Drug-Resistant Tuberculosis in Rural Eastern Cape, South Africa: A Study of Patients' Characteristics in Selected Healthcare Facilities

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Keywords: Drug resistant tuberculosis; Comorbidities; Socioeconomic factors; Rural healthcare; Treatment outcomes; HIV co-infection and Mortality rates

Article

Drug-Resistant Tuberculosis in Rural Eastern Cape, South Africa: A Study of Patients' Characteristics in Selected Healthcare Facilities

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Abstract: This study investigated the characteristics and outcomes of drug-resistant tuberculosis patients in selected rural healthcare facilities in the Eastern Cape, South Africa. A retrospective review of clinical records from 456 patients, covering the period from January 2018 to December 2020, revealed that a statistically significant relationship between DR-TB types and age groups (Chi-square statistic: 30.74, p-value: 0.015). Younger adults (19-35 years) and middle-aged adults (36-50 years) are more frequently affected by RR-TB and MDR-TB, which are the most prevalent forms of DR-TB. Less common types, including Pre-XDR, XDR, and INH TB, were observed in smaller numbers. The study suggests that DR-TB imposes a heavy burden on the working-age population. Gender analysis shows that while the frequency of DR-TB differs between males and females, the percentage distribution of DR-TB types is relatively equal. Both genders are predominantly affected by RR-TB and MDR-TB, which together account for nearly 90% of cases. Pre-XDR, XDR, and INH-resistant TB are much less common, comprising only a small percentage of cases in both males and females. High-risk behaviors such as smoking and drinking are linked to a wider diversity of DR-TB types, while occupations like mining and prison work show higher rates of RR-TB and MDR-TB. In HIV-positive individuals, DR-TB is more common, but the distribution of DR-TB types between HIV-positive and negative groups shows no statistically significant difference. However, HIV-positive individuals have a 20% lower survival rate (65%) compared to HIV-negative patients (85%). Financial stability and comorbidities also significantly influence outcomes, with patients having stable income and fewer high-risk comorbidities experiencing better survival and treatment outcomes. The findings underscore the importance of addressing socioeconomic disparities and strengthening healthcare infrastructure to improve DR-TB treatment outcomes in rural Eastern Cape.

Keywords: drug resistant tuberculosis; comorbidities; socioeconomic factors; rural healthcare; treatment outcomes; HIV co-infection and mortality rates

1. Introduction

The global strategy to end the global tuberculosis (TB) epidemic by 2030 demands an imperative action plan by all countries which is a strategy that is particularly crucial given the significant burden of TB, which remains one of the leading causes of death from infectious diseases worldwide, with an estimated 1.4 million deaths annually attributed to the disease [1]. Despite much progress made by South Africa in lowering the disease burden of TB, human immunodeficiency virus (HIV), and sexually transmitted infections (STIs), these diseases persist as a major public health crisis, particularly in key and other priority populations. Hence, the 5th National Strategic Plan (NSP), 2023-2028 on TB and other communicable diseases, labeled "The People's NSP" was launched by the Deputy President of the Republic of South Africa on the 24th of March 2023 during the commemoration of World TB Day developed an integrated treatment for TB, HIV and sexually transmitted infections armed with the mission to eradicate TB as a public health threat by 2030 [2;3]. TB is a chronic communicable infectious disease caused by *Mycobacterium tuberculosis* [4;5], mostly

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affects the lungs including other parts of the body as well [6;7], and is a major cause of morbidity and fatalities (NSP 2023). The disease spreads through the air when infected people cough, sneeze, or spit [8]. South Africa continues to be one of the hubs of the highest-burdened countries in all three WHO-defined tuberculosis groupings, including TB, multi drug resistant TB (MDR-TB), and TB and HIV coinfection cases. Over 322, 000 new cases of TB are reported per year, out of which 4·4% are drug-resistant [9]. The number of MDR-TB cases keeps rising while the number of drug-susceptible TB cases appears to be declining and this has made TB control and eradication challenging [2;10;11].

TB is one of the leading infectious diseases afflicting global health and its drug-resistant form is burdensome to health systems particularly in poorly resourced settings [12]. Resistance to commonly used drugs includes Rifampicin mono-resistant TB (RMR-TB), Rifampicin-resistant TB (RR-TB), Rifampicin-susceptible, isoniazid-resistant TB (IR-TB), MDR-TB, pre-extensively drug-resistant TB (pre-XDR-TB) and extensively drug-resistant TB (XDR-TB) [13]. RMR-TB is TB resistant to rifampicin and susceptible to isoniazid. RR-TB is TB resistant to rifampicin, regardless of resistance to other drugs. IR-TB though susceptible to rifampicin, is resistant to isoniazid [13]. MDR-TB is TB that is resistant to two main drugs, rifampicin, and isoniazid, and is more complex and pricier to treat than drug-sensitive TB [14;15;16], pre-Extensively drug-resistant tuberculosis (pre-XDR-TB) on the other hand, is TB resistant to rifampicin and any fluoroquinolone while extensively drug-resistant tuberculosis (XDR-TB) whose outbreak was identified in KwaZulu-Natal province at a hospital in Tugela Ferry in 2005 with high [10;17]. is characterized as any resistance exhibited to rifampicin, a fluoroquinolone antibiotic, and any one of the oral medications, bedaquiline and linezolid [13]. Furthermore, between 2008 and 2009, Eastern Cape Province witnessed the emergence of totally drug-resistant TB strains [10].

Rural TB patients typically have lower levels of education than their urban counterparts. This can influence their comprehension of TB symptoms, treatment adherence, and health-seeking behaviors [18]. Rural TB patients have poorer treatment outcomes, with greater rates of loss to follow-up and mortality than urban patients and they face a much higher risk of death, with some studies indicating a 70% increase [19;18]. Socioeconomic inequalities influence when and where a patient seeks care for TB symptoms thereby contributing to delayed healthcare access for TB patients [20], impoverished people hardly seek healthcare or finish treatment, further giving rise to failure in TB control and the scarce healthcare facilities in rural areas also aggravate the delay [21;22]. According some studies, sociocultural beliefs and understanding of the causes and indicators of TB give rise to delays in the search for timely and proper testing and cure for TB [23;24]. Patient characteristics such as gender, age, socioeconomic status, and level of education have been observed to determine healthcare-seeking behavior among TB patients [25;26]. Population groups such as miners, inmate populations, and people living in close, overcrowded conditions are vulnerable and at risk of TB infection [27;28]. Vulnerable populations concurrently hold deprived socioeconomic positions, have elevated risks of contracting tuberculosis, and experience barricades to excellent and appropriate TB care. Many patients in vulnerable populations experience income insecurity, which hampers their ability to seek and adhere to TB treatment. Healthcare providers have noted that financial constraints, including transportation costs and food insecurity, are major barriers to treatment adherence. This is a result of patients often struggling to attend appointments or afford necessary food while undergoing treatment, even though TB medications are provided free of charge [29;30].

