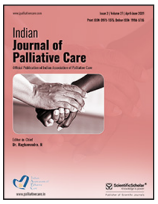

Review Article

Palliative Care in Drug Resistance Tuberculosis: An Overlooked Component in Management

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ABSTRACT

Palliative care should be an important component in the management of drug resistant tuberculosis (DRTB); however, it is not given much importance. Even in the current scenario, many patients and their caregivers consider multidrug-resistant and extensively drug-resistant tuberculosis (TB) as a terminal illness and considering it almost as a death sentence, this group of patients also require palliative care. There is a misconception about considering palliative care as a treatment component in the terminal stage of an illness where curative treatment has no role in improving the survival of the patient. However, the real meaning of palliative care is to relieve suffering in all stages of the disease and is not limited to end-of-life care only. Palliative care in DRTB aims to improve the quality of life, intractable symptoms and physical, psychosocial and spiritual suffering of patients as well as their caregivers. There is an imminent need to train all TB healthcare workers regarding basic palliative care and integrate palliative care into the TB healthcare system.

Keywords: Multidrug resistant tuberculosis, Extensive drug resistant tuberculosis, Palliative care, End-of-life care

INTRODUCTION

Tuberculosis (TB) is a chronic infectious disease caused by *Mycobacterium tuberculosis* and is one of the leading causes of mortality globally.[1] Palliative care for DRTB, though ignored, should be an important component in the management. Despite TB being a curable disease, a large number of patients develop drug-resistant TB (acquired or *de novo*) every year with a very low cure rate. Multidrug-resistant TB (MDR-TB) and extensively drug-resistant TB (XDR-TB) are still considered life-threatening by a large chunk of patients. Data reports that the treatment success rate is even <30% and 50% for MDR- and XDR-TB, respectively, with the conventional treatment regimens. More than 20% of patients die and almost 20% continue to suffer.[2,3] Added to it, human immunodeficiency virus coinfection with M/XDR-TB further complicates the situation and is a potential threat with challenging management. Despite the greater success and reduced mortality with a new bedaquiline-based regimen, and low treatment initiation due to poor access to new drugs in the private sector, a large proportion of patients with DR-TB are still considered to have a terminal illness and will require an integration of palliative care into the management.[4,5] Here, we are elaborating a comprehensive review on the need to emphasise the overlooked component in the management of DR-TB that is, palliative care. A list of articles has been reviewed and summarised in [Table 1].[6-14]

NEED FOR PALLIATIVE CARE IN DR-TB

The life-threatening nature of MDR- and XDR-TB along with the burden of disease management in terms of symptoms, treatment adverse effects, adherence, stigma and subsequent discrimination and social isolation clearly shows the need for care that addresses the physical, social and emotional aspects of various sufferings by patients. There is a misconception that palliative care is only beneficial in the terminal stage of an illness when the role of life-prolonging or curative treatment has terminated.[5] However, the true meaning of palliative care is that it should aim at relieving suffering in all stages of the disease and is not limited to end-of-life care only. Palliative care may be provided along with curative or life-sustaining remedies. The World Health Organization (WHO) defines palliative care as services that are designed to prevent and relieve suffering for patients and families facing life-threatening illnesses, through early management of pain and other physical, psychosocial and spiritual problems.[15]

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Table 1: Elaborative review of articles related to palliative care in TB reviewed.

