# Prevalence and factors associated with Haematological side effects in MDR/RR-TB Patients on Linezolid-Based Regimens in Uganda: A Multicentre Retrospective Study

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# Abstract

**Background:** Linezolid holds a critical role in the management of multidrug-resistant and rifampicin-resistant tuberculosis (MDR/RR-TB), a severe global health threat. The World Health Organisation strongly recommends its inclusion in treatment regimens for these challenging forms of tuberculosis. Despite its efficacy, linezolid is frequently associated with haematological toxicity, a complication insufficiently documented in resource-limited settings like Uganda.

**Objective:** This study aimed to ascertain the prevalence and identify associated factors of haematological side effects in MDR/RR-TB patients receiving linezolid-based regimens in Uganda.

**Methods:** A multicentre retrospective study was conducted, reviewing patient records from four Ugandan hospitals (2020 – 2024). Data were collected on the prevalence of anaemia**:** Haemoglobin (Hb) level below 12 g/dL for women or below 13 g/dL for men. **Thrombocytopenia:** Platelet count below 150,000/µL. **Leukopenia:** White blood cell (WBC) count below 3,700/mm³.Modified Poisson regression with robust error variance identified independent risk factors for these haematological side effects.

**Results:** Out of 412 eligible patients, 62.9% developed at least one haematological side effect. Thrombocytopenia (56.6%) and leukopenia (56.3%) were the most common, followed by anaemia (43.7%). Most of these side effects occurred within the first month of linezolid initiation. Risk factors for developing at least one of the side effects included rural residence (adjusted Prevalence Ratio (aPR) 1.6; 95% CI: 1.11–2.33), divorced/widowed status (aPR 4.1; 95% CI: 1.58–10.77), and smoking (aPR 1.7; 95% CI: 1.28–2.80). Despite the high prevalence of side effects, 86% achieved treatment success (cure and completion); however, loss to follow-up was higher among those with toxicities, at 15.1% (39/259) and 5.9% (9/153) in those without hematologic side effects.

**Conclusion**: Linezolid-related haematological toxicities are common and occur early in treatment. Targeted monitoring of high-risk patients may improve treatment adherence and outcomes.


# Introduction

Multidrug-resistant and rifampicin-resistant tuberculosis (MDR/RR-TB) continues to represent a formidable global public health challenge, complicating treatment strategies and necessitating advanced therapeutic approaches.(1). Despite a cumulative reduction in the overall tuberculosis (TB) incidence rate from 2015 to 2021, the prevalence of drug-resistant TB has unfortunately escalated.(2). Globally, the rate of successful treatment for drug-resistant TB remains suboptimal, standing at a mere 60%(2). This persistent disparity between the identification and effective management of drug-resistant TB brings out the urgent need for more effective and tolerable regimens.

Uganda, being among the 30 high-burden countries affected by both TB and TB-HIV co-infection, experiences an estimated 96,000 new TB cases annually(3). A concerning proportion, approximately 2%,

of these notified TB cases involve drug-resistant TB, which significantly complicates treatment and recovery efforts within the country.(3).

Linezolid (LZD), an oxazolidinone, has emerged as a cornerstone in the treatment of drug-resistant TB due to its demonstrated activity against *Mycobacterium tuberculosis.*(4). It is highly effective and recommended by the WHO as a first-line component of conventional regimens for MDR/RR-TB and pre-XDR-TB and is integral to newer short-course regimens such as BPaL and BPaLM.(4). Linezolid exhibits excellent oral bioavailability, nearing 100%, and is well-distributed throughout the body, effectively reaching lung tissues and inhibiting protein synthesis early in the bacterial replication cycle.

Despite its therapeutic advantages, LZD is associated with a notable incidence of adverse events (AEs), which frequently limit its long-term use.(4). The primary concerns are haematological toxicities, specifically anaemia, thrombocytopenia, and leukopenia. These complications can be severe and typically manifest within the first few weeks of therapy, often after two weeks.(5). Other significant toxicities reported include peripheral neuropathy, optic neuritis, and lactic acidosis.(4) These complications are particularly problematic in low-resource settings like Uganda, where prevalent comorbidities such as HIV co-infection (affecting approximately 35% of notified TB cases) and malnutrition can exacerbate the risks of drug toxicity.(3).

While linezolid's toxicity is recognised globally, its precise prevalence, specific patterns of onset, and associated determinants remain under-documented in real-world settings in sub-Saharan Africa, particularly Uganda. This study aims to address this critical knowledge gap by providing robust, multicentre data on the prevalence, associated factors of linezolid-induced haematological side effects and treatment outcome in MDR/RR-TB patients in Uganda. The findings are crucial for informing evidence-based, appropriate monitoring strategies and improving treatment adherence and overall outcomes in this high-burden setting treatment adherence and overall outcomes in this high-burden setting.

