Review Article

The Impact on The Quality-of-Life Dimensions Amongst Drug-Resistant TB Patients and TB-HIV Co-Infection – Brief Review

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Abstract

Drug-resistant tuberculosis (DR-TB) and Human immunodeficiency virus (HIV) remains a major global public health issue, despite the efforts of the EndTB strategy and global HIV strategies to end these epidemics. There is a dearth of literature on the impact of TB/HIV co-infection on quality of life (QoL). The impact of tuberculosis and TB/HIV co-infection is not limited only to clinical indicators, but also to the quality of life, directly reduced by the disease and treatment, but also indirectly through the nature of the disease. For this short review, the PubMed database was used, using key words such as quality of life, drug-resistant tuberculosis, TB/HIV co-infection, physical, emotional impairment, treatment side effects. Patients with drug-resistant tuberculosis and TB/HIV co-infection face limitations in all areas of quality of life, both at initiation of treatment and at its completion. The impact of these two infectious diseases affects all areas of quality of life, physically, emotionally, professionally and financially. Assessing the health-related quality of life (HQoL) in human immunodeficiency virus positive people and TB-HIV co infected people is of extreme importance in designing strategies and implementing interventional programs on treatment care and support to people living with HIV and AIDS.

Keywords: Tuberculosis, drug-resistance, TB-HIV co-infection, Quality of life

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 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.

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Human immunodeficiency virus (HIV) is an infection that compromises the body's immune system. The most severe phase of this infection is known as acquired immunodeficiency syndrome (AIDS). HIV specifically attacks white blood cells, thereby weakening the immune system and increasing susceptibility to illnesses such as tuberculosis, various infections, and certain cancers. Untreated HIV can progress to AIDS, often after many years. WHO now defines Advanced HIV Disease (AHD) as CD4 cell count less than 200cells/mm³ [3]. HIV remains a major global public health issue, having claimed 40.4 million (32.9–51.3 million) lives so far with ongoing transmission in all countries globally; with some countries reporting increasing trends in new infections when previously on the decline. There were an estimated 39.0 million (33.1–45.7 million) people living with HIV at the end of 2022, two thirds of whom (25.6 million) are in the WHO African Region. In 2022, 630 000 people died from HIV-related causes and 1.3 million people acquired HIV [3].

HIV is transmitted through the body fluids of an infected individual, including blood, breast milk, semen, and vaginal fluids. Treatment and prevention of HIV are possible with antiretroviral therapy (ART). While there is no cure for HIV infection, it has become a manageable chronic health condition with the right prevention, diagnosis, treatment, and care, including management of opportunistic infections. Effective HIV management enables individuals living with the virus to lead long and healthy lives [3]. TB is one of the leading causes of death among people living with HIV worldwide. Without treatment, HIV and TB can interact to significantly shorten lifespan. Having both HIV and TB constitutes an AIDS-defining condition. 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 [4].

the positive impact of DR TB treatment on physical health, much of the burden of TB is associated with deficiencies in quality of life [5], 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 [6].

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 [6]. 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 [7]. 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 [8]. 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 [9]. 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 [9].

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 [10]. 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 [10].

Quality of life is a broad and complex multidimensional concept that encompasses physical, social, psychological, economic and spiritual realms [10]. 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 [10,11]. 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 [10]. 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 [12].

Low performance has been shown to be a strong predictor of mortality [10]. 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 [13].

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 [10,12]. In a study conducted in South Africa, 82% of patients diagnosed with tuberculosis reported stigma [14]. Similarly, literature data from southern India report that 51.2% of patients with drug-resistant tuberculosis felt stigmatized, and stigma was higher during hospitalization [15]. Tuberculosis is associated with a high degree of stigma due to the perceived risk of airborne transmission from patients to other susceptible community members [10]. In other cases, it may be related to the unfavourable association of tuberculosis with HIV infection or poor socio-economic status [10,12].

Among the most common problems reported by patients are loss of friends, disrespect among colleagues, and isolation at work [10]. 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 [10]. 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 [16]. 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 [16].

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 [17]. 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 [17]. 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 [10,12]. Common feelings include fear, isolation and stigma [12]. Prolonged hospitalization and isolation of patients can have important emotional and psychological ramifications [12]. 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 [10].

