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THE IMPACT ON THE QUALITY OF LIFE OF PATIENTS WITH DRUG-RESISTANT TUBERCULOSIS – BRIEF REVIEW

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Abstract

Drug-resistant tuberculosis (DR TB) is a major threat worldwide, despite the fact that the EndTB strategy involves early diagnosis and prompt treatment of all people of all ages with any form of sensitive or drug-resistant tubrculosis. Both forms of tuberculosis imply high morbidity and mortality, but drug-resistant TB accentuates these aspects due to problems arising from the nature of long and difficult to tolerate treatment, which can often lead to abandonment. The impact of tuberculosis is not limited only to clinical indicators, but also to the quality of life, directly reduced by the disease and treatment (weight loss, asthenia, medication side effects, distant sequelae, comorbidities), but also indirectly through the nature of the disease (social inclusion, job loss).

For this short review, the PubMed database was used, using key words such as quality of life, drug- resistant tuberculosis, physical, emotional impairment, treatment side effects. Patients with treatment-resistant tuberculosis face limitations in all areas of quality of life due to tuberculosis, both at initiation of treatment and at its completion. The impact of tuberculosis affects all areas of quality of life, both physically, emotionally, professionally and financially, both at initiation of treatment and post-treatment. The particular aspect of psychological impairment of DR-TB patients requires additional attention from the medical professionals involved in treating these patients and implementing additional support measures to help patients. The quality of life of patients with drug-resistant tuberculosis is an area that requires additional research, having an extremely important role in the success of antituberculosis treatment. Quality of life indicators could shape a more complete picture of TB's impact on patients' lives, both during and after treatment.

Keywords*: tuberculosis, multidrug resistance, quality of life.*

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Rezumat

Tuberculoza drog-rezistentă (TB DR) reprezintă o amenințare majoră la nivel mondial, în ciuda faptului că Strategia EndTB presupune diagnosticarea precoce și tratamentul prompt al tuturor persoanelor de toate vârstele, cu orice formă de tubrculoză sensibilă sau rezistentă la medicamentele antituberculoase. Ambele forme de tuberculoză presupun o morbiditate și mortalitate ridicate, însă tuberculoza drog-rezistentă accentuează aceste aspecte ca urmare a problemelor ce survin din natura tratamentului îndelungat și dificil de tolerat, ce poate conduce adesea la abandon. Impactul tuberculozei nu se rezumă doar la indicatorii clinici, ci și la calitatea vieții, redusă în mod direct de boală și tratament (pierderea în greutate, astenia, efectele secundare ale medicației, sechele la distanță, comorbidități), dar și indirect prin natura bolii (incluziune socială, pierdea locului de muncă).

Pentru acest scurt review a fost utilizată baza de date PubMed, folosind cuvinte cheie precum calitatea vieții, tuberculoză drog-rezistentă, afectare fizică, emoțională, efecte secundare tratament. Pacienții cu tuberculoză rezistentă la tratament se confruntă cu limitări în toate domeniile calității vieții din cauza tuberculozei, atât la inițierea tratamentului, cât și la finalizarea acestuia. Impactul tuberculozei afectează toate domeniile calității vieții, atât din punct de vedere fizic, cât și emoțional, profesional și financiar, atât la inițierea tratamentului cât și post-tratament. Aspectul particular al afectării psihologice a pacienților cu TB-DR necesită atenție suplimentară din partea cadrelor medicale implicate în tratarea acestor pacienți și implementarea unor măsuri suplimentare de sprijin care să vină în ajutorul pacienților. Calitatea vieții pacienților cu tuberculoză drog rezistentă este un domeniu ce necesită cercetări suplimentare, având un rol extrem de important în reușita tratamentului antituberculos. Indicatorii calității vieții ar putea modela o imagine mai completă asupra impactului tuberculozei asupra vieții pacienților, atât în timpul tratamentului, cât și după acesta.

Cuvinte cheie*: tuberculoză, multidrog rezistentă, calitatea vieții.*

General Information

Tuberculosis (TB) is an infectious-contagious disease produced by *Mycobacterium tuberculosis* widespread globally, with mainly airborne transmission and chronic evolution, which untreated or incorrectly treated can have a significant fatality. This condition mainly affects the adult population in the most productive years of life, causing both directly and indirectly significant social consequences[1].

Also, substantial financial resources are consumed to combat it. According to data reported by WHO[2], $13 billion is needed annually for TB prevention, diagnosis and treatment in order to reach the global goal agreed by the UN in 2018. Although it is a preventable and curable disease, tuberculosis is currently the cause of 1.3 million deaths annually, being the most common cause of death caused by a single causative pathogen.

Drug-resistant tuberculosis (DR TB) is a major threat worldwide, despite the fact that the EndTB strategy[1] involves early diagnosis and prompt treatment of all people of all ages with any form of sensitive or drug-resistant tuberculosis[1]. Both forms of tuberculosis imply high morbidity and mortality, but drug-resistant TB accentuates these aspects due to problems arising from the nature of long and difficult to tolerate treatment, which can often lead to abandonment.