# Methods

### Study Design and Setting

A multicentre retrospective cohort study was conducted, reviewing patient medical records from January 2020 to December 2024. The study encompassed four distinct hospitals across Uganda: two regional referrals which included Mbale Regional Referral Hospital and Moroto Regional Referral Hospital, one general hospital, Iganga General Hospital, and one private, not-for-profit St. Kizito Matany Hospital.

### Study Population and Data Collection

The study population included patients with confirmed MDR/RR-TB, diagnosed through standard methods such as Xpert MTB/RIF, Line Probe Assay (LPA), or culture. Patients were eligible for inclusion

if they had received linezolid for a minimum duration of one week and had available complete blood count (CBC) results both before and following the initiation of linezolid therapy. Exclusion criteria, consistent with common practices in similar studies(6), included patients with pre-existing haematological diseases, individuals aged below 18 years. Data were retrospectively extracted from patient medical records, encompassing demographic information (age, sex, residence, marital status, smoking status, alcohol intake), relevant clinical characteristics (e.g., HIV status, other comorbidities documented), and serial laboratory data, with a specific focus on haemoglobin levels, platelet counts, and white blood cell counts. The treatment outcome was also obtained from the files (cure, completion, relapse, failure, and death).

**Study variables**:

Sociodemographic and clinical data were extracted from the participants' charts using a data abstraction form. Sociodemographic variables collected included year of enrolment in care, age, sex, employment status, level of hospital (regional referral, and district hospitals), residence (rural and urban), marital status and any history of alcohol and/or cigarette use. Clinical characteristics included the history of previous TB treatment, HIV serological status, other comorbidities (cancer, hearing impairment, heart failure, hypertension and diabetes mellitus), haemoglobin, hepatic dysfunction was identified by an elevation in liver enzyme levels, specifically Alanine Aminotransferase (ALT) and Aspartate Aminotransferase (AST)ALT/AST greater than 2 times the Upper Limit of Normal (ULN)(7) for our laboratory and Renal Dysfunction was defined as a serum creatinine level exceeding 1.5 mg/dL of the upper limit of normal (ULN) (8)for the testing laboratory, TB resistance profiles, time from diagnosis to treatment initiation, number and type of drugs in the MDR/RR-TB treatment regimen, treatment duration, time to sputum culture conversion, Changes in treatment plan during follow-up like any adjustments made to linezolid during treatment and treatment discontinuation and treatment outcomes. Treatment outcomes were treatment success, which was the sum of TB cure and treatment completion, treatment failure, loss-to-follow-up and death as defined by the WHO.

**Definition of Haematological side effects**

Haematological side effects were defined based on the CBC after initiation of linezolid. **Anaemia**: Haemoglobin (Hb) level below 12 g/dL for women or below 13 g/dL for men(6).

**Thrombocytopenia**

Platelet count below 150,000/μL(6).

**Leukopenia**

White blood cell (WBC) count below 3,700/$mm^3$(6).

**Treatment outcomes.**

- **Cure**: WHO defines cure as having negative sputum smear or culture results at the end of the intensive phase of treatment and on at least one occasion during the continuation phase, with no evidence of treatment failure(9).
- **Treatment Failure**: when sputum smear or culture remains positive at 5 months or later during treatment, or if the patient remains smear or culture positive after 4 months of treatment(9).
- **Relapse**: Relapse occurs when a patient who was initially declared cured later develops a recurrent episode of TB caused by the same strain of Mycobacterium tuberculosis(9).
- **Loss to Follow-Up**: as treatment interruption for at least two consecutive months (9).
- **Death**: if they die for any reason during TB treatment, regardless of the cause(9)

**Data Analysis and Sample Size Estimation**

All participants in the four study sites with MDR/RR-TB were included. Data from the Kobo tool was transferred to an Excel sheet and then exported to STATA version 18 for analysis. Continuous demographic data and outcome predictors were summarised as mean (standard deviation) and median (interquartile ranges). Thereafter, it was presented on tables and graphs. The study outcomes were haematological side effects, defined as: anaemia, thrombocytopenia and leucopenia. These were summarised as proportions of the participants with the given outcome to the total number of study participants.

Factors associated with haematological side effects among MDR/RR-TB patients were tested by bivariate analysis, using the Chi-square test (for categorical variables) to compare proportions. For continuous variables, the t-test was used to compare means, and the Mann-Whitney U test was used to compare medians for groups with and without haematological side effects. Variables with $p < 0.2$ in the bivariate analysis were considered for inclusion in multivariate analysis. We used a modified poison regression model to assess the risk factors associated with developing haematological side effects and treatment success among MDR/RR-TB patients on Linezolid-Based Regimens, with a p-value $< 0.05$ considered statistically significant.

# RESULTS

**Social demographic and clinical characteristics of the participants**

A total of 590 MDR/RR-TB patient's files were identified across the four facilities of Mbale Regional Referral Hospital (190 files), Moroto Regional Referral Hospital (170 files), Iganga General Hospital (115 files), and St. Kizito Hospital Matanyi (120 files). Following the exclusion of patients without CBC results, those without linezolid in their regimen, and those without MDR/RR-TB diagnosis, the numbers were reduced to 186, 90, 34, and 102, respectively. This exclusion process led to a final analytical sample of 412 patients whose data met the inclusion criteria and were therefore used for the study analysis. Figure 1 shows the flow diagram illustrating the selection process of the final study sample.