Prison inmates representative of the vulnerable population are exposed to difficult living conditions including extreme overcrowding, poor ventilation, poor sanitation and hygiene, poor nutrition, and substandard health care which give rise to the high prevalence and transmission of TB in prison settings [31;32]. People living with HIV are also at significant risk of TB infection when compared to HIV-negative people and as such people living with HIV are up to 20 times more likely to fall ill with TB [33]. TB has a more severe impact in resource-poor settings [34], and Eastern Cape Province is one of South Africa's poorest provinces [35]. The Eastern Cape is characterized by high levels of poverty, which significantly contribute to the prevalence of TB [36].

Poverty is closely linked to malnutrition, overcrowded living conditions, and limited access to healthcare, all of which increase the risk of TB transmission and complicate treatment efforts.

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Resource-poor settings often lack the infrastructure necessary for effective TB control, leading to higher rates of infection and mortality. Poverty is closely linked to malnutrition, overcrowded living conditions, and limited access to healthcare, all of which increase the risk of TB transmission and complicate treatment efforts. Resource-poor settings often lack the infrastructure necessary for effective TB control, leading to higher rates of infection and mortality [34;37].

Rural Eastern Cape is not only a poverty-stricken area but also saddled with high levels of TB treatment noncompliance, including drug-resistant TB patients [38]. The healthcare infrastructure in the Eastern Cape is often underfunded and overburdened, which affects the quality of care that patients receive. Limited staffing, shortages of medical supplies, and inadequate disease management strategies contribute to poor TB treatment outcomes. The lack of resources makes it difficult to implement effective TB control measures, further exacerbating the epidemic in this region [39;40].

This study determined the profile of DR-TB patients including their characteristics in selected rural health facilities of the EC province, South Africa

2. Materials and Methods

2.1. Study Design

The study involved a retrospective review of clinical records of DR-TB patients enrolled on treatment in six healthcare facilities between January 2018 and December 2020. Clinical records of DR-TB patients including socio-demographics, clinical, laboratory, and treatment-specific data, were documented. The HIV testing results and co-administration for comorbidity, and the presence of co-morbid conditions, and treatment outcomes were recorded.

2.2. Study Setting

The study population included patients diagnosed with DR-TB in six participating facilities, who met the inclusion criteria of a bacteriologically confirmed diagnosis of DR-TB, MDR-TB or XDR-TB. The researchers purposely and conveniently selected 5 DR-TB clinics and a referral hospital that offers DR-TB, MDR-TB and XDR-TB management services to these clinics.

2.3. Data Collection Methods

We conducted a retrospective review of patients clinic files with DRTB from healthcare facilities. Eligible patients had confirmed DRTB, HIV co-infection, comorbidities and a treatment outcome registered between 2018 and 2020. Socio-demographic and clinical characteristics and TB treatment outcomes were included in data collection.

2.4. Data Analysis Methods

Proportion (%) was calculated when data was categorical while mean or median (± standard deviation) was computed when data was continuous. Student's t-test was performed to assess differences between two means and ANOVA between groups. Either the Chi-square test with and without trend or Fischer's exact test was used to test the degree of association of categorical variables. Chi-Square test (for categorical comparisons) or ANOVA (for comparing group means) were applied to test for significance. ANOVA assumes that the data follows a normal distribution and has homogeneity of variance. If the initial tests (Chi-Square or ANOVA) show significant results, post-hoc pairwise comparison tests were used to identify which specific groups are significantly different from each other. Python version 3.8. and R version 4.1.1 software were used. A $p < 0.05$ was considered to be significant.

3. Results

There were 456 patients with a mean age of 37.5 years (SD = 14.9 years). The ages ranged from 1 year to 86 years, with the 25th percentile at 27.75 years, the median age at 36 years, and the 75th

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percentile at 47 years. This indicates that while the majority of patients are between 27.75 and 47 years old, the age distribution is moderately spread out, with a slight skew towards older ages.

Figure 1 above shows that there is a statistically significant difference in the distribution of DR-TB types across different age groups (Chi-square statistic (χ^2): 30.74, p-value: 0.015). The types of drug-resistant TB (DR-TB) are associated with age groups in a statistically significant way, indicating that certain age groups may be more or less likely to have specific types of DR-TB. The graph highlights that RR-TB and MDR-TB are the most prevalent forms of drug-resistant TB, with young (19-35 years old) and middle-aged adults (36-50 years old) being the most affected age groups. The smaller number of Pre-XDR, XDR, and INH-resistant cases suggests that while these forms of TB exist, they are less common. The age distribution shows a heavy burden of DR-TB on working-age adults, particularly those aged 19-35, indicating a significant impact on this population demographic.

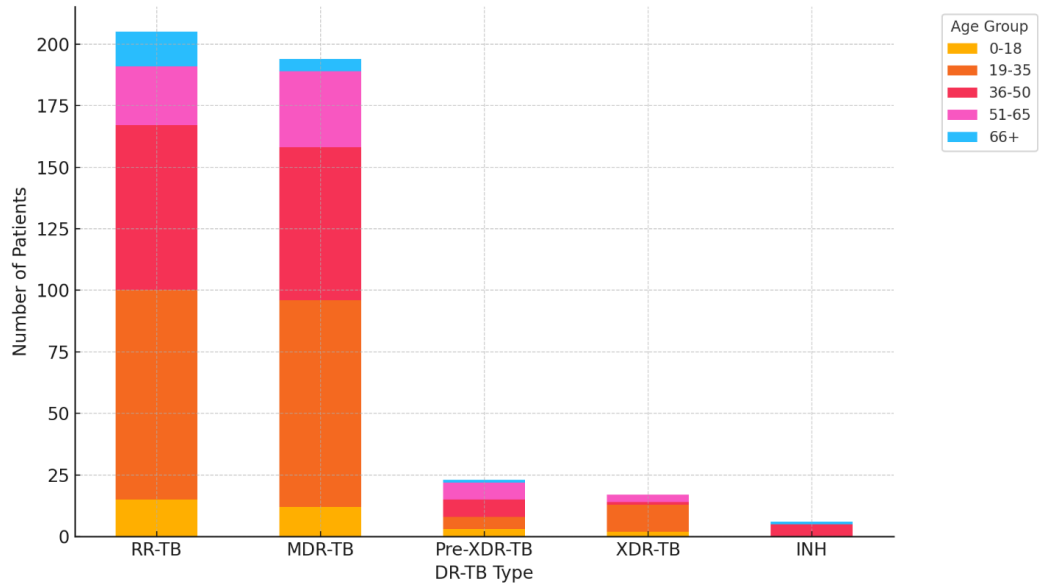

Figure 1. Distribution of DR-TB by age group.

Figure 2 below displays the distribution of different DR-TB types across genders, in terms of both frequency (left graph) and percentage (right graph). The gender difference is more visible in the frequency chart, but when adjusted for percentage, the gender gap is smaller. Both genders have roughly equal proportions for these types. RR-TB and MDR-TB dominate the DR-TB cases in both males and females, accounting for nearly 45% of cases each. Pre-XDR-TB accounts for around 10% of cases in both males and females, with a slight male dominance. XDR-TB and INH make up a very small proportion of the total cases for both genders. XDR-TB accounts for approximately 5-7% of cases, while INH is even smaller, around 2-3% for males and almost 0% for females.