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 [18]. 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 [19]. 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 [20]. Also, factors such as old age, low educational attainment and low socio-economic level were independently associated with mental suffering [10]. Further more, a cross-sectional study conducted in Brazil, observed that 31.4% of patients hospitalized with tuberculosis suffered from depression, 38.4% had anxiety and 23.3% had low self-esteem [21]. 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. 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 [22]. Similarly in southern India, the study conducted by K.K. Shyamala et al, reported the occurrence of depression in 40.8% of tuberculosis patients who received antituberculosis therapy [23]. 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%) [23].

Research in western India by C. Laxmeshwar et al. 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 [17]. 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 et al, showed an improvement in quality of life at the end of DR TB treatment, but without additional post-treatmentimprovement. 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 [24]. Sharma R et al and subsequently Nafees Ahmad et al, demonstrated the importance of affecting emotional health and its implications for TB treatment [6,25]. 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 realized by James Brown et al [26]. Moreover, long-term hospitalization, stigma, and difficulties in maintaining family life predispose people with DR-TB to social isolation [26].

As evidenced by a meta-analysis by Kefyalew Addis Alene et al., multidrug-resistant tuberculosis was associated with a high risk of developing mental disorders, social stressors and a decreased quality of life [27]. 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 [27]. 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 number one cause of mortality from a single infectious disease worldwide [5]. Social refusal, stigma and treatment side effects are examples of indicators of poor quality of life affecting patients' social and professional integration [6]. 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. which finds the significant impact of drug-resistant tuberculosis among patients, the most common manifestations being depression, anxiety and psychosis [27]. 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 [27].

Affecting the financial sector

Patients with tuberculosis are predominantly in the economically active age group, which indirectly produces a significant economic burden [10]. 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 [10]. 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 [10].

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 [10]. A study conducted in northern India, 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 [28]. 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 [29]. A study conducted in Pakistan, observed a significant increase in post- treatment quality of life scores [30]. Prior to this study, in Iraq, J.A. Dujaili et al. showed that physical well-being, functional well-being increased significantly two months after initiation of treatment [31]. 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 [10, 31].

As evidenced by a study conducted in Yemen, both physical and mental scores improved at the end of the intensive treatment phase, with additional improvements observed at the completion of treatment [10]. 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 [32]. In contrast to these studies, the Canadian study conducted by M. Bauer et al., 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 [33]. 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 [10,12]. A Canadian study, conducted by Guo N. et al., reported that major adverse reactions were associated

with significant reductions in several mental and physical subscales of quality of life [5]. This study also showed that patients with low quality of life scores before treatment were more likely to experience adverse drug reactions [5].

A cross-sectional study conducted in Namibia by E.L. Sagwa et al. aimed to correlate the link between adverse effects of treatment and impaired quality of life until completion of treatment [34]. 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. from South Africa, showed a more significant impairment of the quality of life of patients with multidrug-resistant tuberculosis who reported adverse reactions to treatment, especially during the intensive phase of treatment, targeting the psychological and general well-being fields [35]. 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 [10]. Other investigators report substantial impairment in quality of life, even several years after treatment ends [10]. 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) [36]. 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., 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 [36].

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 [10]. A study conducted in northern India by A.N. Siddiqui et al., showed that patients with tuberculosis and diabetes experienced a lower quality of life at the beginning of treatment compared to patients without diabetes [37]. 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 [38]. 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 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 [39]. Similar study 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 [40]. These findings were echoed in 2019 in a cross-sectional study conducted in India by Jha D.K. et al [41].

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 [42]. A study by W. Kittikraisak et al., 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 [43]. Another South African study conducted by T. Mthiyane et al. indicated an overall improvement in quality of life among co-infected TB/HIV patients during TB treatment [44]. 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 [44].

Globally, numerous quality of life (QOL) studies have been conducted among patients with HIV infection [46,47] and those with tuberculosis (TB) [48,49]. However, there is a lack of literature on the QOL of patients co-infected with TB and HIV [39]. TB and HIV co-infection are associated with special diagnostic and therapeutic challenges and constitute an immense burden on healthcare systems of heavily infected

countries [39]. Various studies have consistently shown that socio-demographic, clinical, psychological, and behavioral factors, immunological status, presence of symptoms, depression, stigma, and social support are the most frequently reported factors associated with health-related quality of life (HRQOL) among individuals with HIV mono-infection and those co-infected with TB/HIV [50]. In the following we will present the impact on the quality of life domains of patients co-infected with TB/HIV starting from a conceptual framework for factors associated with the health-related quality of life (HRQOL) of individuals with HIV mono-infection and TB/HIV co-infection derived from various studies [39,50-54].