The study included 412 participants with a mean age of 40.2 (± 17.5) years. Most participants resided in rural areas (83.5%), and 60.2% were male. 22.7% had elevated liver enzymes. Substance use was reported by 46.3% for cigarette smoking and 49.8% for alcohol use. Adverse events during follow-up occurred in 72.7%, and 14.4% had changes in their treatment plan. Sociodemographic and clinical characteristics are shown in Table 1

Table 1
Social demography and clinical characteristics of the participants

| Characteristic | Frequency | Percentage |
|---|---|---|
| Age (Mean and Standard deviation) | 40.2 (± 17.5) | |
| Residence | | |
| Rural | 344 | 83.5 |
| Urban | 68 | 16.5 |
| Sex | | |
| Female | 164 | 39.8 |
| Male | 248 | 60.2 |
| Pregnancy and breastfeeding status at baseline (n = 164) | | |
| Breastfeeding | 12 | 7.5 |
| Not Pregnant | 142 | 88.8 |
| Pregnant | 6 | 3.8 |
| Nature of Employment | | |
| Employed | 40 | 9.7 |
| Self employed | 71 | 17.3 |
| Unemployed | 300 | 73.0 |
| Marital Status | | |
| Divorced | 38 | 9.4 |
| Married | 270 | 66.8 |
| Single | 71 | 17.6 |
| Widowed | 25 | 6.2 |
| Cigarette smoking | | |
| No | 168 | 53.7 |
| Yes | 145 | 46.3 |
| Alcohol use | | |
| No | 157 | 50.2 |
| Yes | 156 | 49.8 |
| Hypertension | | |

| Characteristic | Frequency | Percentage |
|---|---|---|
| Hypertensive | 6 | 2.2 |
| Not Hypertensive | 265 | 97.8 |
| Renal Dysfunction | | |
| Known Renal Dysfunction | 8 | 3.0 |
| No known Renal Dysfunction | 263 | 97.0 |
| Hepatic Dysfunction | | |
| Elevated Liver enzymes | 61 | 22.7 |
| Unknown | 208 | 77.3 |
| Hearing impairment | | |
| No | 253 | 61.4 |
| Yes | 159 | 38.6 |
| Documentation of adverse events during follow-up | | |
| No | 74 | 27.3 |
| Yes | 197 | 72.7 |
| Changes in treatment plan during follow-up | | |
| No | 232 | 85.6 |
| Yes | 39 | 14.4 |

**Prevalence of haematological side effects among MDR/RR-TB patients on Linezolid-Based Regimens**

Out of 412 participants, 62.9% (95% CI: 58.0%-67.5%) developed linezolid-induced haematological side effects. The most common haematological side effects were thrombocytopenia (56.6%, 233/412) and leukopenia (56.3%, 232/412). Anaemia was reported in 43.7% (180/412) of the participants. Among those who experienced side effects, the majority occurred within the first month (54.0%, 81/150), followed by the second month (14.0%, 21/150). Figure 2 presents the monthly distribution of haematological side effect onset.

Bivariable analysis for social demographic and clinical factors associated with different haematological side effects among patients on linezolid-containing MDR/RR- TB regimens in Uganda

Thrombocytopenia was significantly more prevalent among rural residents compared to urban residents (177 [76.0%] vs. 56 [24.0%], $p < 0.001$). Additionally, smokers were more likely to have thrombocytopenia

than non-smokers (102 [64.6%] vs. 56 [35.4%], p < 0.001). Thrombocytopenia was also more common in participants with elevated liver enzymes (59 [25.7%] vs. 2 [5.1%], p = 0.005).

Leukopenia followed similar trends, being more common among rural residents (176 [75.9%] vs. 56 [24.1%], p < 0.001), and among smokers (102 [64.6%] vs. 56 [35.4%], p < 0.001). It was also significantly associated with elevated liver enzymes (59 [25.8%] vs. 2 [5.0%], p = 0.004). Although HIV-positive individuals accounted for 17.2% of cases with leukopenia, this association was not statistically significant (p = 0.114).

Anaemia was significantly more frequent in male participants than females (120 [66.7%] vs. 60 [33.3%], p = 0.018), and in rural compared to urban residents (140 [77.8%] vs. 40 [22.2%], p = 0.006). Similarly, a higher proportion of anaemia cases occurred among smokers (78 [63.9%] vs. 44 [36.1%], p = 0.004) and HIV-positive individuals (35 [19.4%] vs. 26 [11.2%], p = 0.020). Furthermore, the mean age of participants with anaemia was significantly higher than those without anaemia (42.7 ± 17.7 vs. 38.3 ± 17.0 years, p = 0.011). Anaemia was also more common in patients who had documented adverse events during follow-up (141 [78.8%] vs. 38 [21.2%], p = 0.002).