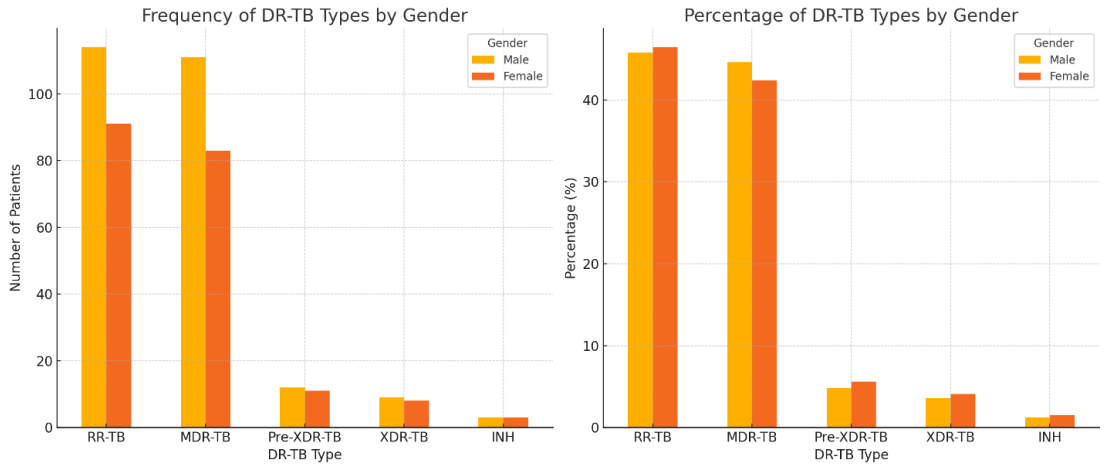

Figure 2. Frequency and percentage of DR-TB by gender.

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MDR and RR are the most common DR-TB types across all social history categories, reflecting broader trends. Patients with multiple high-risk behaviors, like smoking and drinking, tend to have a greater diversity of DR-TB types, indicating that these behaviors may increase disease severity or complexity (Figure 3).

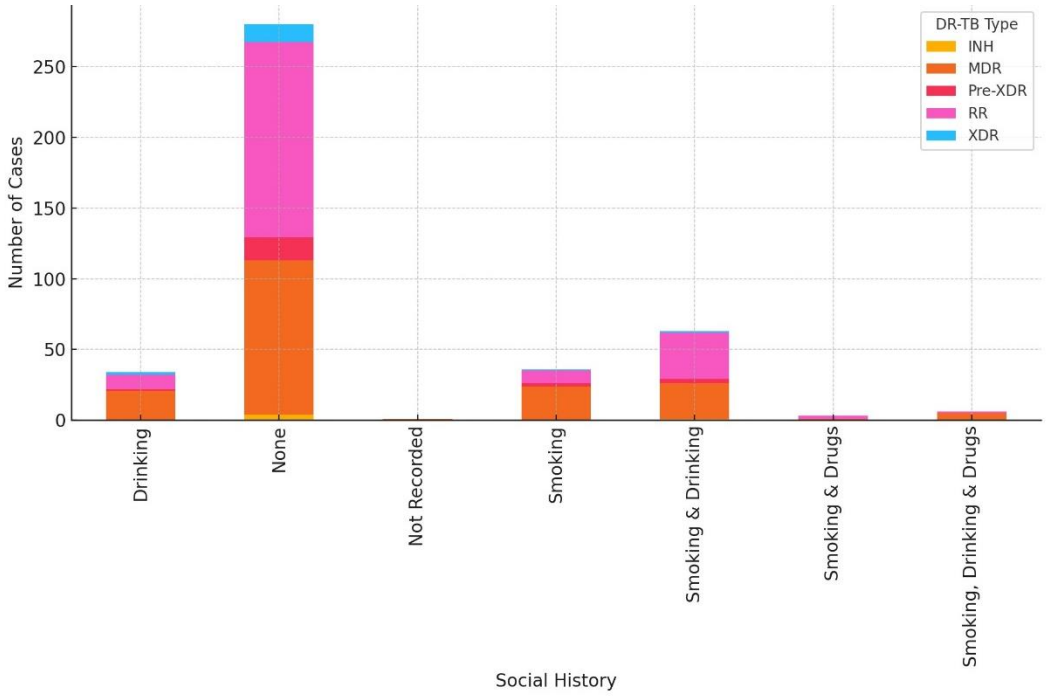

Figure 3. Distribution of different DR-TB types based on patients' social history.

MDR and RR are the most common DR-TB forms across all work history categories, with a higher prevalence observed in high-risk occupations like mining and prison work (Figure 4)

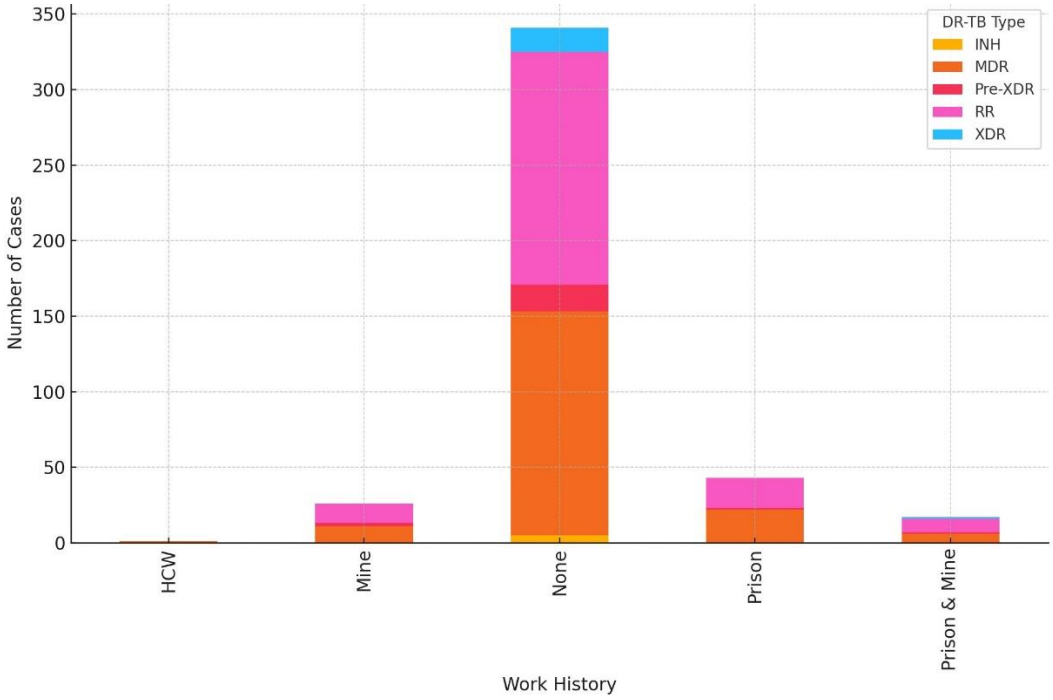

Figure 4. Comparison of DR-TB Type and Patient Work History.