Citing studies	Year	Title	Type of manuscript	Concluding message
Drenth *et al.*, South Africa[6]	2018	Palliative care in South Africa	Review Article	TB or M/XDR-TB patients can be provided with palliative care at home, in palliative TB care hospices, in palliative care facilities, in TB hospitals and/or general hospitals, or in primary healthcare facilities
Dheda and Migliori, Cape Town, South Africa[9]	2017	The epidemiology, pathogenesis, transmission, diagnosis and management of MDR, XDR and incurable TB	Review Article	In high-burden settings, the need to strike a balance between inpatient palliation and palliative care delivered in the home must be tailored to local conditions.
World Health Organization[10]	2008	Guidelines for the programmatic management of drug-resistant TB: An emergency update.	Guidelines	Discussed end-of-life supportive measures, addressing pain and symptom control, nutritional support, need for medical intervention after treatment cessation management of psychological morbidity, ensuring the appropriate place of care, preventive care and infection control.
Upshur *et al.*, Toronto[11]	2009	Apocalypse or redemption: Responding to XDR-TB	Perspectives	Embracing palliative care will contribute to ensuring that patients are 'permitted to live out their life with minimal suffering and loss of dignity'.
Arias-Casais *et al.*, Europe[7]	2019	EAPC Atlas of Palliative Care in Europe 2019	BOOK (Action Plan)	Preliminary data on the integration of palliative care into different fields are encouraging though inequalities between countries and sub-regions persist.
Harding *et al.*, London.[13]	2012	Palliative and end-of-life care in the global response to MDR TB	Review article	Good end-of-life care needs to be understood and practised as a standard by all attending clinicians in TB. Robust palliative and end-of-life research to identify better ways to care for patients with MDR-TB.
Morrison *et al.*, New York, USA.[14]	2008	Cost savings associated with US hospital palliative care consultation programs	Comparative study (Palliative care patients vs. Usual care patients)	Estimating costs for palliative care patients assuming that they did not receive palliative care resulted in projected costs that were not significantly different from usual care costs.
Hatziandreu *et al.*, England[12]	2008	The potential cost savings of greater use of home- and hospice-based end-of-life care in England.	Review Article	Palliative and end-of-life care provides cost savings and is fairly easy to deliver in high-income countries.
Gwyther *et al.*, Cape Town, South Africa.[13]	2009	Advancing palliative care as a human right	Review Article	Describes recent advocacy activities and explores practical strategies for the palliative care community to use within a human rights framework to advance palliative care development worldwide.
World Health Organization. Regional Office for Europe.[8]	2021	Review on palliative care with a focus on 18 high TB priority countries, 2020	Review Article	Discussed the minimal sets of standards on palliative care in drug-resistant TB care for discussion and development.
Lanken *et al.*[42]	2008	An Official American Thoracic Society Clinical Policy Statement: Palliative Care for Patients with Respiratory Diseases and Critical Illnesses	Official Statement	Palliative care is foremost centred on the patient and the patient's family. Identification of, and respect for, the preferences of patients and families, symptomatic or life-threatening diseases.

MDR: Multidrug-resistant tuberculosis XDR-TB: Extensively drug-resistant tuberculosis, TB: Tuberculosis

Around 500,000 deaths are attributed to TB globally and many suffer serious health suffering requiring palliative care.[16] In a cohort analysis of XDR-TB patients from South Africa, the majority were coinfected with HIV, nearly a quarter died before initiation of treatment for their disease, and almost half of them subsequently died in the 1st year of treatment.[17] The WHO end TB strategy of zero new infections, zero deaths and zero suffering for TB patients requires four basic elements to be followed at various healthcare levels.[18] Along with prevention, early diagnosis and treatment, there is an urgent need to focus on the last but not the least component which is palliation. The WHO

identified DRTB as one of the most common conditions in adults requiring palliative care.[19]

There is a strong link between DRTB and HIV coinfection. Data say that HIV infection has been detected in 70% of patients with TB among 30 high-burden countries with TB and HIV coinfection. According to the WHO Global Report 2021, India is red squared in all three global lists of high-burden countries for TB, HIV-associated TB and MDR/rifampicin resistant tuberculosis (RR-TB) in the period 2021–2025.[20] Although palliative care in lone HIV patients is growing at a good rate in the US, it needs to be focused in our country to provide special attention to HIV-TB coinfection patients when providing them with psychological assistance.

PALLIATIVE CARE SERVICES FOR DRTB PATIENTS

The availability of palliative care should not replace the intention to successfully treat all patients, which means that both palliative and curative treatment should be given side by side. In general, drug-resistant TB (DRTB) has a high burden of symptoms; hence, staff caring for these patients should have some familiarity with palliative care, and how it should be administered.[21,22] Palliative care aims to improve the quality of life of patients as well as their families and treatment of intractable symptoms and other physical, psychosocial and spiritual suffering. Breathlessness, pain stress, anxiety and financial constraints are some of the most burdensome palliative care problems experienced by patients with drug-resistant TB that require psychological advice and social support[23-36] [Table 2].