The impact of tuberculosis is not limited only to clinical indicators, but also to the quality of life, directly reduced by the disease and treatment (weight loss, asthenia, side effects of medication, distant sequelae, comorbidities), but also indirectly by the nature of the disease (social inclusion, job loss).

According to data from the specialized literature, multiple studies have highlighted the problem of decreasing the quality of life of patients with multidrug-resistant tuberculosis.

Patients with drug-resistant tuberculosis (DR TB) frequently have associated comorbidities and previous treatments, leading to additional social, family and financial challenges. DR TB treatment is long-lasting, more complex, frequently associated with significant adverse effects and less favorable outcomes. Consequently, it is reasonable to assume that components of the quality of life of patients diagnosed with DR TB are significantly compromised[3].

Despite the positive impact of DR TB treatment on physical health, much of the burden of TB is associated with deficiencies in quality of life[4], which is highly relevant given that TB is the number one cause of mortality from a single infectious disease worldwide. Social refusal, stigma and treatment side effects are examples of indicators of poor quality of life affecting patients' social and professional integration[5].

A study conducted in northern India by R. Sharma et al. (2014) showed that patients with multidrug-resistant tuberculosis have a lower quality of life compared to patients with sensitive tuberculosis undergoing treatment[5].

Compared to a study conducted by A.A. Roba et al (2018) in Ethiopia which found a similar reduction in quality of life among DR TB patients and patients with treatment-sensitive tuberculosis[6]. However, DR TB patients reported lower overall health scores and experienced a significant degree of stigma. In a retrospective study conducted in India by M. Das et al. (2014) on 61 patients diagnosed with drug- resistant tuberculosis and HIV, up to 16% initially experienced depression, but almost all showed a favorable course under tuberculosis treatment and psychological support[7]. A follow-up study conducted in Pakistan by N. Ahmad et al.

(2016) indicated a severe impairment of quality of life of DR TB patients in all areas prior to initiation of treatment[8]. After 12 months of treatment, there was minimal improvement, and at the end of treatment, although there was significant progress, scores remained below average, thus suggesting a significant impairment in quality of life[8].

Currently, the diagnosis and treatment of tuberculosis are based on the clinical and microbiological characteristics of this disease. However, tuberculosis is not only responsible for affecting physical health, but can influence to a large extent both the psychological, economic and social component, therefore, our attention must turn to the quality of life of patients[9]. Disease influences all areas of quality of life and adds substantially to patient morbidity, and these complex and multidimensional interactions pose challenges in accurately quantifying QOL deterioration[9].

Quality of life is a broad and complex multidimensional concept that encompasses physical, social, psychological, economic and spiritual realms[9]. It is therefore difficult to define and measure, but it can be described as individuals' perception of their position in life in a cultural context, as well as in terms of the value systems in which they live, and in relation to their goals, expectations, standards and concerns[9,10]. Thus, the areas of impairment of quality of life can be grouped as follows.

Affecting the physical domain

Physical functioning is defined by an individual's ability to carry out basic activities, as well as by the ability to function both at work and in society or within the family[9].

The physical effects secondary to tuberculosis are variable in nature and depend largely on the patient's state of health, associated comorbidities, as well as on the severity and duration of the disease. The most common general symptoms are fatigue, physical asthenia and weight loss[11]. Low performance has been shown to be a strong predictor of mortality[9]. In a meta-analysis conducted in 2023 by Temesgen Yihunie Akalu et al. aimed at quantifying the prevalence and types of physical sequelae associated with patients diagnosed with MDR-TB and XDR-TB, respiratory, auditory, musculoskeletal, neurological, renal, hepatic and visual sequelae were found to be common among patients with multidrug-resistant tuberculosis. However, there was a significant difference in the prevalence of sequelae between MDR-TB and XDR-TB patients[12].

Affecting the social domain

The social stigma associated with tuberculosis is one of the most important components of affecting the quality of life, both at family and community level[9,11]. In a study conducted in South Africa, 82% of patients diagnosed with tuberculosis reported stigma[13].

Similarly, literature data from southern India report that 51.2% of patients with drug-resistant tuberculosis felt stigmatized, and stigma was higher during hospitalization[14].

Tuberculosis is associated with a high degree of stigma due to the perceived risk of airborne transmission from patients to other susceptible community members[9]. In other cases, it may be related to the unfavourable association of tuberculosis with HIV infection or poor socio-economic status[9,11].

Among the most common problems reported by patients are loss of friends, disrespect among colleagues, and isolation at work[9]. The degree of stigma associated with the disease may be higher among the female sex, with both inability to marry and increased divorce rates frequently reported in developing countries[9]. In a review conducted by Melisane Regina Lima Ferreira et al. (2023) based on social protection as a right of people affected by tuberculosis, scientific evidence was systematized that includes social protection measures and strategies, including adequate nutrition, income insurance, housing, the right to free medical services, as well as extensive rights involving social assistance[15].

