



**Adverse Drug Reactions related to Drug-Resistant
Tuberculosis (DR-TB) Treatment in Ethiopia:
Active Tuberculosis Drug-Safety Monitoring and
Management**

December 2023

Addis Ababa, Ethiopia

Acknowledgement

EFDA would like to thank and appreciate the healthcare providers working in MDR-TB clinics, and pharmacy department for reporting ADRs.

The authority is indebted to the national TB program for their leadership and collaboration during the implementation of aDSM in the MDR-TB program in the country.

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List of Abbreviations/Acronyms

ADRs	Adverse Drug Reactions
ADEs	Adverse Drug Events
PV	Pharmacovigilance
MDR-TB	Multidrug-Resistant Tuberculosis
NTP	National TB Program
TICs	TB Treatment Initiation Centers
EFDA	Ethiopian Food and Drug Authority
TLD	Tenofovir, Dolutegravir, Lamivudine
TFCs	Treatment follow-up centers
ARV	Antiretroviral
aDSM	Active Drug Safety Monitoring
DTG	Dolutegravir
Am	Amikacin
Bdq	Bedaquiline
Cm	Capreomycin
Cfz	Clofazimine
Cs	Cycloserine
Dlm	Delamanid
E	Ethambutol
H	Isoniazid
Km	Kanamycin
Lfx	Levofloxacin
Lnz	Linezolid
Mfx	Moxifloxacin
PAS	Paminosalicylic acid
Pto	Prothionamide
Z	Pyrazinamide
R	Rifampicin
STR	Short Term Regimen
LTR	Long Term Regimen
SAE	Serious Adverse Event
TMP/SMX	Trimethoprim and Sulfamethoxazole
3TC	Lamivudine
TDF	Tenofovir
NVP	Nevirapine
HAART	Highly Active Antiretroviral Treatment
LPV _r	Lopinavir

Executive Summary

Background:

As part of the global recommendation, the national TB program and Ethiopian Food and Drug Authority have set active TB-drugs safety monitoring and management (aDSM) as an essential requirement during the introduction of new anti-TB drugs and regimens. Hence, proper implementation of aDSM is evaluated by the presence of effective monitoring, detection, management, recording, and reporting of adverse drug events of MDR-TB drugs.

Since the implementation of aDSM, ADR reports have been received by EFDA from TICs throughout the country. In December 2021, these national ADR data were comprehensively aggregated and analyzed to generate national level information for decision-making. The report was disseminated to relevant national stakeholders and feedback was provided to the NTP. This report, therefore, presents the description of the national ADR data received by EFDA between December 2021-December 2023 to shed light primarily on the common AEs and SAEs, regimens/drugs suspected to cause the ADRs, and factors contributing to the occurrence of ADRs.

Objective:

To assess the number and types of adverse drug reactions related to DR-TB treatment in Ethiopia from 2021-2023.

Methods

There are 67 DR-TB treatment initiating centers (TICs) throughout the country. ADR reports were collected by EFDA from reporting TICs through the monthly AE line listing form, yellow form, and e - reporting from December 2021 to December 2023. An excel version 22 data aggregation form was prepared using the monthly adverse events line listing form and data entered to the data aggregation tool. After thorough data cleaning, data was exported to SPSS version 25 for data analysis. Simple descriptive statistics was used to present the data including frequency, percentage, and mean. Tables and figures were used to present the data.

Results:

Of the total 293 patients who were reported to have ADRs, a total of 333 valid ADRs were identified which gives an average number of 1.14 ADRs per patient. The most common ADRs were peripheral neuropathy (60,18.0%), nausea and vomiting (49,14.7%), optic neuritis (32, 9.6%), gastritis/dyspepsia (25, 7.5%), drug induced liver injury (DILI) (20, 6.0%), and arthralgia/arthritis (24, 7.2%). Based on system affected, close to half of the ADR reports were GI (70, 24.3%) and neurologic (65, 22.6%) related problems. Linezolid was the most suspected medicine for the ADR accounting for (87, 29.7%) of the ADRs reported, followed by cycloserine (23, 7.8%) and long-term regimen (LTR) (21, 7.2%). Majority of the reported cases were mild (135, 46.1%) while only 3 (0.9%) of the cases were reported as life threatening. Of the total ADRs reported, only 169 of them were labeled causality by the TICs. Of these causality classification, 74 (25.3%) were classified as probable/Likely, followed by possible (48, 16.4%) and certain (28, 9.6%). Almost half of the reported ADRs 145 (49.5%) were resolved, whereas it was unknown in 49 (16.7%) of the cases and 35 (11.9%) of the ADRs were resolving.