An Ethiopian study realized by Amare Deribew et al. compared the QOL of persons with HIV infection with and without active TB by Amharic version of the WHOQOL-HIV instrument. In this study, patients co-infected with TB and HIV exhibited lower quality of life (QOL) across all domains

of the WHOQOL-HIV compared to individuals living with HIV alone. The presence of two stigmatizing diseases can negatively impact QOL by affecting physical, social, and mental well-being. Other studies have shown that HIV patients generally have a lower QOL compared to the general population [39,47] and that TB patients experience a lower QOL compared to their neighbors [39, 49]. Various studies have identified multiple factors that affect the quality of life (QOL) of patients. A multi-country study among HIV patients found that women, older age groups, and those with lower education levels had a lower QOL [46]. Research among African American HIV-positive participants indicated that stigma and the presence of HIV symptoms were linked to poor QOL [55]. Additionally, depression and lower income were associated with poorer physical, social, and environmental QOL domains [39]. Depression not only decreases QOL [56] but can also be a consequence of poor QOL. Perceived stigma
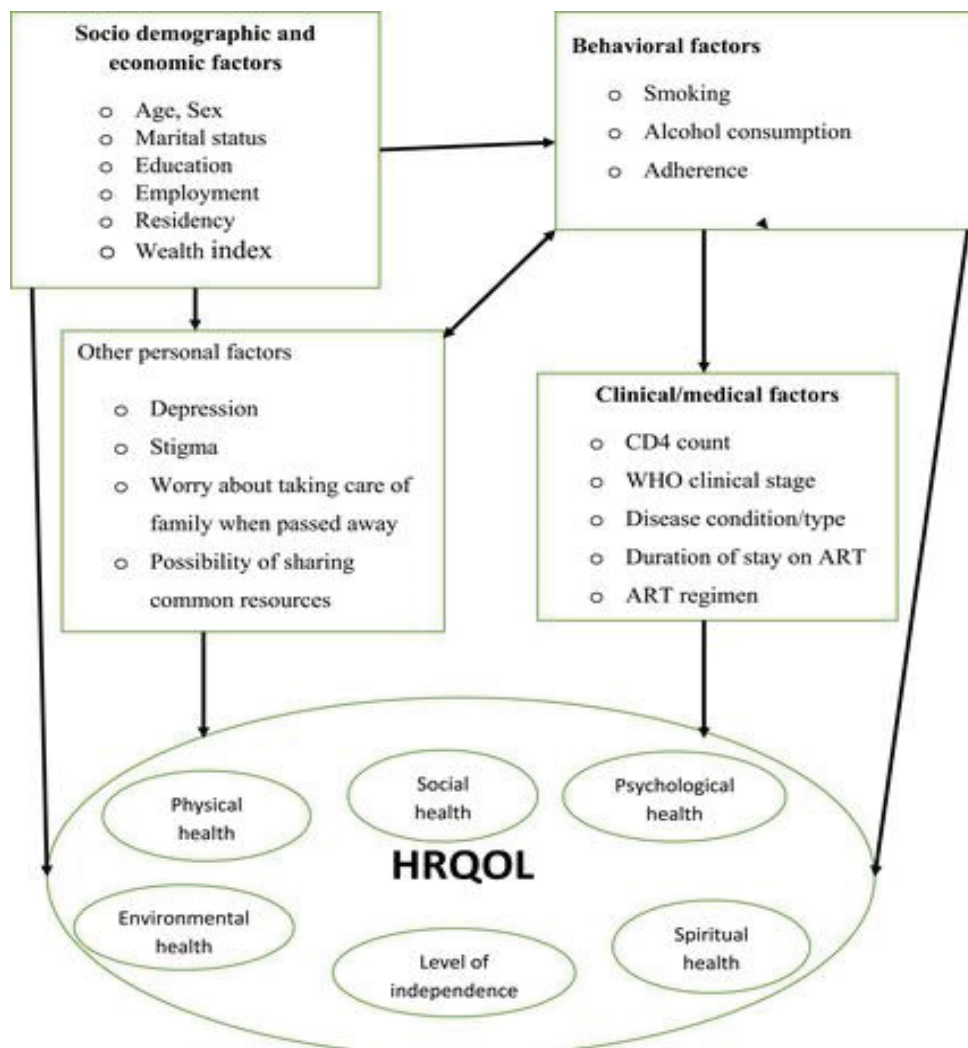

Figure 1: Conceptual framework for factors associated with the health-related quality of life (HRQOL) of individuals with HIV mono-infection and TB/HIV co-infection.

was linked to the psychological domain of QOL, with Yen et al. in Taiwan also reporting its impact on QOL [57].