Thus, it was identified that ensuring such rights to patients with sensitive and drug-resistant tuberculosis contributed both to improving general health and to increasing the quality of life and adherence to treatment, thus reducing the cost of hospitalizations in case of tuberculosis[15].

Affecting the psychological domain

As evidenced by the study conducted by Laxmeshwar C. & Stewart A. G. (2019) one of the most affected areas is mental health, followed by social relations and the environment[16]. Job loss due to DR TB negatively affects the last two areas. Other factors involved included physical factors (damage largely due to adverse effects of treatment), psychological factors, social factors and environmental factors[16].

A wide and complex range of psychological reactions are associated with the diagnosis of tuberculosis. The diagnosis may come as a shock to the patient, being subsequently associated with denial of the diagnosis[9,11]. Common feelings include fear, isolation and stigma[11]. Prolonged hospitalization and isolation of patients can have important emotional and psychological ramifications[11]. Symptoms specific to depression such as mood disorders, namely feelings of sadness, hopelessness or outbursts of anger, irritability and frustration, fatigue and lack of energy, low sex drive, sleep disorders are common[9].

Cross-sectional data conducted by the World Health Survey on approximately 250.000 adults in low- and middle-income countries showed a higher prevalence of depression episodes in patients diagnosed with drug-resistant tuberculosis compared to patients diagnosed with sensitive tuberculosis[17]. Also, patients diagnosed with drug-resistant tuberculosis are more likely to develop symptoms of depression. Thus, a study conducted in Nigeria by B.A. Issa et al., identified using the PHQ (The Patient Health Questionnaire) as a screening method that 27.7% of patients diagnosed with tuberculosis suffer from depression[18]. These data are correlated with the study conducted

by K. Peltzer et al. on tuberculosis patients in South Africa, showing that 32.9% of them had a psychological condition and 8.3% received antidepressant treatment[19]. Also, factors such as old age, low educational attainment and low socio-economic level were independently associated with mental suffering[9].

Further more, a cross-sectional study conducted in Brazil by A.P. Dos Santos, T.K. Lazzari, D.R. Silva (2017) observed that 31.4% of patients hospitalized with tuberculosis suffered from depression, 38.4% had anxiety and 23.3% had low self-esteem[20]. Patients with depression or anxiety also had lower overall quality of life scores compared to patients who did not develop symptoms of depression. Also, the analysis conducted by F. Ambaw et al. (2018) in Ethiopia, supports the data previously presented, respectively showed that 53.9% of tuberculosis patients were classified as having probable depression at the beginning of treatment, and factors such as decreased quality of life, therapeutic dropout and mortality were significantly higher in this subgroup[21]. Similarly in southern India, the study conducted by K.K. Shyamala, R.S. Naveen, B. Khatri (2018) reported the occurrence of depression in 40.8% of tuberculosis patients who received antituberculosis therapy[22]. The majority of patients had mild or moderate depression, with a higher prevalence of lung involvement compared to extrapulmonary tuberculosis (80.4% vs. 19.6%)[22].

Research in western India by C. Laxmeshwar et al. (2019) has highlighted that the psychological and physical domains are most commonly affected among DR TB patients undergoing treatment, having a significant impact on social and environmental relationships[16]. Despite this, quality of life indicators were not as low as reported in other studies and were not influenced by drug resistance. Another study conducted in Yemen by A.A.S. Jaber, B. Ibrahim (2019) showed an improvement in quality of life at the end of DR TB treatment, but without additional post-treatment improvement. The duration of illness prior to diagnosis of drug-resistant tuberculosis played a crucial role in improving quality of life scores, especially in the physical and mental fields[23].

Sharma R et al (2014), subsequently Nafees Ahmad et al (2016) demonstrated the importance of affecting emotional health and its implications for TB treatment[5,24].

TB-DR is associated with an increased risk of developing psychological comorbidities, with symptoms of anxiety and depression being very common, according to the study by James Brown et al (2015)[25]. Moreover, long-term hospitalization, stigma, and difficulties in maintaining family life predispose people with DR-TB to social isolation[25].

As evidenced by a meta-analysis by Kefyalew Addis Alene et al. (2018), multidrug-resistant tuberculosis was associated with a high risk of developing mental disorders, social stressors and a decreased quality of life[26]. A generalized prevalence estimate showed that one in four DR-TB patients experienced depression (25%) and anxiety (24%), and one in ten DR-TB patients experienced a psychotic syndrome (10%). Stigma, discrimination, isolation and lack of social support are frequent indicators among patients with multidrug-resistant tuberculosis[26].

Despite the positive impact of DR-TB treatment on physical health, much of the burden of TB is associated with deficiencies in quality of life, which is highly relevant given that tuberculosis is the No. 1 cause of mortality from a single infectious disease worldwide[4].

Social refusal, stigma and treatment side effects are examples of indicators of poor quality of life affecting patients' social and professional integration[5].

This aspect of the psychological impairment of DR-TB patients requires additional attention from the medical professionals involved in treating these patients and implementing additional support measures to help patients. These aspects are supported by the meta-analysis conducted by Kefyalew Addis Alene et al. (2018) which finds the significant impact of drug-resistant tuberculosis among patients, the most common manifestations being depression, anxiety and psychosis[26].