Conclusion and recommendations

Of the total patients who were reported to have ADRs, the most common ADRs were peripheral neuropathy, nausea and vomiting, optic neuritis, gastritis/dyspepsia, drug induced liver injury (DILI), and arthralgia/arthritis. Based on system affected, close to half of the ADR reports were GI and neurologic related problems. Linezolid was the most suspected medicine for the ADRs reported followed by cycloserine and long-term regimen (LTR). The majority of the reported cases were mild cases. Of the total ADRs having causality classification by the TICs, a quarter of it were classified as probable/Likely followed by possible and certain. Regarding the outcome of ADRs, almost half of the reported ADRs were resolved.

Based on the findings of this report, the following recommendations were forwarded.

- The implementation of aDSM have shown a benefit in ensuring patient safety in DR-TB treatment and it should be strengthened at TICs throughout the country to better ensure patient safety on DR-TB treatment.
- ADR data analysis should be conducted regularly to see if there are new signals
- aDSM program should be strengthened to ensure safety of newly introduced regimens such as BPAL/M
- Continuous training and supervision of professionals working in TICs should be conducted to increase reporting rate and quality of reports.
- EFDA should revise and distribute uniform AE line listing form to TICs for consistency and data quality.
- Data handling system should be strengthened at EFDA and TICs including digitization.
- EFDA should improve feedback mechanism to reporting professionals and TICs.

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1. Background

Drug-resistant TB continues to be a major global health threat. In 2021 alone, 450,000 incident MDR/RR-TB cases were estimated to have emerged. About 3.6% of new TB cases and 18% of previously treated TB cases were having MDR/RR-TB globally. Ethiopia has transitioned out of the list of the high burden countries for MDR/RR-TB in 2020 but DR-TB remains an important public health threat in the country. An estimated 1.1% of these new TB cases and 7.5% of previously treated TB cases had drug resistant TB in 2021 and an estimated 1800 MDR/RR-TB cases emerging in 2021.

Management of MDR-TB is a significant challenge to the global healthcare system due to the complexity and long duration of the MDR-TB treatment. Health programs that systematically monitor patient safety are in a better position to prevent and manage Adverse Drug Reaction (ADR) and improve treatment outcomes and health-related quality of life. Likewise, national TB programs (NTP) that actively pursue drug-safety monitoring and management are better prepared to introduce and implement new tuberculosis (TB) drugs and novel regimens.

Ethiopia has been implementing different regimens for treatment of RR/MDR-TB and introduced new MDR-TB drugs (Bedaquiline (Bdq) and delamanid (Dlm) and repurposed drugs (clofazimine and linezolid) for treatment of DR-TB following WHO recommendations supported by in-country multi-site observational studies. The safety profiles of new drugs are not well established as these drugs did not complete their 3rd phase of clinical trial and the safety profiles of repurposed drugs are not yet fully understood when used in the DR-TB regimen for a longer period.

The WHO recommends that countries introducing new drugs and novel treatment regimens for MDR-TB should develop and implement a system for active pharmacovigilance (PV) as one of the five conditions to be met when these drugs are used to treat MDR-TB patients allowing for detection, management, and reporting of ADRs.

Ethiopia has introduced Active Drug safety monitoring and management (aDSM) as part of the introduction of new TB drugs and novel MDR-TB regimens. All NTP sites (TB treatment initiation centres (TICS) treating eligible patients with new and repurposed medicines, and novel MDR-TB regimens require to implement aDSM and hence monitor, manage, record and report ADEs experienced by patients treated with MDR-TB drugs. The recording and reporting activities of

aDSM primarily target the serious adverse events (SAEs) as a priority requirement. MDR-TB treatment sites may also monitor other ADEs that are of clinical significance or of special interest to the program, as part of comprehensive aDSM.

Since the introduction of aDSM, MOH-NTP and EFDA in collaboration with the USAID GHSC-PSM project and other partners have been conducting different activities to strengthen aDSM. Some of the activities include program sensitization workshops, face to face discussions, targeted and integrated supportive supervisions to TICs and TFCs, printing and distribution of ADE reporting tools, development, and provision of PV training to HCP.