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Figure 5 compares the proportions of different types of DR-TB across six healthcare facilities (HCFs). RR-TB, represented by the darkest purple color, is the most common type across all healthcare facilities. In several facilities, such as HCF 3, HCF 4, and HCF 5, RR-TB accounts for more than 50% of the cases, highlighting its prevalence. MDR-TB, represented by the blue color, shows variability across the facilities. HCF 2 and HCF 6 have a significant proportion of MDR-TB cases, whereas in HCF 4 and HCF 5, MDR-TB is less prevalent. The green color representing Pre-XDR TB is more visible in HCF 1, indicating a higher proportion of this type in that facility compared to others. XDR-TB (yellow) and INH-resistant TB (light green) are less common overall. XDR-TB is present in very small proportions in some facilities, such as HCF 1 and HCF 6, but is almost negligible in others.

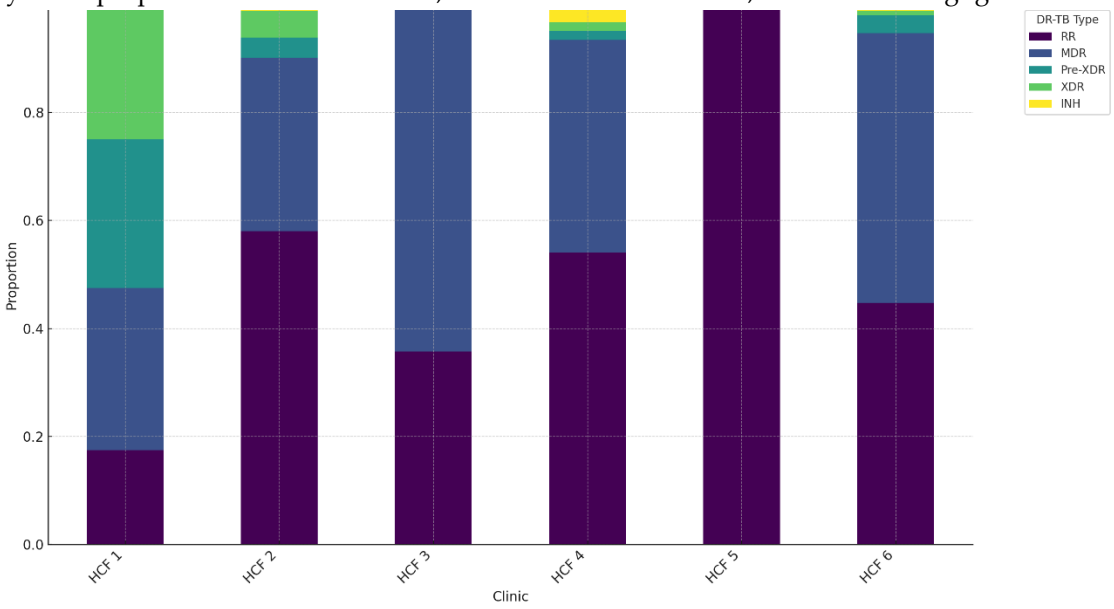

Figure 5. Proportions of DR-TB Types by Clinic.

Figure 6, indicates that DR-TB is more common in HIV-positive individuals compared to HIV-negative ones when using absolute count numbers. Additionally, among both HIV-positive and negative groups, the most prevalent forms of DR-TB are RR and MDR types. However, when comparing the proportions of different DR-TB cases between HIV-positive and HIV-negative groups, there is no statistically significant difference in the proportions of each DR-TB type between HIV-positive and HIV-negative individuals.

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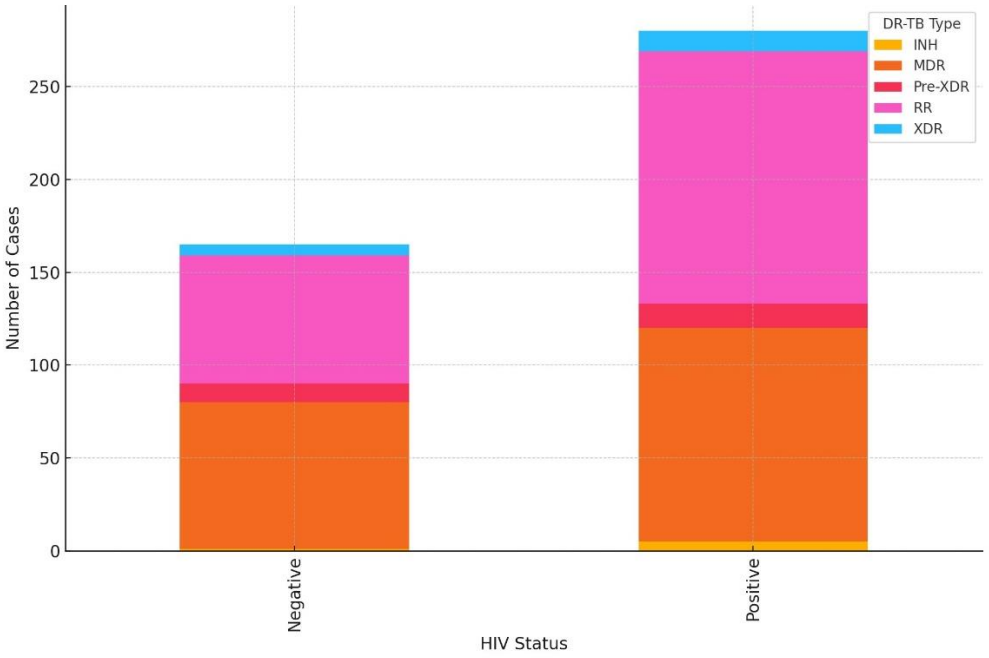

Figure 6. Distribution of DR-TB types within each HIV status.

The survival rate for HIV-positive TB patients is approximately 65%, indicating a significant impact of HIV on TB treatment outcomes. In contrast, HIV-negative TB patients have a higher survival rate of about 85%, suggesting that a greater proportion of HIV-negative individuals survive compared to those who are HIV-positive (Figure 7).