In addition, social stressors such as stigma, discrimination, isolation and lack of social support, commonly found in DR-TB patients, are the main factors responsible for affecting the quality of life of these patients[26].

Affecting the financial sector

Patients with tuberculosis are predominantly in the economically active age group, which indirectly produces a significant economic burden[9]. Prolonged hospitalization, respectively the physical inability to perform normal activities are contributing factors to job loss, respectively to the decrease and even loss of income. A study conducted in Thailand observed that adult patients diagnosed with tuberculosis allocated more than 15% of their income to the diagnosis and treatment of tuberculosis[9]. Another study conducted in southern India reported that financial harm to patients could reach up to 40% of their own income, through medical costs of diagnosis and treatment in the private health sector[9].

Side effects of treatment

A limited number of expert studies have conducted longitudinal quality-of-life assessments in cohorts of adult patients undergoing tuberculostatic treatment, particularly in regions with a high prevalence of the disease. The most substantial improvement in quality of life appears to occur in the first 2-3 months after initiation of treatment[9]. In a study conducted in northern India, S.A. Dar et al. (2019) reported a significant improvement in the quality of life of patients at the end of the intensive phase of treatment, after which the quality improved considerably by the end of treatment[27]. Comparable results were reported in another study from northern India, conducted by M. Dhuria et al. in which all areas of quality of life except the social field showed improvement after three months of treatment and further improvements were observed at the completion of treatment[28].

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In a study conducted in Pakistan, S. Saleem et al. (2018) observed a significant increase in post- treatment quality of life scores[29]. Prior to this study, in 2015 in Iraq, J.A. Dujaili et al. showed that physical well-being, functional well-being increased significantly two months after initiation of treatment[30]. All areas of quality of life, except social, economic and spiritual well-being, showed improvement at the end of treatment, making a significant contribution to treatment adherence[9,30].

As evidenced by a study conducted in Yemen, by A.A. Jaber, A.H. Khan, S.A. Syed Sulaiman, N. Ahmad, M.S. Anaam (2016), both physical and mental scores improved at the end of the intensive treatment phase, with additional improvements observed at the completion of treatment[9]. In the same year, similar results are supported by the study conducted by S.M. Kisaka et al., thus showing significant improvement in the physical and mental domains at the end of the intensive treatment phase, demonstrating an upward improvement by the end of treatment[31].

In contrast, another study conducted by M. Bauer, S. Ahmed, A. Benedetti, C. Greenaway, M. Lalli, A. Leavens, et al. in 2015 in Canadian patients showed that while psychological and emotional domain scores showed improvement over the course of treatment, the physical component score improved slightly over the 2-4 month treatment period, only to show a further decline thereafter[32]. On the other hand, adverse effects of tuberculostatic treatment can sometimes paradoxically worsen patients' quality of life. For example, gastrointestinal disorders, visual impairment or peripheral neuropathy may impede physical functioning[9,11]. A Canadian study, conducted by Guo N., F. Marra, et al. in 2010, reported that major adverse reactions were associated with significant reductions in several mental and physical subscales of quality of life[4]. This study also showed that patients with low quality of life scores before treatment were more likely to experience adverse drug reactions[4].

A cross-sectional study conducted in Namibia by E.L. Sagwa et al. (2016) aimed to correlate the link between adverse effects of treatment and impaired quality of life until completion of treatment[33]. Assessments of quality of life domains were moderately low, but showed no direct correlation with adverse reactions to treatment, which were mostly mild. By comparison, the study conducted by T. Sineke et al. (2019) from South Africa, showed a more significant impairment of the quality of life of patients with multidrug-resistant tuberculosiswho reported adverse reactions to treatment, especially during the intensive phase of treatment, targeting the psychological and general well-being fields[34]. However, in both studies, most

adverse events occurred before quality of life was quantified, and some persisted for different durations.

The long-term impact of tuberculosis treatment on quality of life is not yet clear. Limited studies demonstrate that in patients treated 12-24 months ago, quality of life was largely similar to that in the general population[9]. Other investigators report substantial impairment in quality of life, even several years after treatment ends[9]. Apart from the overall assessment, individual facets of quality of life can have a significant impact for patients. Another essential element that plays a significant role in maintaining and amplifying stimgatization is the particular way of administration of treatment, respectively under direct observation (DOT)[35]. This is a major barrier to successful completion of treatment. Patients diagnosed with tuberculosis must face repeated exposure to stigma according to strict treatment requirements. Thus, stigma can shape the extent of access to and adherence to treatment. A study conducted in India by Arupkumar Chakrabartty et al. (2019) showed that stigmatization of tuberculosis patients is an important predictor for their adherence to directly observed treatment. Strategies to reduce stigma should still be designed to improve adherence to treatment. The present study recommends further qualitative research to gain more information about the extent, form of stigma and how it influences treatment adherence[35].