Palliative care can be generalised or specialised. The timely identification, and addressing, of adverse events occurring during the treatment course, is considered general palliative care for those receiving curative treatment while specialised palliative care is for more complex problems. General palliative care may be provided by any healthcare professional whereas specialised palliative care is given by palliative care professionals. Any patient whose treatment is discontinued either due to refusal of treatment or unlikely to respond should be eligible to receive specialised palliative care services. All TB professionals should be familiar with basic palliative care principles and symptom management and should use these skills while caring for their patients. Some TB patients die within several weeks of withdrawal from active treatment; however, many survive for months or years.[37] The 5-year survival rate for XDR-TB is 23%.[37] Especially in M/XDR-TB patients coinfected with HIV patients, the main aim of palliative care is to address suffering, various adverse drug reactions to anti-retroviral therapy (ART) and anti-tubercular treatment (ATT), education and counselling at the time of immune reconstitution inflammatory syndrome and hence preventing abrupt stoppage of treatment due to increasing signs/symptoms. Further, it aids in maximising these patients' function and quality of life.

This approach to palliative care has been emphasised in other countries such as South Africa, which has an integrated community-based home care model wherein TB or M/XDR-TB patients are provided with palliative care at home,[6] and Armenia has a national law on palliative care.[7] Similarly, Scotland has its palliative care guidelines mentioning a holistic approach to care enabling patients and families to set realistic goals and priorities during their terminal illness.[38] At present, we have palliative care policy documents of 18 high-priority countries for TB in the WHO European region.[7]

TB and M/XDR-TB is a contagious disease and, if not treated properly, threatens the people surrounding the infected person, including healthcare workers and patients' families.[39] Due to the risk of infection, TB patients are often abandoned by their families and it is difficult to employ and retain staff for the provision of palliative care.

There are three main categories of DRTB patients that require different palliative care services:

1. M/XDR-TB treatment failure patients going into the community. These patients often do not have any specific residence to live in due to the lost links with family, socioeconomic issues and denial by community residents due to concerns about the spread of infection. Patients ultimately end up residing in single rooms with other family members. Patients with advanced illness, and their caregivers, frequently experience profound financial and social strain.
2. The DRTB patients who are unamenable to treatment or approaching death beds have immediate requirements of community residential and palliative treatment care facilities, by adapting existing structures, if necessary, to prevent continuing transmission within hospitals and communities. Such facilities should be available not only for dying patients, ensuring that their end of life occurs in a safe and dignified setting but also for people for whom treatment has failed to provide them somewhere that they could reside on a long-term voluntary basis. These facilities would provide social, educational and recreational opportunities and would also be places where patients would receive good nutrition and care from support groups and multidisciplinary teams in an infection-controlled setting.
3. Treatment-responsive DRTB patients require generalised palliative care delivered by healthcare worker trained in palliative care. This includes management of adverse drug effects during treatment, counselling for adherence and addressing symptoms.

It is generally recommended that two specialised palliative care services (one home care team and one hospital team) should be available for every 1 lakh population.[7] Specialised palliative care services must be available in the community or may be provided within government-run TB facilities

Table 2: Summarising basic palliative care services required to be implemented in NTEP to reduce patient suffering.

Component	Symptoms	Drug	Administrative action
Physical suffering	Pain[23-25]	Mild-paracetamol, NSAIDs Moderate-codeine, tramadol Severe-morphine Neuropathic pain- amitriptyline,[26] pregabalin,[27] pyridoxine	All the NTEP Doctors, Nurses, Lab Technicians and DOTS providers should be trained in basic palliative care.
	Cough[28-30]	Dry – antihistaminic, chlorpheniramine, codeine, dextromethorphan, lidocaine inhalation Productive – steam inhalation, mucolytic	
	Haemoptysis[31]	A haemostatic agent, BAE	
	Dyspnoea	Oxygen[32] and morphine[33]	
	Anxiety/Fatigue[34]	Psychostimulants and antidepressants	
	Nausea[35]	Metoclopramide	
Psychological suffering	Delirium	Haloperidol and lorazepam	The programme should include social workers, psychologists, grief counsellors or trained and supervised lay counsellors
	Depression[34]	Sertraline, fluoxetine, mirtazapine, amitriptyline	
Social Suffering			Cash transfers for daily living, children's school tuition, transportation to healthcare facilities or funeral costs; food packages etc.
Spiritual suffering[36]			Counselling with counsellor

NSAIDs: Non-steroidal anti-inflammatory drugs, BAE: Bronchial artery embolisation

and programmes. A specialised service should have an interdisciplinary team and should meet the standards required of palliative care operations. Home care teams work in patients' homes or long-term care facilities, in collaboration with basic health teams or nursing home staff.