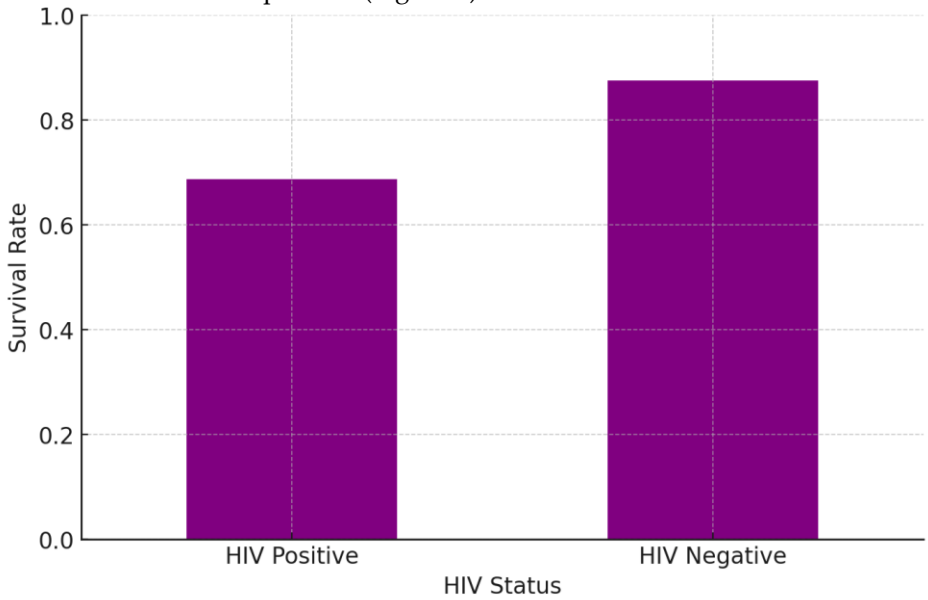

Figure 7. Survival Rates for TB and HIV Co-Infection.

Since time-to-event data was not available, we used the survival rates provided to compare the two groups (HIV-positive and HIV-negative). The difference in survival rates was 0.20 or 20% higher survival rate for HIV-negative individuals. This difference is likely clinically meaningful, especially in the context of DR-TB and HIV co-infection.

In the Figure 8 below, the majority of DR-TB cases are either RR-TB or MDR-TB, together accounting for approximately 85% of the total cases. Pre-XDR-TB, XDR-TB, and INH-resistant TB are less common, with each making up a smaller proportion of the cases. The data highlights the need

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for targeted treatment strategies, especially for the more prevalent RR-TB and MDR-TB types, which pose significant challenges in terms of management and control.

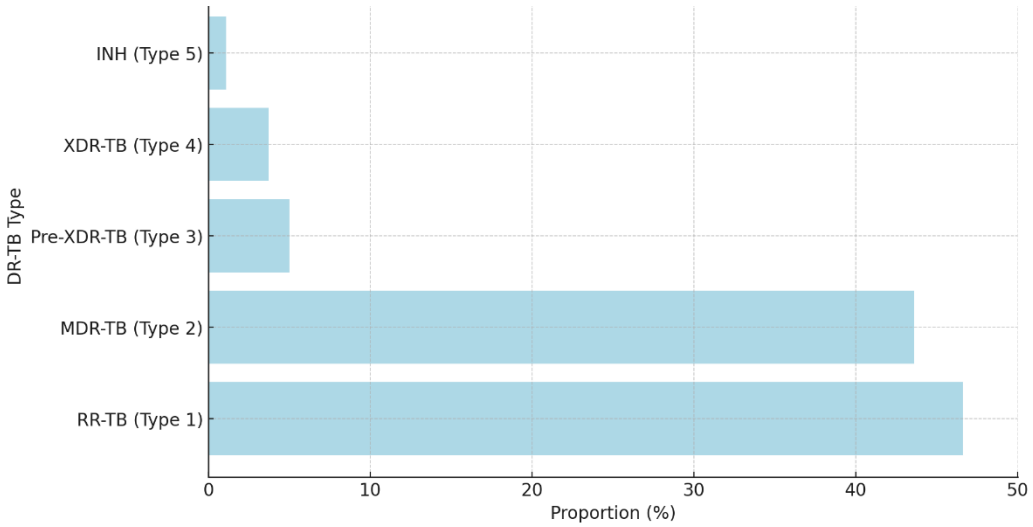

Figure 8. The proportions of DR-TB types in patients with comorbidities.

Patients with stable income (Salary or Wages) generally experience better treatment outcomes, including higher cure rates and fewer adverse outcomes. In contrast, those with no income or relying on social grants (DG) are more vulnerable, with a higher prevalence of adverse outcomes such as death and treatment failure, indicating that financial instability can negatively impact TB treatment success (Figure 9).

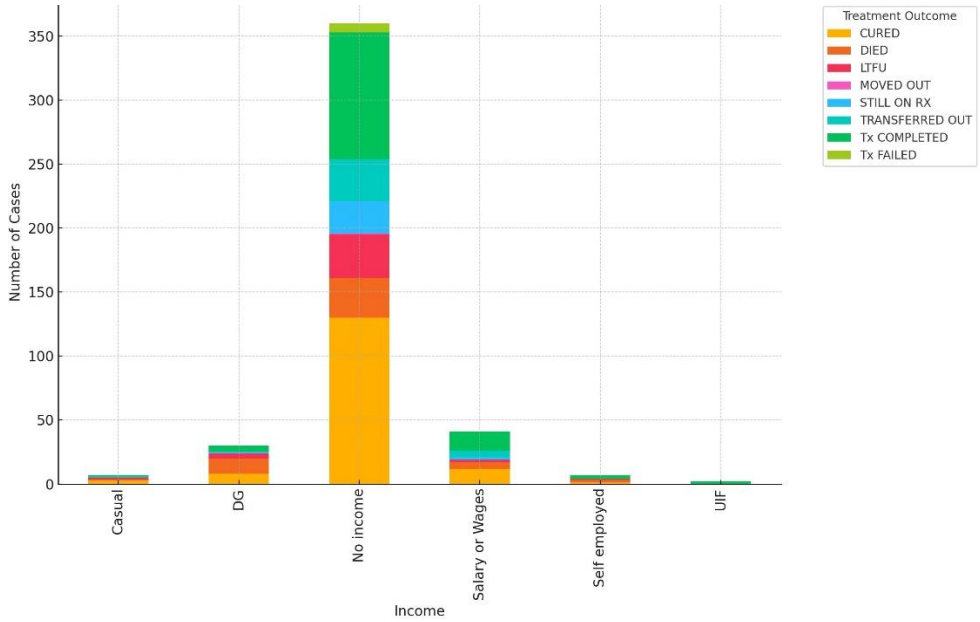

Figure 9. Impact of income on treatment outcomes.

Underweight patients face significant challenges with high rates of LTFU and treatment failure, while normal BMI patients have better outcomes but still experience notable adverse events; overweight and obese patients show relatively balanced and more favorable outcomes, suggesting that being underweight is a greater risk factor for poor DR-TB treatment outcomes compared to higher weight categories (Figure 10).