As shown in Table 2, we compared sociodemographic and clinical characteristics of patients on linezolid-based regimens who developed haematological abnormalities with those who did not.

Patients residing in rural areas were 1.6 times as likely to develop haematological side effects (any of anaemia, thrombocytopenia and leucopenia) compared to urban residents [aPR 1.6, 95% CI: 1.108–2.33, p = 0.012]. Divorced or widowed patients were 4.1 times as likely to develop haematological side effects compared to those who never married [aPR 4.1, 95% CI: 1.583–10.771, p = 0.004]. The patients who were smokers were 1.7 times as likely to develop haematological side effects [aPR 1.7, 95% CI: 1.277–2.796, p = 0.005] as shown in Table 3 below.

Table 3
Factors associated with haematological side effects among MDR/RR-TB patients on linezolid-based treatment regimen

| Variable | cPR (95% CI) | P-Value | aPR (95% CI) | P-Value |
|---|---|---|---|---|
| **Residence** | | | | |
| Urban | 1 | | 1 | |
| Rural | 2.6(1.517–4.451) | 0.001 | 1.6(1.108–2.33) | **0.012** |
| **Nature of Employment** | | | | |
| Employed | 1 | | 1 | |
| Self employed | 1.4(0.627–2.977) | 0.432 | 1.5(0.56–3.952) | 0.425 |
| Unemployed | 0.7(0.339–1.274) | 0.214 | 0.5(0.233–1.226) | 0.139 |
| **Marital Status** | | | | |
| Single never married | 1 | | 1 | |
| Divorced/ widowed | 3(1.488–6.088) | 0.002 | 4.1(1.583–10.771) | **0.004** |
| Married | 1.2(0.704–2.074) | 0.492 | 1.1(0.496–2.349) | 0.848 |
| **Cigarette smoking** | | | | |
| Yes | 2.7(1.237–4.712) | 0.008 | 1.7(1.277–2.796) | **0.005** |
| No | 1 | | 1 | |
| **HIV status** | | | | |
| Negative | 1 | | 1 | |
| Positive | 1.5(0.877–2.611) | 0.136 | 1.2(0.565–2.393) | 0.683 |
| **Alcohol use** | | | | |
| No | 1 | | 1 | |
| Yes | 1.1(0.678–1.677) | 0.782 | 1.1(0.637–1.843) | 0.766 |
| **Previous history of TB treatment** | | | | |
| No | 1 | | 1 | |
| Yes | 1(0.663–1.533) | 0.971 | 1.3(0.735–2.147) | 0.404 |

**Haematological side effects and treatment outcome among patients with MDR/RR-TB who received a Linezolid-based regimen**

Among patients who developed haematological side effects during linezolid-based treatment (n = 259), 83.0% (215/259) achieved cure/completion, while 1.9% (5/259) died during treatment, and 15.1%

(39/259) were lost to follow-up. For patients who did not experience haematological side effects (n = 153), the cure rate was 93.5% (143/153), with 0.7% (1/153) dying and 5.9% (9/153) being lost to follow-up. As illustrated in Fig. 3, treatment outcomes differed between patients with and without haematological side effects.

Figure 3 illustrates these differential treatment outcomes between patients with and without haematological side effects. While the majority of patients in both groups achieved cure, those with side effects were more than twice as likely to be lost to follow-up (15.1% vs 5.9%). Mortality rates remained low and relatively comparable between groups (0.7–1.9%), suggesting haematological abnormalities primarily impact retention in care rather than survival in this MDR-TB cohort.

Factors associated with treatment success among patients with MDR/RR-TB who received a Linezolid-based regimen

Patients with MDR/RR-TB who were HIV positive were 1.1 times as likely to have treatment success compared to those who were HIV negative [aPR: 1.1; 95% CI (1.022–1.196)]. Patients who reported as non-alcohol users were 1.9 times as likely to have treatment success compared to those who consume alcohol [aPR: 1.9; 95% CI (1.016–2.213)]. Unemployed patients were 10% less likely to have treatment success compared to those who were employed [aPR: 0.9; 95% CI (0.765–0.961)]. Table 4

Table 4
Factors associated with treatment success among patients with MDR/RR-TB who received a Linezolid-based regimen

| Variable | cPR (95% CI) | P-Value | aPR (95% CI) | P-Value |
|---|---|---|---|---|
| Residence | | | | |
| Urban | | | | |
| Rural | 1.1(0.998–1.17) | 0.057 | 1(0.933–1.169) | 0.454 |
| Marital Status | | | | |
| Single never married | | | | |
| Divorced/ widowed | 0.9(0.808–1.045) | 0.198 | 1.2(0.849–1.226) | 0.832 |
| Married | 0.9(0.87–1.031) | 0.206 | 1.6(0.858–1.116) | 0.748 |
| HIV status | | | | |
| Negative | | | | |
| Positive | 1.2(1.097–1.224) | < 0.001 | 1.1(1.022–1.196) | **0.012** |
| Alcohol use | | | | |
| Yes | | | | |
| No | 1.2(1.075–1.285) | < 0.001 | 1.9(1.016–2.213) | **0.021** |
| Cigarette smoking | | | | |
| Yes | | | | |
| No | 1.1(1.025–1.217) | 0.012 | 1.5(0.929–1.096) | 0.829 |
| Nature of Employment | | | | |
| Employed | | | | |
| Self employed | 1(0.943–1.11) | 0.585 | 1.1(0.973–1.195) | 0.148 |
| Unemployed | 0.9(0.804–0.957) | 0.003 | 0.9(0.765–0.961) | **0.008** |
| Previous history of TB treatment | | | | |
| No | | | | |