Many developing countries including India have palliative care services in juvenile stages, available at a few centres. It is estimated that nearly 5.4 million patients need palliative care every year; however, it is accessible to only 1% of them. The concept of palliative care was introduced in India in the mid-1980s and the Medical Council of India launched the MD Palliative medicine post-graduate programme in 2012. However, the number of institutions offering this course and the number of graduates each year is far below the current projected needs of the country. India currently ranks 59th out of 81 countries in the quality of death index.[40]

Ideally, palliative care for TB patients should be linked to local palliative care and hospice teams. Unfortunately, minimal access to and availability of palliative care in resource-limited countries inevitably contribute to the challenges in the organisation of palliative care for TB patients. Delivery of palliative care by existing staff in respiratory clinical service must be established with an effort to provide additional training and develop clear referral criteria to palliative care specialists for complex cases, which, at present, are available in a few countries worldwide.[41,42] In South Africa, for example, patients with TB or M/XDR-TB can be provided with palliative care at home, in palliative TB care hospices, in palliative care facilities, in TB hospitals and/or general hospitals or in primary healthcare facilities.[8]

Overall, there are plenty of challenges and suggestions that can be made to implement palliative care in DRTB patients. A few of them are listed below.

CHALLENGES

1. Palliative care is in a pre-mature state at present with very few specialised centres in our country
2. Training of all healthcare workers in the field of palliative care
3. Provision of a community facility for all DRTB patients who are in the end-stage of the disease
4. Financial support to the caregivers
5. Training regarding infection control practices
6. Easy availability of drugs used for palliative care like morphine at designated centres.

SUGGESTIONS TO BE CONSIDERED

1. Do not treat only TB patients but rather the whole family, address their financial issues and reduce their social sufferings
2. While assessing patients for palliative care, they should focus on the main physical symptoms along with emotional, psychological and spiritual aspects
3. All health workers should receive at least basic training in palliative care like we are providing basic life support training, to enable them to undertake a routine

assessment of patients with TB and to provide symptom control and support for their problems
4. Drugs for pain control and symptom control should be readily available throughout the health system
5. Primary palliative care curriculum for non-palliative care specialists and primary care clinicians should be enforced to train clinicians regarding managing pain and symptoms and discuss care goals with patients and their families
6. Palliative care teleconsultation and education can help rural providers deliver care
7. There should be a collaboration between palliative care providers and TB professionals
8. There should be universal access to palliative care, irrespective of diagnosis, disease stage or place of care
9. Patients should refer to a specialised palliative care team for breathlessness, fatigue, cachexia and end-of-life crises such as haemoptysis and acute respiratory failure and alleviate the anxiety of patients and their families
10. Infection control is a component of care that is essential, especially if patients are managed in their homes
11. A good death should be an articulated goal of care for all services
12. Unmet a need for research in this field to know the burden of symptoms, and social suffering and find out the best model of palliative care.

CONCLUSION

Palliative care for multidrug-resistant (M/XDR-TB) TB is an unmet need of the hour. The life-threatening nature of MDR- and XDR-TB is associated with higher mortality and has been associated with various physical, social and emotional sufferings by patients as well as their caregivers. TB, being a social disease, should not be treated as an individual disease; instead, treatment should be focused on reducing the suffering of the whole family. Palliative care should be implemented on an urgent basis at all healthcare and should be limited to end-of-life care management rather than at all stages of the disease.

Declaration of patient consent

Patient's consent was not required as there are no patients in this study.

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Conflicts of interest

There are no conflicts of interest.

Use of artificial intelligence (AI)-assisted technology for manuscript preparation

The authors confirm that there was no use of artificial intelligence (AI)-assisted technology for assisting in the writing or editing of the manuscript and no images were manipulated using AI.

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