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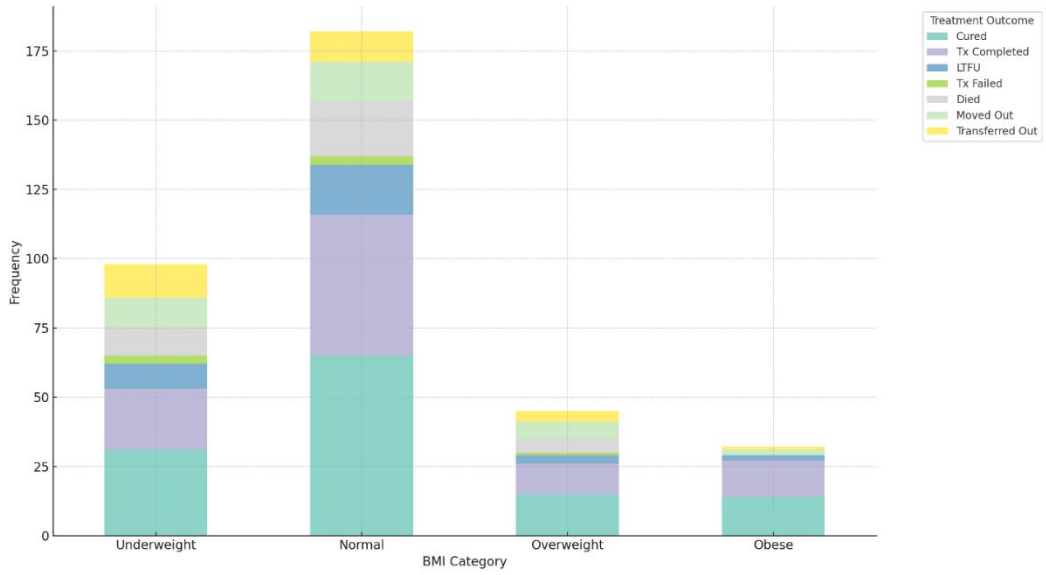

Figure 10. Comparison of BMI and treatment outcomes.

In the younger age groups (19-35 and 36-50), individuals with stable income (Salary or Wages) and self-employment show lower death rates compared to those with no income or receiving DG (Social grant), suggesting that financial stability may protect against the worst outcomes. There is an increased vulnerability with Age as the age increases, the protective effect of income appears to diminish, with deaths occurring across all income categories, especially among the elderly (51+), indicating that age-related factors may outweigh the benefits of financial stability (Figure 11).

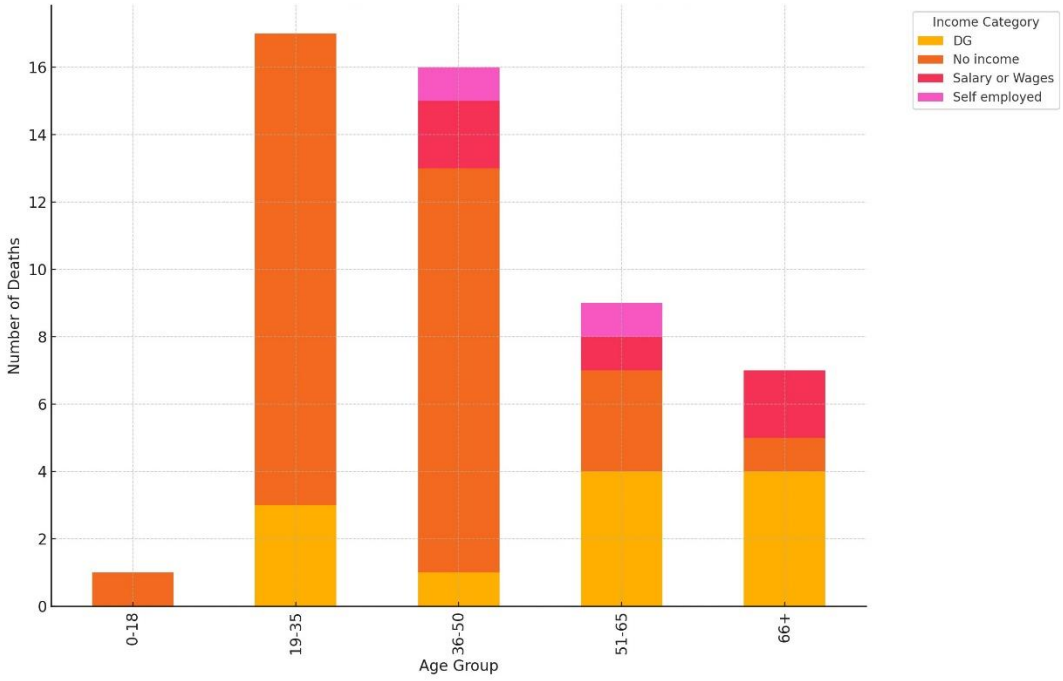

Figure 11. Death rate by age group and income category.

High-risk comorbidities like epilepsy and T2DM have the highest death rates, nearly 30%, making DR-TB patients with these conditions particularly vulnerable while moderate-risk comorbidities like mental illness and hypertension present moderate risks, with death rates between 15% and 25%, requiring significant attention in DR-TB management. The lower-risk comorbidities like allergies and hearing loss have relatively lower death rates (~10%), indicating that these conditions, while risky, are less critical compared to epilepsy, T2DM, and mental illness (Figure 12).

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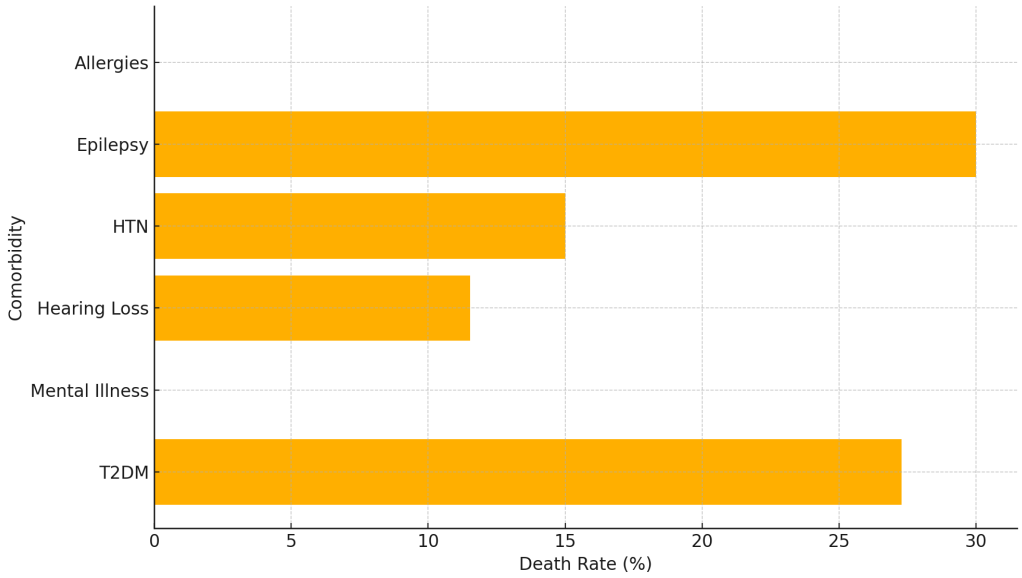

Figure 12. Death rate by specific comorbidity.