| Variable | cPR (95% CI) | P-Value | aPR (95% CI) | P-Value |
|---|---|---|---|---|
| Yes | 1.2(0.9–1.064) | 0.612 | 1.4(0.953–1.137) | 0.368 |
| Having haematological abnormalities | | | | |
| No | | | | |
| Yes | 0.8(0.773–0.93) | < 0.001 | 0.9(0.767–1.026) | 0.108 |

# DISCUSSION

The study (n = 412) found that 62.9% of MDR/RR-TB patients on linezolid-based regimens developed haematological side effects, with thrombocytopenia (56.6%) and leukopenia (56.3%) being the most prevalent, followed by anaemia (43.7%). The high prevalence is attributed to myelosuppressive properties and cumulative exposure(10, 11).

Comparatively, our study reported higher rates than those from South Africa (12), Indonesia, (13) Nigeria, (14%), China 46.05%, with thrombocytopenia at 31.58%, leukopenia at 21.05% and anaemia at 6.58% (14) and low prevalence found by A. Oehadian et al at only 5.4% (15).

The discrepancies between our findings could stem from differences in patient demographics, comorbidities, the significantly larger sample size of our study (n = 412) and study designs employed, or linezolid dosing and monitoring practices. For instance, the Indonesian study attributed its relatively lower cytopenia rates to conservative dosing and shorter treatment duration of linezolid(13). Globally, reported frequencies of linezolid-induced haematological abnormalities vary widely (ranging roughly from 5% to over 70% in different cohorts), reflecting the heterogeneity in study populations and program practices(16). Nonetheless, the consistently observed pattern is that linezolid can frequently cause cytopenia's, especially when used for extended durations, warranting vigilant blood count monitoring across all settings.

This study identified several factors associated with hematological side effects, Patients residing in rural areas were 1.6 times as likely to develop haematological side effects, possibly due to delayed healthcare access and limited monitoring (17), a finding contrasting with A Oehadian, also found a lower prevalence of haematological effects; however, they found no factors to be significantly associated with haematological-related AEs (16)

Divorced or widowed patients were 4.1 times as likely to develop haematological side effects potentially linked to psychosocial stress and reduced social support(18).

Additionally, smokers were 1.7 times more likely to develop haematological side effects, suggesting that smoking induced oxidative stress may exacerbate linezolids myelosuppressive influence (19).These comparisons suggest that regional disparities in healthcare delivery may largely influence these outcomes. Haematological side effects significantly reduce treatment success among MDR/RR-TB patients on linezolid-based regimens, primarily due to their impact on treatment adherence leading to higher rate of loss to follow up. (20).

In this study, patients without haematological side effects achieved a cure rate of 93.5%, compared to 83% among those with toxicity, with nearly threefold higher Loss to follow-up (15.9% vs. 5.1%), aligning with findings study by Kumar et al.(21). And also consistent with a Systematic review and meta-analysis which found 83% of patients had a favorable outcome, defined as either cure or treatment completion(22)

While a systematic review and meta-analysis by (23) noted high rate of linezolid adverse events often requiring interruption, Studies in more advanced health systems like, the TB-PRACTECAL trial (24) and BPaL regimen in South Africa (25) showed that toxicities did not significantly affect treatment success due to robust monitoring and patient support. This discrepancy highlights systemic issues in Uganda, such as limited timely laboratory tests and patient support, which exacerbate the impact of these side effects on treatment outcomes in the local context.

In this study, haematological side effects were initially associated with a lower rate of treatment success in the bivariate analysis. However, when we adjusted for other potential confounding variables in the multivariable analysis, the association between haematological side effects and treatment success lost its statistical significance. This suggests that while haematological side effects are indeed common, their direct influence on treatment success may be mediated by other factors such as baseline disease severity, HIV co-infection and treatment adherence. similar findings were reported by Sotgiu et al. (2012) and the TB-PRACTECAL trial, where adverse drug reactions directly impact on success diminished after accounting for confounders. This highlights the importance of a nuanced approach to treatment outcomes, emphasizing holistic care, adherence support, and addressing other clinical issues.

**Strength**

The multicentre retrospective cohort study design, encompassing four distinct hospitals across Uganda, enhances the generalizability of the findings within the Ugandan context.