Impact of associated comorbidities

A large number of patients diagnosed with drug-resistant tuberculosis have associated comorbidities, which can play a significant role in affecting the quality of life. More specifically, diabetes stands out as a common association[1]. However, most studies that focus on assessing quality of life under specific health conditions usually either exclude patients with coexisting diseases that could complicate quality of life assessment, or overlook these associated clinical conditions. As a result, there is a shortage of data in this area[9].

A study conducted in northern India by A.N. Siddiqui et al. (2017) showed that patients with tuberculosis and diabetes experienced a lower quality of life at the beginning of treatment compared to patients without diabetes[36]. In another study by H. Shahdadi et al, involving patients diagnosed with tuberculosis and diabetes in Iran, researchers observed a significant inverse relationship between quality of life and hemoglobin A1c levels. This suggests that inadequate control of blood glucose levels could significantly reduce quality of life among pulmonary tuberculosis patients[37].

The second common association is coexistence with HIV/AIDS infection. Approximately 9% of tuberculosis patients are co-infected with HIV, and the existence of this nefarious association seems to play a significant role in the recurrence of tuberculosis in developed countries[1]. A study conducted in Ethiopia by A. Deribew et al., showed that people co-infected with TB/HIV had a significantly reduced quality of life in all areas compared to TB patients without HIV[38]. Similarly, another Ethiopian studyconducted by A. Deribew et al. demonstrated significant impairment of quality of life in co-infected TB/HIV patients compared to HIV-positive persons without TB, and adherence to treatment showed a substantial improvement in quality of life, in all its fields[39]. These findings were echoed in 2019 in a cross-sectional study conducted in India by Jha D.K., Jha J., Jha A.K., B. Achappa, R. Holla[40]. In

contrast, a Brazilian study conducted by D.W. Dowdy et al., found that areas of quality of life were equally affected among patients undergoing treatment for HIV infection, active TB and TB/HIV co-infection, with the most significant impairment being that of the physical domain among co-infected individuals[41]. A study by W. Kittikraisak et al. (20012) focused on HIV co-infected tuberculosis patients treated in Thailand documented significant impairment in the areas of physical and mental health, of which physical symptoms improved considerably with initiation of treatment, but in mental health no improvement was observed, on the contrary, it worsened in about two-thirds of patients[42].

Another South African study conducted by T. Mthiyane et al. (2016) indicated an overall improvement in quality of life among co-infected TB/HIV patients during TB treatment[43]. This improvement seemed similar both among those who received simultaneous antiretrovial therapy and among those who did not. However, patients with CD4 lymphocyte counts below 200/µL had lower quality of life both before, during, and after treatment[43].

Conclusions

According to the International Standards of Tuberculosis Care, it is essential to establish a patient- centered therapeutic approach aimed at increasing adherence to treatment, improving quality of life and reducing suffering[1]. Unfortunately, the quality of care for this pathology remains suboptimal, especially in endemic countries[44]. Currently, significant delays persist in diagnosing tuberculosis, thus leading to the loss of more patients before treatment is initiated[44]. In addition, many patients perceive current treatment methods, under direct observation, as rigid and intrusive, often preferring unsupervised but less effective treatment. The non- medical aspects of TB are still inadequately addressed by most TB programmes, having a direct impact on patients' quality of life. These problems can negatively affect the pace of recovery and treatment outcomes, indirectly contributing to decreased quality of life[35].

A radical change is needed on the perception and approach of patients diagnosed with tuberculosis, namely changing the perspective centered on traditional markers of disease severity and response to treatment, towards capturing the general state of health, placing greater emphasis on the patient's perspective, rather than relying only on the clinician's point of view[9,15]. Tuberculosis control programmes should extend their scope beyond clinical and microbiological aspects, encompassing the socio-economic, cultural and psychological

dimensions influencing both disease and its treatment in evaluation and monitoring tools. As a result, quality of life indicators could be more frequently associated with routine indicators for assessing response to treatment and could be included in future guidelines. This integration could enable healthcare providers to identify specific aspects of mental and physical health that are negatively affected by the disease or its treatment[15].

Another objective is to raise awareness and initiate relevant social reforms. Understanding the origins of misconceptions about tuberculosis and addressing the lack of knowledge about the disease is essential. Effective communication, especially during diagnosis and initiation of treatment, is vital, and integrating psychological counselling into tuberculosis management is imperative[15]. Patients diagnosed with tuberculosis who have social support from family, friends and community tend to experience a better quality of life[15]. Therefore, there is a potential benefit in implementing psychological support programs at family or community level to improve quality of life. Culturally relevant psychosocial support interventions tailored to people undergoing TB treatment, especially during the intensive phase, can play a significant role in the rapid reintegration of patients into their communities.

More broadly, policymakers should advocate for both social protection and initiatives aimed at strengthening livelihoods, such as poverty reduction measures and ensuring food security[15]. In addition, a comprehensive set of interventions is needed to diminish stigma related to tuberculosis. Educational and support programs targeting healthcare providers, tuberculosis patients, and at-risk community members can be very effective[4]. Addressing stigma also involves implementing support groups, effective communication, community mobilisation and support for marginalised groups and women who disproportionately bear the stigma associated with a TB diagnosis. Establishing support groups or social networks for patients can facilitate their interaction as well as more effective management of various situations[4,15].