4. Discussion

Tuberculosis patients in rural areas face a complex interplay of socioeconomic disadvantages, healthcare access issues, and demographic trends that significantly impact their treatment outcomes and overall health. Age has a significant impact on TB treatment outcomes, influencing factors such as treatment efficacy, adherence, recovery rates, and the likelihood of complications. Studies indicate that the risk of unsuccessful TB treatment outcomes increases with age. Specifically, older patients (aged above 45 years) tend to have lower treatment success rates compared to younger patients. This is attributed to higher default rates, increased mortality, and the presence of comorbidities that complicate treatment [41]. Study by [42]. found that patients aged under 20 years had an 84% lower likelihood of achieving successful treatment outcomes compared to those aged above 60. This finding suggests that younger patients may engage in riskier behaviors (e.g., substance abuse) that negatively impact their treatment adherence and outcomes. Children generally have less developed immune systems, which can make them more vulnerable to severe forms of TB. However, younger patients often respond well to treatment if it is started early and managed effectively.

RR-TB and MDR-TB were the most prevalent TB types in our study, each with over 200 cases, mainly affecting patients aged 19-35 and 36-50. These types were less common in the 0-18 and 66+ age groups. Individuals aged 19-50 had higher exposure to TB due to their active social and economic involvement in environments like workplaces and public transportation, increasing their risk of contracting drug-resistant strains [43]. In contrast, the 0-18 and 66+ age groups have lower exposure, as younger individuals are often under guardians' care and older adults are more likely to be retired or less mobile, reducing their risk [44]. Pre-XDR-TB, XDR-TB, and INH-resistant TB are less common overall but predominantly affect the 19-35 and 36-50 age groups due to their higher exposure to TB, challenges with treatment adherence, and delayed healthcare access. Several studies found that pre-XDR-TB cases were more common among young adults aged 15-34 years while One study reported that 70% of pre-XDR-TB cases were in this age group [45;46]. These factors are less pronounced in the youngest and oldest populations, leading to minimal cases in these age groups. The higher prevalence of DR-TB in the 19-35 and 36-50 age groups is likely due to several factors like stress, malnutrition, and co-existing conditions like HIV can weaken their immune systems, making it harder to combat TB infections [13;44]. Inconsistent treatment adherence, driven by work commitments and limited healthcare access, further contributes to the development of DR-TB strains [47]. Economic pressures, migration, urbanization, and occupational risks in this demographic also play significant roles in the spread and worsening of DR-TB [48].

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To fully understand the gender-based differences in DR-TB prevalence, it's essential to consider factors like age, socioeconomic status, geographic location, co-existing health conditions, and occupational risks. Men show a slightly higher prevalence of DR-TB, which could be influenced by their roles in high-risk occupations, socioeconomic barriers, and health conditions like HIV [49;50;51]. While gender differences are present, the percentage representation of DR-TB types across genders is nearly equal, indicating the need for balanced resource allocation and focused interventions that address both gender-specific risks and broader demographic factors.

The social history of patients with DR-TB in this study highlights the significant impact of socio-economic factors on treatment outcomes. Patients from lower socioeconomic backgrounds, especially those receiving social grants/ DG or without stable income, face poorer outcomes, including higher rates of loss to follow-up and mortality. Economic instability contributes to inadequate access to healthcare, poor living conditions, and insufficient nutrition, all of which exacerbate the challenges of managing DR-TB [52;53]. A study examining public healthcare expenditure from 1996 to 2016 found that despite increases in government health expenditure, the relationship between healthcare spending and economic development is complex. The research indicated that higher unemployment rates correlate with poorer healthcare performance, suggesting that economic challenges hinder effective healthcare delivery, particularly for diseases like TB and [54]. Higher death rates among these patients emphasize the critical role of economic factors in treatment adherence and overall health. Additionally, social stigma and the lack of support systems in impoverished communities further complicate TB management. These findings suggest that effective TB control must address socio-economic conditions through interventions like economic support, stigma reduction, and community-based support systems, alongside medical care, to improve treatment outcomes for vulnerable populations in rural Eastern Cape.

Tuberculosis, is known as a disease of poverty and it disproportionately affects socially and economically underprivileged people [55;56]. Low-income patients face significant challenges in accessing and adhering to TB treatment due to financial constraints, inconsistent access to healthcare, poor living conditions, inadequate nutrition, psychosocial stress, and limited social support [57;55]. These challenges contribute to higher rates of adverse outcomes, such as loss to follow-up or death during treatment, highlighting the need for focused interventions to support these vulnerable populations. These findings highlight the need for economic support and social services for low-income patients to improve treatment adherence and overall health outcomes.

The analysis reveals that death rates are highest among those receiving social grants/Disability Grants (DG) and the Self-employed, with rates nearing 60%, predominantly in older age groups (51-65 and 66+). The No Income group also shows a significant death rate of about 45%, entirely within the 66+ age group. In contrast, individuals with stable incomes, such as those receiving salaries or wages, exhibit lower death rates, around 25%. Casual workers and those on UIF have the lowest death rates, with the latter showing no deaths. This highlight that older individual, particularly those in the DG and self-employed categories, are more vulnerable to higher mortality, likely due to limited access to healthcare, financial instability, and existing health [58;59]. In contrast, income stability appears to be linked to better health outcomes and lower death rates. Socioeconomic factors significantly impact health outcomes, particularly for DG recipients and the self-employed as well as economic instability that often leads to inadequate healthcare, poor living conditions, and insufficient nutrition, exacerbating health problems [60;61,62]. Additionally, both groups may live or work in environments with poor housing, sanitation, or safety, further increasing their health risks and mortality rates. For DG recipients, the barriers to adequate care are compounded by their health conditions, while for the Self-employed, the uncertainty and pressures of their work significantly contribute to poorer health outcomes.

HCF 1 has a diverse distribution of DR-TB types, including notable proportions of Pre-XDR and XDR cases, alongside RR and MDR. HCF 3, 4, and 5 are dominated by RR-TB with few cases of other DR-TB types, indicating a less diverse distribution. HCF 2 and HCF 6 show a significant presence of both MDR-TB and RR-TB, reflecting a broader spectrum of drug resistance compared to HCF 4 and HCF 5. This suggests that while RR-TB is the most prevalent type of DR-TB across all HCFs, this

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agrees with [63]. who also reported prevalence of RR-TB. There are variations in the distribution of other types like MDR, Pre-XDR, and XDR, which is highlighting the ongoing challenge of managing drug resistance in TB [64]. These differences may reflect variations in patient populations, healthcare practices, or the stage of diagnosis at each facility. The population demographics and characteristics served by each healthcare facility influence TB type distribution. Areas with higher poverty, overcrowding, or migration may have more cases of drug-resistant TB due to poor living conditions and inconsistent healthcare access [65]. The facilities serving populations with higher HIV rates may see more severe TB forms, as HIV-positive individuals are more susceptible to developing DR-TB due to weakened immune [63]. Healthcare practices and resources significantly influence TB type distribution. Facilities with advanced diagnostic tools are better at identifying and classifying severe forms of drug-resistant TB, leading to higher reported incidences of Pre-XDR and XDR [51]. The facilities with strong treatment adherence support tend to have lower rates of drug-resistant TB, as they can better ensure patients complete their treatment regimens, reducing the likelihood of resistance developing. Factors such as patient awareness, trust in healthcare providers, and support systems significantly influence treatment adherence, ultimately impacting the development of DR-TB [64;65]. Referral patterns and case complexity affect TB type distribution. Referral centers that handle more complex TB cases, including those with severe drug resistance, tend to report higher proportions of MDR, Pre-XDR, and XDR TB [66]. Facilities managing severe cases often see higher rates of drug-resistant TB, as they receive patients who have failed treatment elsewhere or have a history of inconsistent treatment. The history of TB treatment in an area influences the distribution of TB types. Areas with past treatment interruptions or inadequate TB control programs tend to have higher rates of drug-resistant TB [67]. Additionally, inconsistent drug supply or the use of substandard medications can contribute to the development of drug resistance, impacting the prevalence of DR-TB in different facilities. The presence of more severe forms of drug resistance (Pre-XDR and XDR) in certain facilities like HCF 1 indicates potential hotspots that may require focused interventions and closer monitoring.