**limitations**

The study's retrospective design, based on existing patient medical records, results in variable data availability and completeness. This variability can lead to missing information on some variables and uncertainties about the precise timing and severity of adverse events.

# Conclusion

This study identified a high prevalence (62.9%) of linezolid-induced haematological side effects, predominantly thrombocytopenia and leukopenia, among MDR/RR-TB patients in Uganda, with most occurring within the first month, underscoring the need for early monitoring.

Rural residence divorced or widowed marital status, and smoking were independently associated with these abnormalities, suggesting that clinical, socioeconomic, and behavioural factors influence susceptibility to toxicity and necessitate enhanced monitoring and psychosocial support. While most patients with haematological abnormalities still achieved treatment success, they experienced higher rates of loss to follow-up, indicating compromise to adherence and continuity of care rather than increased mortality; thus, strengthening pharmacovigilance and patient support is recommended.

The findings reflect the multifactorial nature of adverse events in MDR/RR-TB care, with prevalence aligning with reports from other high-burden settings. Integrating laboratory surveillance with psychosocial and nutritional assessments is crucial, and future research should focus on pharmacovigilance and dose-optimization trials to ensure safe long-term linezolid use.

# Abbreviations

MDR-TB: Multidrug-Resistant Tuberculosis

RR-TB: Rifampicin-Resistant Tuberculosis

LZD: Linezolid

CBC: Complete Blood Count

Hb: Hemoglobin

WBC: White Blood Cells

AE: Adverse Event

ALT: Alanine Aminotransferase

AST: Aspartate Aminotransferase

aPR: Adjusted Prevalence Ratio

CI: Confidence Interval

WHO: World Health Organization

# Declarations

**Ethics Approval and Informed Consent**

The Mbale Regional Referral Hospital Research and Ethics Committee (Reference Number MRRH-2024-497) approved the study. The same committee provided a waiver of consent for the use of the data. The study was conducted in accordance with the ethical standards of the institutional research committee and with the 2013 revision of the Declaration of Helsinki.

**Clinical trial**

Clinical trial number: Not applicable.

**Consent for publication**

Not applicable.

**Availability of data and material**

The datasets used during this study are available from the corresponding author upon reasonable request.

**Competing interests**

The authors declare no competing interests**.**

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No funding was received for this study.

**Authors' contributions:**

EA: Conceptualisation, Methodology, Data Curation, Formal Analysis, Writing, Original Draft Preparation and Project Administration.

JBB, RK: Writing – Review & Editing, Validation, Supervision.

PJM, DB: contributed to the design and ensured adherence to the research protocols during implementation.

EK, ON, JI, JK: contributed to the conceptualisation of the study and data collection.

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## Table 2

Table 2 is available in the Supplementary Files section.