The current literature review shows the substantially negative impact of drug-resistant tuberculosis on patients' quality of life. A wide variety of tools have been used in assessing quality of life, making it difficult to fully understand the impact of the disease[4]. The current review suggests that assessing the quality of life of patients with drug-resistant tuberculosis is a growing field of research, lacking at present a TB-specific psychometric instrument, a critical step in the future being the design of an applicable, reliable and valid TB-specific assessment instrument.

References

1. Western Pacific regional framework to end TB: 2021-2030. World Health Organization. ISBN: 978-92-9-061970-3.

2. The End TB Strategy. World Health Organization; 2014. http://www.who.int/tb/strategy/end-tb/en/. Accessed March 14, 2019.

3. Cioran Nicoleta Valentina, Dumitrescu Andreea, Moisoiu Adriana, Popa George Cristian, Popa Marcela Cristina, Popescu Gilda Georgeta, Spînu Victor. National Guideline Management of Multi drug-resistant Tuberculosis 2023. Romanian Society of Pneumology- TB Section. Marius Nasta Institute of Pneumology. Ministery of Health.

4. Guo N, Marra F, Marra CA. Measuring health-related quality of life in tuberculosis: a systematic review. Health Qual Life Outcomes. 2009;7: 14.

5. Sharma R et al. acta Med Iran. 2014. Quality of life of multi drog resistant tuberculosis patient: a study of north India.

6. Aklilu Abrham Roba ,Tamirat Tesfaye Dasa,Fitsum Weldegebreal,Abyot Asfaw,Habtamu Mitiku,Zelalem Teklemariam,Mahantash Naganuri,Bahubali Jinnappa Geddugol,Frehiwot Mesfin,Hilina Befikadu,Eden Tesfaye.

Internal Medicine

General Reviews

Tuberculosis patients are physically challenged and socially isolated: A mixed methods case-control study of Health Related Quality of Life in Eastern Ethiopia. Published: October 15, 2018. https://doi.org/10.1371/journal.pone.0204697

7. Srinath Satyanarayana, Ada Kwan,Benjamin Daniels, Ramnath Subbaraman, Andrew McDowell, Sofi Bergkvist et al. Use of standardised patients to assess antibiotic dispensing for tuberculosis by pharmacies in urban India: a cross-sectional study. Published:August 24, 2016DOI:https://doi.org/10.1016/S1473-3099(16)30215-8.

8. Muhammad Abubakar,Nafees Ahmad,Abdul Ghafoor, Abdullah Latif,Izaz Ahmad,Muhammad Atif,Fahad Saleem,Shereen Khan,Amjad Khan Amjad,Amer Hayat Khan. Treatment Outcomes of Extensively Drug-Resistant Tuberculosis in Pakistan: A Countrywide Retrospective Record Review. Front. Pharmacol., 31 March 2021Sec. Drugs Outcomes Research and Policies. Volume 12 - 2021 | https://doi.org/10.3389/fphar.2021.640555

9. Ashutosh N. Aggarwal.Quality of life with tuberculosis.Journal of Clinical Tuberculosis and Other Mycobacterial Diseases,Volume 17,2019,100121,ISSN 2405-5794. https://doi.org/ 10.1016/j.jctube. 2019.100121.

10. The world health organization quality of life assessment (WHOQOL): position paper from the World Health Organization. Soc Sci Med, 41 (10) (1995), pp. 1403-1409.

11. N.N. Hansel, Wu A.W., Chang B., G.B. Diette.Quality of life in tuberculosis: patient and provider perspectives. Qual Life Res, 13 (3) (2004), pp. 639-652, 10.1023/B:QURE.0000021317.12945.

12. Temesgen Yihunie Akalu,Archie C.A. Clements, Haileab Fekadu Wolde,Kefyalew Addis Alene. Prevalence of long-term physical sequelae among patients treated with multi-drug and extensively drug-resistant tuberculosis: a systematic review and meta-analysis. eClinicalMedicine. 2023 Mar; 57: 101900. Published online 2023 Mar 10. doi: 10.1016/ j.eclinm. 2023.101900.PMCID: PMC10023854.PMID: 36942158.

13. A.L. Cremers, M.M. de Laat, N. Kapata, R. Gerrets, K. Klipstein-Grobusch, M.P. Grobusch. Assessing the consequences of stigma for tuberculosis patients in urban Zambia. PLoS One, 10 (3) (2015), Article e0119861, 10.1371/journal.pone.0119861.

