









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 stigmatization 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 Chakrabarty 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].

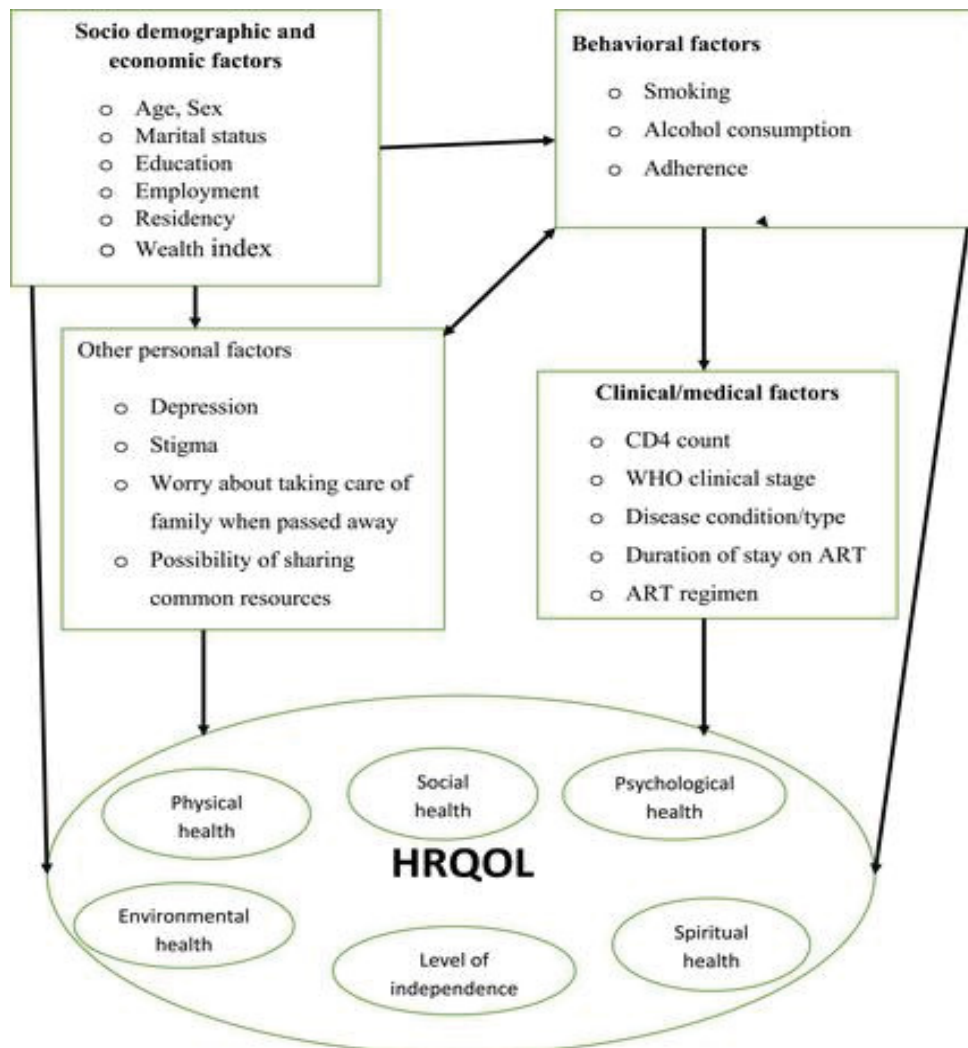
In contrast, a Brazilian study conducted by D.W. Dowdy et al., found that areas of quality of life were equally affected among patients undergoing treatment for HIV infection, active TB and TB/HIV co-infection, with the most significant impairment being that of the physical domain among co-infected individuals [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 antiretroviral therapy and among those who did not. However, patients with CD4 lymphocyte counts below 200/ $\mu$ L 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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