A lack of social support, lower levels of education, and income have been associated with poor quality of life (QOL) among TB patients [49,58]. Similar studies indicate that income, depression, and lack of family support are predictors of poor QOL among those co-infected with TB and HIV. Participants without adequate income and family support may experience poor nutritional and immune status, which can further impact their QOL [39]. These findings were similar to results obtained in comparable studies carried out as HIV-infected patients with active TB exhibited poorer quality of life (QOL) across all domains compared to HIV-infected patients without TB. According to Beck's Depression Inventory, most co-infected patients experienced mild mood disturbances, whereas the majority of HIV-infected patients without TB were found to be normal [41]. A cross-sectional study conducted in Iran revealed that patients older than 35 years had significantly lower scores in overall quality of life (QOL), social relationships, and spirituality/religion/personal beliefs compared to younger participants [59].

Another study assessing the impact of HIV/AIDS on QOL among individuals in Chitradurga district, Karnataka, found that the highest mean scores were in the psychological domain. QOL was influenced by factors such as education, income, occupation, antiretroviral therapy (ART) status, duration of ART treatment, and clinical disease categories [60]. Similarly, a study in North India investigating the impact of HIV/AIDS on QOL highlighted associations with education, income, occupation, family support, and clinical disease categories among patients [41, 61]. Another correlation has been found between HIV-TB co-infected patients and their CD4 count, revealing lower CD4 counts compared to HIV-infected patients without TB [41]. These findings were similar to results obtained in comparable studies when comparing the quality of life (QOL) of HIV-infected patients with and without active TB, it was found that those with TB scored lower across all domains of the WHOQOL-HIV instrument (physical health, psychological health, level of independence, social relationships, environmental health, and spiritual health). Educational status showed a strong association with QOL among HIV-TB co-infected patients. For HIV patients without TB, being on antiretroviral therapy (ART) was identified as a determinant of QOL. Additionally, having family support emerged as a predictor of QOL among HIV patients [41].

In addition to its biological and physical challenges, HIV/AIDS is associated with numerous social consequences such as stigma and discrimination, which significantly impact quality of life (QoL) [40,62]. QoL is also influenced by various clinical and socio-demographic factors. A prospective cohort study conducted among 947 HIV-infected adults starting highly active antiretroviral therapy (ART) in Uganda between 2003 and 2004 found that overall QoL scores significantly improved from baseline, with most gains observed by the third month of therapy. Initially, several clinical, psychosocial, and socio-demographic factors predicted QoL at ART initiation, but financial dependence on others remained the sole predictor after accounting for time on ART [63]. Another cohort study involving men in the USA demonstrated that higher family support and baseline CD4 lymphocyte counts predicted improvements in physical and social functioning over time, whereas higher depressive symptoms at baseline were associated with diminished role functioning, emotional well-being, and general health perception [64]. Meanwhile, a prospective cohort study of 1,053 patients in France identified baseline CD4 lymphocyte count, time since HIV diagnosis, undetectable viral load, and fewer self-reported symptoms as predictors of QoL [65]. Other predictors of QoL include poor social support, depression, unemployment or financial dependence on others, older age and being female [40]. Many studies have documented significant improvements in QoL during ART [40,63,66].

A follow-up study conducted in Ethiopia among patients with HIV infection, both with and without TB, aimed to assess changes in quality of life (QoL) over a 6-month period and identify predictors of these changes. The study found that there was a statistically significant improvement in physical, psychological, social, environmental, and spiritual QoL at the 6-month follow-up compared to baseline for both groups of patients. The improvement in QoL across all dimensions was more pronounced among TB/HIV co-infected patients compared to HIV-infected patients without TB [40]. This study demonstrates that all dimensions of quality of life (QoL) significantly improved after 6 months of treatment, including physical, psychological, social relationships, environmental, spiritual, and level of dependence. However, the improvement in QoL was notably greater for TB/HIV co-infected patients. The substantial enhancement in the physical QoL of TB/HIV co-infected patients may be attributed to the relief of TB symptoms during anti-TB treatment [40]. Previous studies have indicated that the most significant gains in QoL among HIV-infected patients occur within the first three months of initiating antiretroviral therapy (ART) [40,67]. It has been demonstrated that lack of social support, absence of income, and poor adherence to ART negatively impact the physical dimension of QoL for all patients. These predictors of QoL change are closely associated with severe forms of Common Mental Disorders (CMD), which further exacerbate the physical QoL among TB/HIV co-infected individuals [40].