14. R. Shivapujimath, A.P. Rao, A.R. Nilima, D.M. Shilpa. A cross-sectional study to assess the stigma associated with tuberculosis among tuberculosis patients in Udupi district, Karnataka. Indian J Tuberc, 64 (4) (2017), pp. 323-326, 10.1016/j.ijtb.2016.10.002

15. Ferreira, M.R.L., Bonfim, R.O., Bossonario, P.A. et al. Social protection as a right of people affected by tuberculosis: a scoping review and conceptual framework. Infect Dis Poverty 12, 103 (2023). https://doi.org/10.1186/s40249-023-01157-1

16. Laxmeshwar C et al. Int J Tuberc Lung dis. 2019. Beyond "cure" and "treatment success": quality of life of patients with multidrug-resistant tuberculosis. Int J Tuberc Lung Dis, 23 (1) (2019), pp. 73-81, 10.5588/ijtld.18.0149

17. A. Koyanagi, D. Vancampfort, A.F. Carvalho, J.E. DeVylder, J.M. Haro, D. Pizzol, et al. Depression comorbid with tuberculosis and its impact on health status: cross-sectional analysis of community-based data from 48 low- and middle-income countries. BMC Med, 15 (1) (2017), p. 209, 10.1186/s12916-017-0975-5

18. B.A. Issa, A.D. Yussuf, S.I. Kuranga. Depression comorbidity among patients with tuberculosis in a university teaching hospital outpatient clinic in Nigeria. Ment Health Fam Med, 6 (3) (2009), pp. 133-138

19. K. Peltzer, P. Naidoo, G. Matseke, J. Louw, G. McHunu, B. Tutshana. Prevalence of psychological distress and associated factors in tuberculosis patients in public primary care clinics in South Africa. BMC Psychiatry, 12 (2012), p. 89, 10.1186/1471-244x-12-89

20. A.P. Dos Santos, T.K. Lazzari, D.R. Silva. Health-Related quality of life, depression and anxiety in hospitalized patients with tuberculosis. Tuberc Respir Dis (Seoul), 80 (1) (2017), pp. 69-76, 10.4046/ trd.2017. 80.1.69

21. F. Ambaw, R. Mayston, C. Hanlon, G. Medhin, A. Alem. Untreated depression and tuberculosis treatment outcomes, quality of life and disability, Ethiopia. Bull World Health Organ, 96 (4) (2018), pp. 243-255, 10.2471/blt.17.192658

22. K.K. Shyamala, R.S. Naveen, B. Khatri. Depression: a neglected comorbidity in patients with tuberculosis. J Assoc Physicians India, 66 (12) (2018), pp. 18-21

23. Jaber, A.A.S., Ibrahim, B. Health-related quality of life of patients with multidrug-resistant tuberculosis in Yemen: prospective study. Health Qual Life Outcomes 17, 142 (2019). https://doi.org/10.1186/s12955-019-1211-0

24. Nafees Ahmad, Arshad Javaid, Syed Azhar Syed Sulaiman, Anila Basit, Afsar Khan Afridi, Ammar Ali, Saleh Jaber, Amer Hayat Khan. Published: July 28, 2016. Effects of Multidrug Resistant Tuberculosis Treatment on Patients' Health Related Quality of Life: Results from a Follow Up Study.

25. James Brown, Santino Capocci, Colette Smith, Steve Morris, Ibrahim Abubakar, Marc Lipman. International Journal of Infectious Diseases. 2015. Health status and quality of life in tuberculosis.

26. Kefyalew Addis Alene, Archie C A Clements, Emma S McBryde, Ernesto Jaramillo, Knut Lönnroth, Debebe Shaweno, Amelia Gulliver, Kerri Viney,Mental health disorders, social stressors, and health-related quality of life in patients with multidrug-resistant tuberculosis: A systematic review and meta-analysis. Journal of Infection,Volume 77, Issue 5,2018,Pages 357-367,ISSN 0163-4453. https://doi.org/10.1016/j.jinf.2018.07.007

27. S.A. Dar, N.N. Shah, Z.A. Wani, D. Nazir. A prospective study on quality of life in patients with pulmonary tuberculosis at a tertiary care hospital in Kashmir, Northern India. Indian J Tuberc, 66 (1) (2019), pp. 118-122, 10.1016/j.ijtb.2018.07.002

28. M. Dhuria, N. Sharma, S. Narender Pal, J. Ram Chander, R. Saha, I. Gopal Krishan. A study of the impact of tuberculosis on the quality of life and the effect after treatment with dots. Asia Pac J Public Health, 21 (3) (2009), pp. 312-320, 10.1177/1010539509336242

29. S. Saleem, A. Malik, A. Ghulam, J. Ahmed, H. Hussain. Health-related quality of life among pulmonary tuberculosis patients in Pakistan. Qual Life Res, 27 (12) (2018), pp. 3137-3143, 10.1007/s11136-018-1954-9

30. J.A. Dujaili, S.A. Sulaiman, M.A. Hassali, A. Awaisu, A.Q. Blebil, J.M. Bredle. Health-related quality of life as a predictor of tuberculosis treatment outcomes in iraq. Int J Infect Dis, 31 (2015), pp. 4-8, 10.1016/j.ijid.2014.12.004