Since the implementation of aDSM, ADR reports experienced by DR-TB patients have been received by EFDA from TICs throughout the country. In December 2021, these national ADR data were comprehensively aggregated and analyzed to generate information for decision-making. The report was disseminated to national stakeholders and feedback was provided to the NTP. After December 2021, EFDA has continued receiving ADR reports and it is important to analyze the ADR reports so far to identify the common AEs and SAEs, regimens/drugs suspected to cause the ADRs and factors contributing to the occurrence of ADRs. This report therefore presents the description of the national ADR data received by EFDA between December 2021-December 2023.

2. Objectives

2.1 General Objective

- To assess the number and types of adverse drug reactions related to DR-TB treatment in Ethiopia from 2021-2023.

2.2 Specific Objectives

- To determine the frequency of ADRs reported on patients with DR-TB
- To identify the common types of ADRs reported
- To determine ADRs reported by severity and seriousness
- To identify suspected medications related with ADRs
- To identify outcomes of ADRs reported
- To assess the measures taken to manage ADR

3. Methodology

3.1 Study-site and period

This study was conducted in healthcare facilities providing clinical care for DR-TB patients. There are 67 TICs nationally, and this study includes 37 of these centers because they were the TICs that sent ADR reports during the period. These TICs are situated across nine regions and two city administrations of Ethiopia, namely Addis Ababa, Oromia, Amhara, Tigray, Dire-Dawa, South Ethiopia, Central Ethiopia, Afar, Harari, Sidama, and Somali. The collection of ADR reports took place from December 2021 to December 2023.

3.2 Study Design

This study utilized a facility-based prospective observational active surveillance called active TB-drugs safety monitoring and management (aDSM). Each participant in the study was followed throughout the treatment period starting from the initiation of treatment using the standard operating procedure set nationally for aDSM implementation. This includes clinical and laboratory assessment, clinical management and recording and reporting of ADRs while patients have regular follow-up in the TICs and TFCs. After treatment initiation at the TICs, patients were connected to the TFCs for follow-up and medication refill. Patients were consistently monitored for the presence or absence of ADRs, managed for ADRs when identified, monitored for improvement of previously experienced ADRs, as well as the severity and seriousness of ADRs. Moreover, expert clinicians identified the suspected medication related to the identified ADR and report to EFDA.

3.3 Source and Study Population

All individuals with confirmed DR-TB and on DR-TB medications served as a source population. Patients who have developed at least one ADR during the treatment period, were included as study population.

3.4 Sampling and Sample Size Determination

All patients who developed ADRs and whose ADR reports sent to EFDA are included in this study and this happened in 37 TICs. Accordingly, in the current report, 293 patients were included in the analysis.

3.5 Study variables

Dependent variable

- Type and number of ADRs
- Outcome of AEs

Independent variable

- Socio-demographic characteristics (age, sex, weight at baseline).
- Clinical characteristics (regimen, comorbidity, suspected medication, and concomitant drug use).

3.6 Data Collection and Management

Data Collection Procedure

Data was collected by trained healthcare providers from 37 TICs. Pharmacovigilance experts from EFDA and GHSC-PSM project supervised the overall aDSM implementation.

Data Collection Instrument

ADR reports were received by EFDA through the monthly AE line listing form, yellow form, and e - reporting system from the TICs. The data collection tools contain information regarding socio-demographic characteristics, clinical characteristics, details of ADR occurrences and reporter information.

Data Quality Assurance

The reporting forms consist of established and standardized information. Additionally, the data collectors received training, and supervisors conducted regular monitoring of the aDSM.

3.7 Data Analysis and Interpretation

The data was entered using MS excel version 22, exported to, and analyzed using statistical package for social science (SPSS) version 25. Mean and standard deviation (SD) for continuous variables and frequency and percentage for categorical variable were computed using descriptive statistics.

3.8 Ethical Consideration

Patient anonymity was maintained throughout this study.

3.9 Operational Definitions

- **Adverse drug event** means any untoward medical occurrence that may be present during treatment with a medicine but does not necessarily have a causal relationship with this

treatment, that is, an adverse outcome that occurs while the patient is taking the medicine but is not, or not necessarily, attributable to it.