A comparative cross-sectional study indicated that age, sex, marital status, occupational status, educational status and residence of the study participants were significantly

associated with the HRQOL of patients. The HRQOL scores of the TB/HIV co-infected patients were low in all domains compared with those of HIV mono-infected patients [50]. Moreover, this finding is comparable with other studies conducted in Brazil, Nigeria and Ethiopia [50, 68, 69]. In most HRQOL domains, TB/HIV co-infected patients had higher depressive symptom scores compared to HIV mono-infected patients. Similarly, stigma scores were also higher in TB/HIV co-infected patients than in those with HIV alone [50]. The age of patients was significantly associated with the psychological domain of HRQOL among HIV mono-infected individuals, with older age correlating with better psychological health. This finding aligns with a study conducted in India, which suggests that older age is positively related to quality of life [50,70].

The sex of patients was significantly associated with HRQOL, with females exhibiting lower levels of independence compared to males in the mono-infected group. This finding is consistent with a study conducted in the United States [50,71]. Marital status was significantly associated with the HRQOL of patients, with married individuals exhibiting improved social relationships compared to unmarried participants. This finding aligns with a study conducted in South India on the psychosocial impact and QOL of people with HIV/AIDS, which also found that being married positively influenced the social relationships domain of QOL [50,72]. Occupational status was significantly associated with the HRQOL of patients. Studies revealed that being employed positively influenced the physical domain of HRQOL among HIV mono-infected patients [50]. Educational status was significantly associated with the physical, social, and environmental domains of HRQOL for both HIV mono-infected and TB/HIV co-infected patients. Additionally, it was significantly associated with the psychological and independence level domains of HRQOL for HIV mono-infected patients. This finding is consistent with studies conducted in Ethiopia and Nepal, which show that higher education levels are significantly associated with improved QOL in most domains [50,69]. The duration of ART treatment was found to be a significant determinant in the spiritual domain of HRQOL, with longer treatment duration positively associated with spiritual health among HIV mono-infected patients. This result aligns with findings from a study conducted in Addis Ababa, Ethiopia, on the HRQOL of HIV mono-infected individuals on combined ART [50,73]. Depressive symptoms were significantly associated with all HRQOL domains, except the level of independence domain, in HIV mono-infected patients. In HIV/TB co-infected patients, depressive symptoms were significantly associated with the social, environmental, and spiritual domains of HRQOL [50]. Stigma was significantly associated with the social, environmental, and spiritual domains of HRQOL in HIV mono-infected patients. For HIV/TB co-infected patients, stigma was significantly associated with the psychological and environmental domains of HRQOL. Participants who experienced stigma had lower HRQOL in these domains [50]. Wealth status was positively associated with all domains of HRQOL except the spiritual domain in HIV mono-infected patients. Similarly, it had a positive association with the physical and psychological domains of HRQOL in TB/HIV co-infected patients [50]. The CD4 count was positively related to the psychological domain of HRQOL in HIV mono-infected patients. The WHO clinical stage was significantly related to the spiritual domain of HRQOL in both HIV mono-infected and HIV/TB co-infected patients. Specifically, HIV mono-infected patients in lower stages (I and II) had better spiritual health compared to those in stage III, while in TB/HIV co-infected patients, stage III individuals had better spiritual health compared to stage IV participants [50].