31. S.M. Kisaka, E. Rutebemberwa, S. Kasasa, F. Ocen, J. Nankya-Mutyoba. Does health-related quality of life among adults with pulmonary tuberculosis improve across the treatment period? a hospital-based cross sectional study in Mbale Region, Eastern Uganda. BMC Res Notes, 9 (1) (2016), p. 467, 10.1186/s13104-016-2277-y

32. M. Bauer, S. Ahmed, A. Benedetti, C. Greenaway, M. Lalli, A. Leavens, et al. Health-related quality of life and tuberculosis: a longitudinal cohort study. Health Qual Life Outcomes, 13 (2015), p. 65, 10.1186/s12955-015-0250-4

33. Sagwa EL, Ruswa N, Mavhunga F, Rennie T, Leufkens HG, Mantel-Teeuwisse AK. Adverse events and patients' perceived health-related quality of life at the end of multidrug-resistant tuberculosis treatment in Namibia. Patient Prefer Adherence. 2016 Nov 23;10:2369-2377. doi: 10.2147/PPA.S116860. PMID: 27920503; PMCID: PMC5125758.

34. Sineke T, Evans D, Schnippel K, van Aswegen H, Berhanu R, Musakwa N, Lönnmark E, Long L, Rosen S. The impact of adverse events on health-related quality of life among patients receiving treatment for drug-resistant tuberculosis in Johannesburg, South Africa. Health Qual Life Outcomes. 2019 May 31;17(1):94. doi: 10.1186/s12955-019-1155-4. PMID: 31151398; PMCID: PMC6545023.

35. Arupkumar Chakrabartty, Pampa Basu, Kazi Monjur Ali, Debidas Ghosh. Tuberculosis related stigma attached to the adherence of Directly Observed Treatment Short Course (DOTS) in West Bengal, India,Indian Journal of Tuberculosis,Volume 66, Issue 2,2019,Pages 259-265,ISSN 0019-5707. https://doi.org/10.1016/j.ijtb.2019.03.005.

36. Ali Nasir Siddiqui, Khalid Umer Khayyam, Nahida Siddiqui, Rohit Sarin, Manju Sharma Diabetes prevalence and its impact on health-related quality of life in tuberculosis patients.. First published: 04 September 2017 https://doi.org/10.1111/tmi.12968

37. Shahdadi, Hosien, Salarzaee, Morteza, Balouchi, Abbas. 2017/09/01. Quality of Life of Diabetic Patients with Smear Positive PTB in Southeastern Iran: A cross-Sectional study in a poor region of Iran. DOI - 10.1016/j.ijtb.2017.08.035Indian Journal of Tuberculosis

38. Deribew A, Tesfaye M, Hailmichael Y, Negussu N, Daba S, Wogi A, Belachew T, Apers L, Colebunders R. Tuberculosis and HIV co-infection: its impact on quality of life. Health Qual Life Outcomes. 2009 Dec 29;7:105. doi: 10.1186/1477-7525-7-105. PMID: 20040090; PMCID: PMC2809048.

39. Deribew, A., Deribe, K., Reda, A.A. et al. Change in quality of life: a follow up study among patients with HIV infection with and without TB in Ethiopia. BMC Public Health 13, 408 (2013). https://doi.org/10.1186/1471-2458-13-408

40. Jha DK, Jha J, Jha AK, Achappa B, Holla R. Quality of life among HIV-tuberculosis co-infected patients. Perspect Clin Res. 2019 Jul-Sep;10(3):125-129. doi: 10.4103/picr.PICR_99_18. PMID: 31404188; PMCID:

PMC6647895.

41. Dowdy DW, Israel G, Vellozo V, Saraceni V, Cohn S, Cavalcante S, Chaisson RE, Golub JE, Durovni B. Quality of life among people treated for tuberculosis and human immunodeficiency virus in Rio de Janeiro, Brazil. Int J Tuberc Lung Dis. 2013 Mar;17(3):345-7. doi: 10.5588/ijtld.12.0123. Epub 2013 Jan 14. PMID: 23321341; PMCID: PMC3718256.

42. Kittikraisak W, Kingkaew P, Teerawattananon Y, Yothasamut J, Natesuwan S, Manosuthi W, Chongsuvivatwong V, Whitehead SJ. Health related quality of life among patients with tuberculosis and HIV in Thailand. PLoS One. 2012;7(1):e29775. doi: 10.1371/journal.pone.0029775. Epub 2012 Jan 11. PMID: 22253777; PMCID: PMC3256183.

43. Roos R, Myezwa H, van Aswegen H. Factors associated with physical function capacity in an urban cohort of people living with the human immunodeficiency virus in South Africa. S Afr J Physiother. 2019 Sep 9;75(1):1323. doi: 10.4102/sajp.v75i1.1323. PMID: 31616799; PMCID: PMC6780000.

44. Jacob Bigio, Angelina Sassi, Zelalem Temesgen, Madhukar Pai, Improving the quality of tuberculosis care in the post-pandemic world,Journal of Clinical Tuberculosis and Other Mycobacterial Diseases,Volume 23,2021,100212,ISSN 2405-5794. https://doi.org/10.1016/j.jctube.2021.100212.