Income stability plays a crucial role in treatment outcomes for TB patients. Those with stable or higher income sources, such as salaries or self-employment, are more likely to achieve successful outcomes, including being cured or completing [68;69]. which is the same in this study. Individuals with stable incomes are known to afford healthcare services, such as regular doctor visits, diagnostic tests, and medications, allowing them to adhere to treatment plans without interruptions caused by financial constraints [69]. Additionally, higher income enables timely healthcare seeking, which is crucial for early diagnosis and effective TB treatment, reducing the risk of complications and improving the chances of a cure. Patients with stable incomes can consistently purchase necessary medications throughout their treatment, reducing the risk of drug resistance and treatment failure [35]. Better financial resources enable them to afford transportation to healthcare facilities, ensuring regular check-ups and timely access to medications. Patients with higher incomes typically have better living conditions, such as less crowded housing and better ventilation, which reduce the risk of TB transmission and support recovery [70;71]. The stable income enables access to better nutrition, strengthening the immune system and improving the body's ability to fight TB, leading to more favorable treatment outcomes [72]. In contrast, low-income patients, particularly those with no income or relying on casual work or disability grants, face greater challenges, resulting in higher rates of adverse outcomes like loss to follow-up or death during treatment [73]. Patients from low socioeconomic backgrounds are less likely to seek medical attention and have lower treatment outcomes [56]. Low income, unemployment, and a lack of social support all contribute to greater rates of loss to follow-up and increased death while in treatment. According to [31]. patients with low socioeconomic status are less likely to seek medical attention and have poor treatment outcomes. Low income, unemployment, and a lack of social support all contribute to greater rates of loss to follow-up and increased death while in treatment.

In our study HIV-positive patients with TB had a lower survival rate compared to those who are HIV-negative, largely due to the weakened immune system associated with HIV, which hinders effective TB treatment. There are significantly lower survival rates among HIV-positive TB patients

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compared to those who are HIV-negative. The weakened immune system in people living with HIV is a major contributor to this disparity, highlighting the importance of early diagnosis, prompt initiation of [74;38]. In a study conducted in KwaZulu Natal, the HIV-positive patients had a higher mortality rate (9.67%) compared to HIV-negative patients (2.91%) with overall treatment success rate lower for HIV-positive patients, indicating that HIV significantly affects TB treatment outcomes and survival rates in South Africa [32]. This emphasizes the need for strengthening integrated care strategies that address both HIV and TB simultaneously, including more aggressive treatment, closer monitoring, and additional patient support. TB treatment for HIV-positive individuals is more complex because they often need to manage both TB medications and antiretroviral therapy (ART) for HIV. Drug interactions between TB medications such as rifampicin and ART can reduce the effectiveness of both treatments, requiring careful selection and adjustment of drug regimens. A study that reviewed the management of individuals requiring ART and TB treatment in South African patients emphasized that rifampicin is a potent inducer of cytochrome P450 enzymes, which can reduce the plasma concentrations of non-nucleoside reverse transcriptase inhibitors (NNRTIs) and protease inhibitors (PIs). This reduction can lead to inadequate ART plasma concentrations and inferior treatment outcomes, necessitating careful selection and adjustment of drug regimens [75].

The complexity of managing multiple medications increases the risk of non-adherence, making patient education and support essential.

The underweight category had a high frequency of lost to follow up and treatment failure, while normal BMI patients have better treatment outcomes. Underweight individuals experience social stigma, lack of support, or mental health issues that contribute to a higher likelihood of discontinuing treatment [76;77]. Nutritional deficiencies and a compromised immune system can lead to poorer responses to treatment and underweight patients may also have less physiological reserve to cope with illness, leading to complications [79]. Normal BMI patients often have better access to resources and support systems, which can enhance their commitment to treatment protocols. A normal BMI is often associated with better overall health, which can facilitate more effective treatment responses and lower rates of complications. Overweight patients had fewer patients but have a balanced distribution of treatment outcomes. Research indicates that overweight patients generally experience a mild baseline disease severity and lower mortality rates compared to their underweight counterparts. This suggests that being overweight may confer some protective effects against severe outcomes related to TB, although the exact mechanisms remain under investigation [80;81;82].

This study highlights the significant challenges associated with managing TB in patients with comorbidities with death rate for patients with any comorbidity is estimated at 11.14%. Comorbidities complicate TB treatment by requiring multiple medications, which can interact negatively with TB drugs, leading to reduced treatment effectiveness, increased side effects, and higher mortality rates [83;84]. Patients often struggle with treatment adherence due to the complexity of managing multiple conditions, side effects, or the burden of taking many medications, increasing the risk of treatment failure. Comorbidities can also cause TB to progress more rapidly into severe forms, which are harder to treat and associated with higher mortality rates [83]. For example, HIV-positive individuals are more prone to developing extrapulmonary TB, which is harder to manage and has a higher risk of death. Mental health issues, such as depression and anxiety, further complicate TB treatment by reducing patients' motivation to adhere to their medication regimen. Specific comorbidities like epilepsy and hypertension further complicate TB treatment. Epilepsy medications can interact with TB drugs, reducing their effectiveness and increasing the risk of seizures and drug resistance [84]. Hypertension, combined with TB, increases the risk of cardiovascular events and makes treatment adherence more difficult due to side effects and the need for frequent monitoring [84].

Overall, the study underscores the need for comprehensive management of different significant patients characteristics alongside TB treatment to improve patient outcomes and reduce mortality.

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5. Conclusions

This study highlights the complex interplay of socioeconomic factors, comorbidities, and healthcare access challenges in managing DR-TB in rural Eastern Cape. The findings underscore the critical need for integrated care strategies that address both medical and socioeconomic determinants to improve treatment outcomes. Higher mortality rates among patients with unstable income, comorbid conditions like HIV, and those facing treatment adherence challenges point to the necessity of focused interventions, including enhanced patient support, closer monitoring, and improved healthcare infrastructure. To effectively combat DR-TB in resource-limited settings, future efforts should focus on reducing socioeconomic disparities, ensuring comprehensive management of comorbidities, and strengthening the capacity of healthcare facilities. Addressing these issues holistically could lead to better patient outcomes and contribute significantly to the broader goal of controlling and eventually eradicating TB in high-burden regions.

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