## Figures

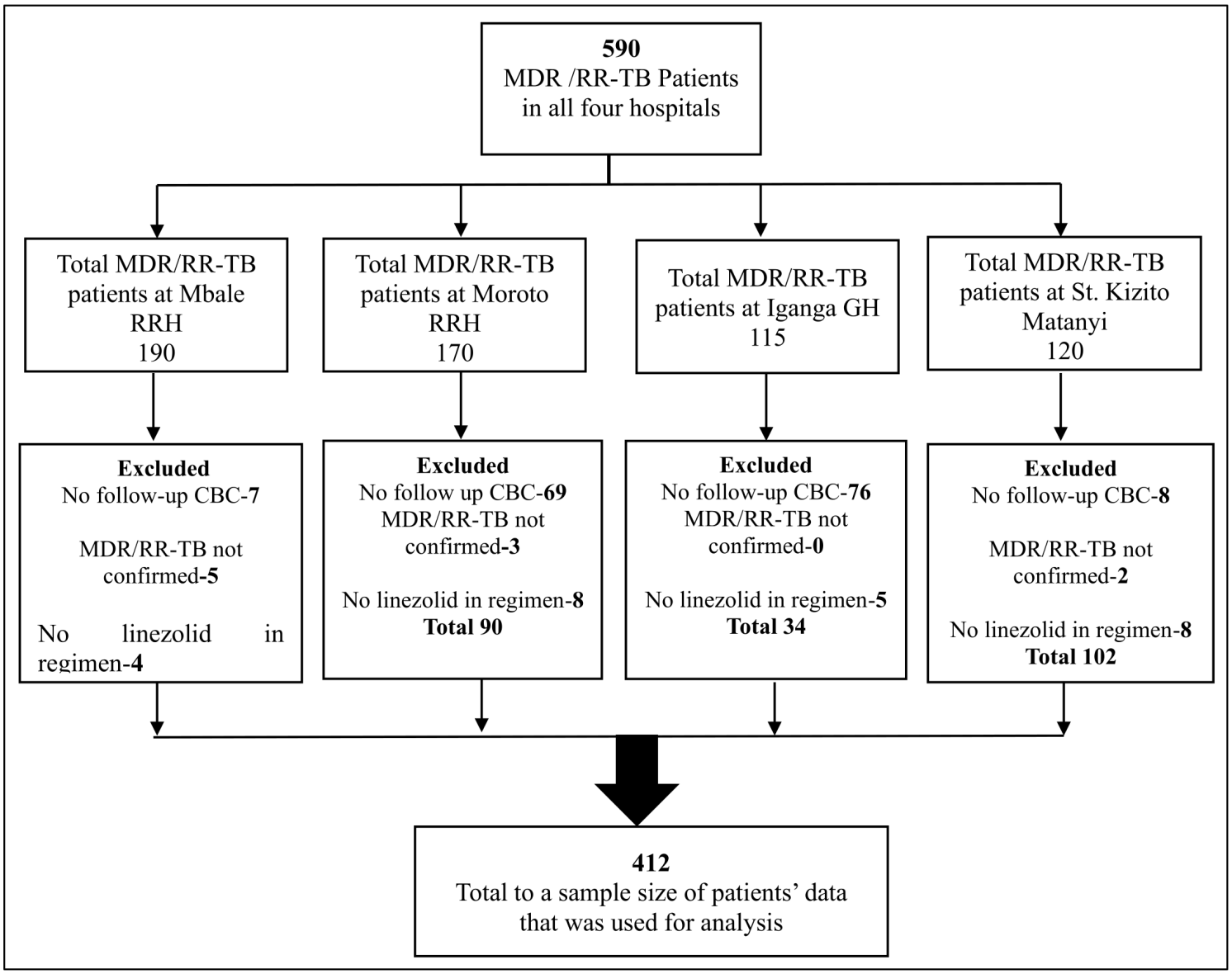



**Figure 1**

Study flow diagram

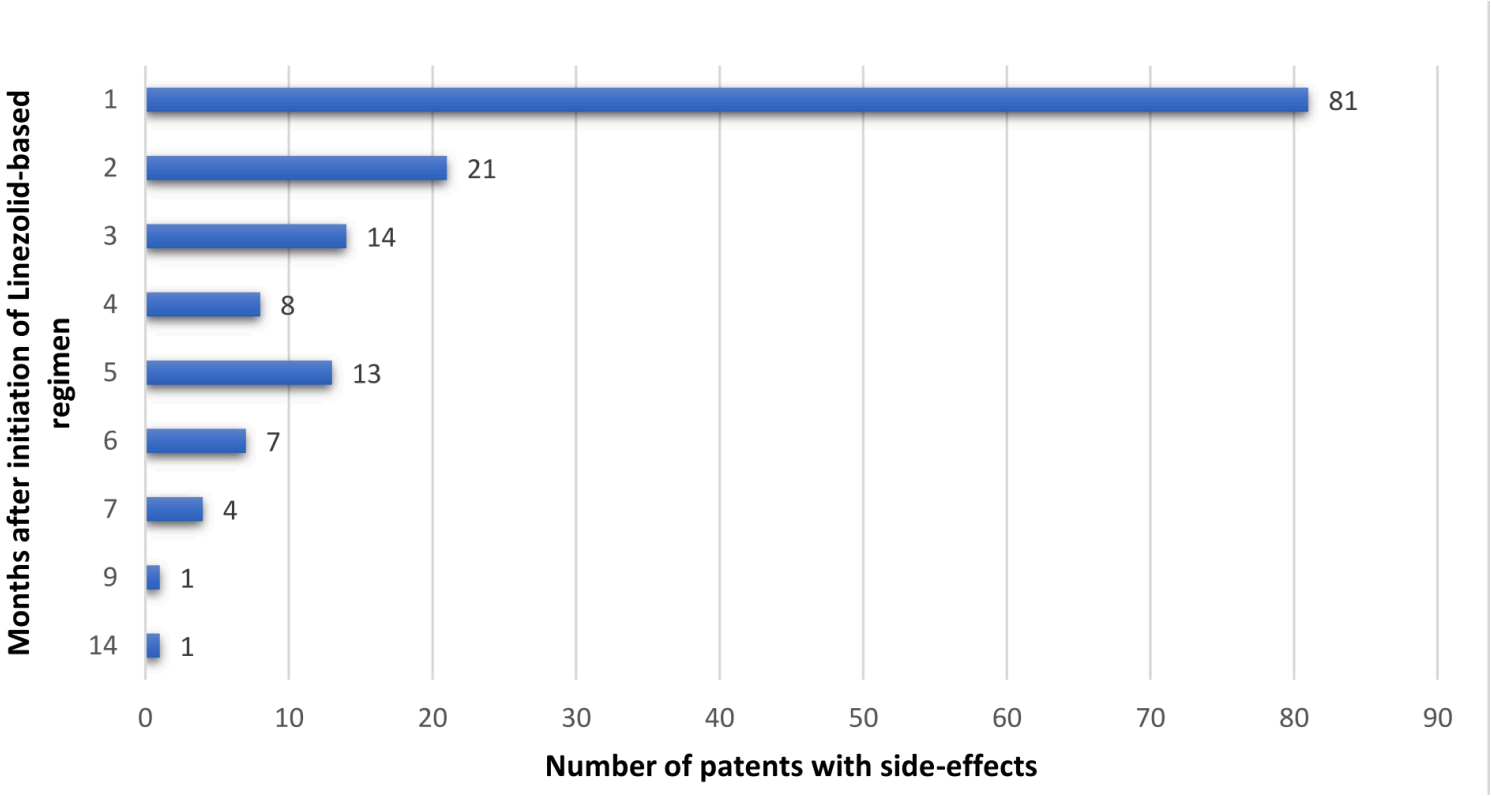
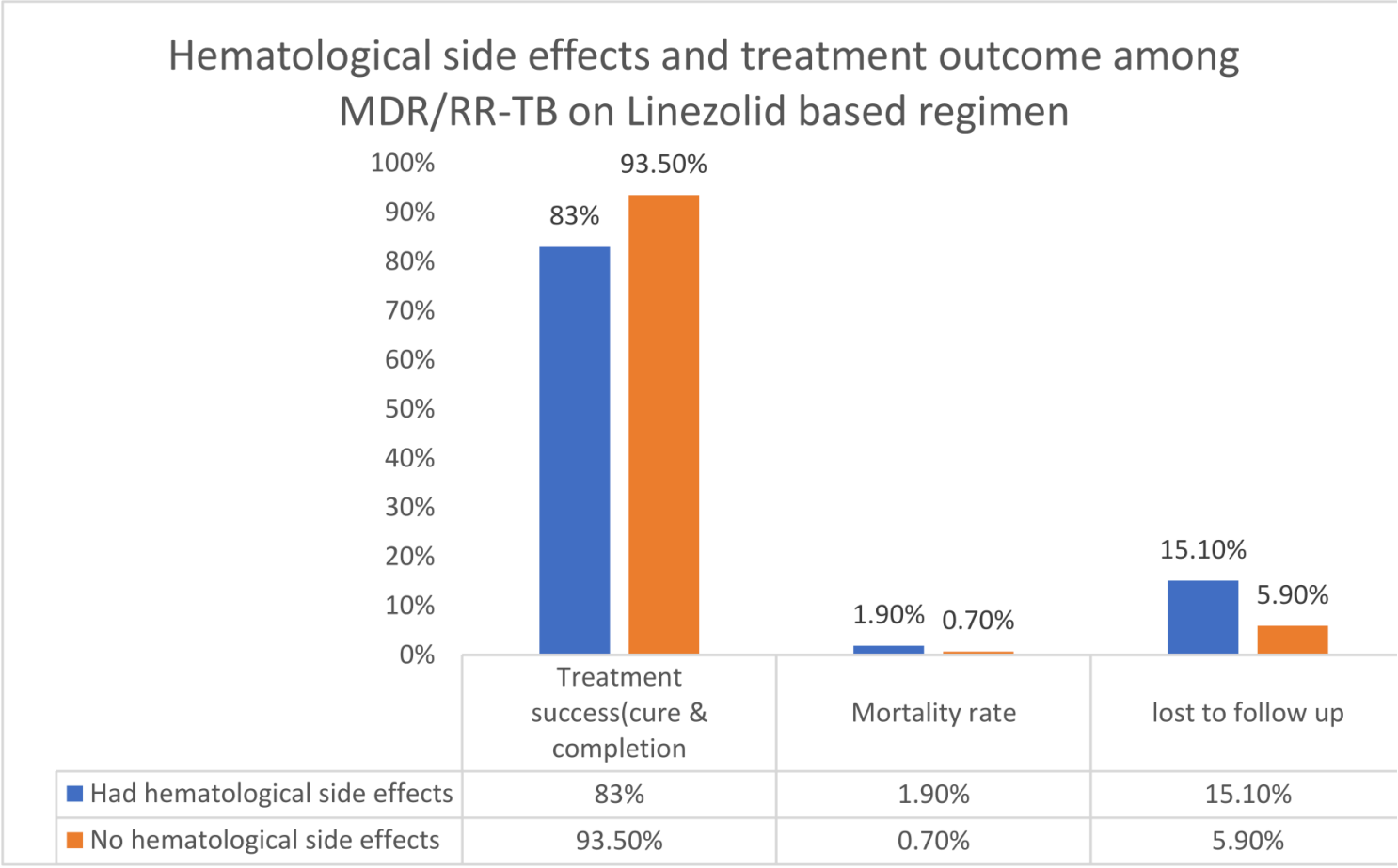



**Figure 2**

Number of MDR/RR-TB patients that developed haematological abnormalities, Months after initiation of the Linezolid-based regimen




| | Treatment success(cure & completion | Mortality rate | lost to follow up |
|---|---|---|---|
| Had hematological side effects | 83% | 1.90% | 15.10% |
| No hematological side effects | 93.50% | 0.70% | 5.90% |

**Figure 3**

Factors associated with treatment success among patients with MDR/RR-TB who received a Linezolid-based regimen

## Supplementary Files

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- Table2.docx