A study conducted in Nigeria highlighted that stigma and discrimination are major obstacles to treatment adherence, significantly reducing patients' quality of life [74]. Similarly, a study in Northern Ethiopia found that high perceived stigma was strongly linked to poorer psychological quality of life [75]. These outcomes negatively affect patients' family and personal lives, including their sexual relationships. These findings are consistent with similar studies conducted in Ibadan, Nigeria [76]. The co-occurrence of HIV and TB, both stigmatizing diseases, synergistically impacts negatively on the quality of life (QOL) of patients [74]. Such individuals are more prone to depression and less likely to receive support from close partners or engage in sexual relationships. Recent studies indicate a high prevalence of depression among HIV patients, and depression diagnosis is a significant predictor of poor QOL [77]. The combination of depression and lack of family support has also been linked to poorer QOL among co-infected patients [74]. According to Akpa et al. [78], individuals from families affected by HIV/AIDS experience significantly poorer QOL compared to those from unaffected families.

A study conducted in Kathmandu, Nepal, assessed the quality of life and depression among people living with HIV/AIDS and TB-HIV co-infection [79]. The study found that TB-HIV co-infected patients had lower quality of life across all domains compared to HIV-infected patients without TB. Additionally, the prevalence of depression was higher among TB-HIV co-infected individuals compared to those with HIV/AIDS alone. The study identified several factors significantly associated with QoL domains, including CD4 count, educational status, occupation, family size, and depression. There was a notable association between CD4 counts and depression with QoL across all domains except physical health and level of independence [79]. Health-related quality

of life (HRQOL) among TB/HIV co-infected patients was lower across all dimensions compared to HIV mono-infected patients. In HIV mono-infected patients, factors significantly associated with all HRQOL domains included education, adherence to treatment, depression, and wealth status. Specifically, education and adherence were linked to the physical, social relationships, and environmental domains, while stigma affected the psychological and environmental domains. Wealth status influenced the level of independence, social relationships, environmental, and spiritual domains, and depression impacted the social relationships and environmental domains. Furthermore, TB/HIV co-infected study participants showed significantly lower CD4 counts compared to HIV mono-infected patients without TB.

Conclusion

According to the International Standards of Tuberculosis Care, establishing a patient-centered therapeutic approach is crucial for enhancing treatment adherence, improving quality of life, and reducing suffering. Many TB programs inadequately address the non-medical aspects of TB, which directly impact patients' quality of life. These challenges can hinder recovery and treatment outcomes, thereby indirectly contributing to a decreased quality of life. There is a pressing need for a radical shift in the perception and approach to patients diagnosed with tuberculosis (TB). This change involves moving away from focusing solely on traditional markers of disease severity and treatment response towards capturing the overall health status, with a greater emphasis on the patient's perspective rather than solely relying on the clinician's viewpoint.

TB control programs should broaden their scope beyond clinical and microbiological aspects to include socio-economic, cultural, and psychological dimensions that influence both the disease and its treatment in evaluation and monitoring tools. By integrating quality of life indicators more frequently into routine assessment metrics for treatment response, future guidelines can better reflect patient-centered outcomes. This approach will allow healthcare providers to identify specific mental and physical health aspects that are adversely affected by the disease or its treatment. Assessing the health-related quality of life (HRQoL) and depression among people living with human immunodeficiency virus (HIV) and those co-infected with tuberculosis (TB-HIV) is crucial for designing effective strategies and implementing intervention programs aimed at treatment, care, and support for individuals affected by HIV and AIDS.

TB/HIV co-infected patients exhibited poor quality of life (QOL) across all domains of the WHOQOL-HIV instrument. Depression, income, and family support emerged as significant factors strongly linked to QOL. It is imperative for TB control programs to develop strategies aimed at enhancing the QOL of TB/HIV patients. Interventions targeting depression and self-stigma are crucial to improving QOL outcomes. Additionally, counseling and education initiatives for families of patients should be implemented to maximize family support and thereby enhance QOL. The introduction of antiretroviral therapy (ART) and anti-TB treatment has been shown to enhance all dimensions of quality of life (QoL). Common mental disorders (CMD) significantly predict poorer QoL outcomes. Therefore, integrating mental health services into TB/HIV programs is essential. Healthcare providers should be trained to promptly identify and treat CMD to effectively improve QoL.

The current literature review shows the substantially negative impact of drug-resistant tuberculosis and the TB/HIV co-infection on patients' quality of life. Therefore, greater emphasis should be placed on the medical management of co-morbid patients to enhance their physical health. Additionally, there is a critical need to integrate mental health services and expand psychosocial support for these patients and their caregivers. This approach aims to reduce stigmatization and rejection, improve their self-worth, and foster a positive outlook on life. Such comprehensive care strategies can significantly enhance the overall well-being of individuals facing both HIV and TB infections.

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