- **Adverse Drug Reaction** means a response to a medicine which is noxious and unintended, and which occurs at doses normally used in man for the prophylaxis, diagnosis, or therapy of disease, or for the modification of physiological function.
- **Onset of ADR:** The time gap in days between being put on the treatment to the development of the first episode of adverse drug reactions.
- **Active TB-drugs Safety Monitoring and Management (aDSM):** An aDSM is defined as active and systematic clinical and laboratory assessment of patients while on treatment. It applies to all DR-TB patients who are on treatment including patients on treatment with new and repurposed anti-TB drugs, novel MDR-TB regimens, and regimens for extensively drug-resistant TB (XDR-TB).

4. Results

4.1 Sociodemographic Characteristics

Out of the total 293 patients who experienced ADR, 173 (59.0%) were males and 118 (40.3%) were females. On average the weight of patients who experienced ADR was 49.5kg (range 8-79.6kg). The mean age of patients who experienced ADR was 33.8 years (range 1-67 years); the most common age range who experienced ADRs was 19-34 years, which accounts 48.5% of the total cases reported (table 1). Most of the reports were received through the monthly AE line listing form followed by the yellow form.

Table 1: Sociodemographic characteristics, December 2021-December 2023, N=293.

Characteristics	Category	Frequency (%)
Sex	Male	173 (59.0%)
	Female	118 (40.3%)
	Missing	2 (0.7%)
Age	<=18	21 (7.2%)
	19-34	142 (48.5%)
	35-49	86 (29.%)
	>=50	40 (13.7%)
	Missing	4 (1.4%)

4.2 Types of DR-TB Regimens Prescribed

Of the total 293 patients who were reported to have ADRs, more than half of the patients 159 (54.3%) were on long-term regimen (LTR) followed by short-term regimen 83 (28.3%) (figure 1).

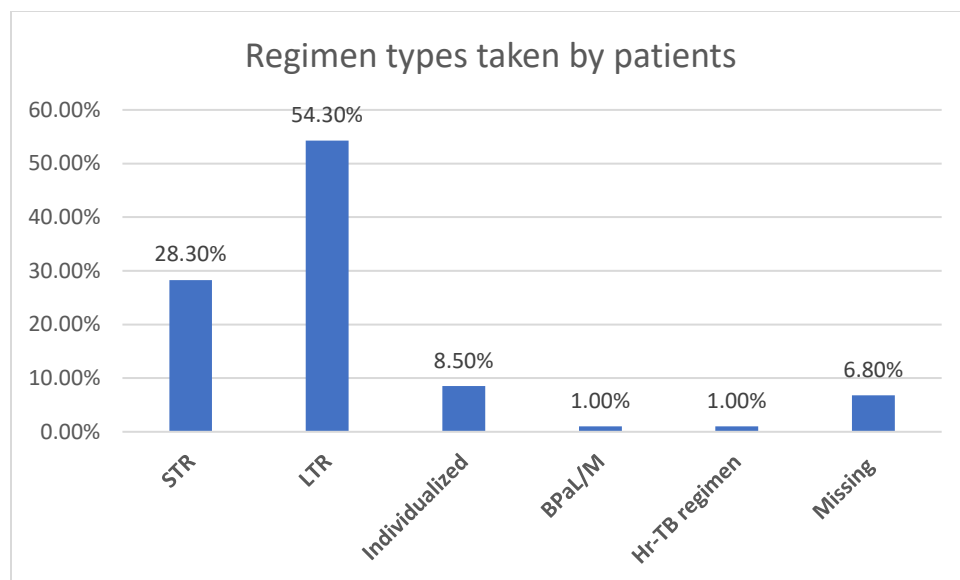


Figure 1: Regimen type among DR-TB patients, December 2021-December 2023, N=293.

4.3 Concomitant Medications

Of the total 293 patients, 113 (38.6%) were taking at least one concomitant medications at the time of ADR occurrence. Among the prescribed concomitant medications, Vitamin B₆ (57, 19.5%) and ARVs (40, 13.7%) were the most common ones. The concomitant medications are described in table 2.

Table 2: Concomitant medications among DR-TB patients, December 2021-December 2023, N=293.

Concomitant medications	n (%)
Yes	113 (38.6)
No	180 (61.4)
Types of concomitant medications	n (%)
Vitamin B ₆	57 (19.5)
ARVs	40 (13.7)
Insulin	4 (1.4)
Metformin	2 (0.7)
Depo-Provera	2 (0.7)
Others*	9 (3.1)

* Salbutamol, Furosemide, Phenytoin, Propranolol, PTU, Anticoagulant, Omeprazole, Risperidone, Cimetidine

4.4 Comorbid Conditions

As indicated in table 3 below, only 52 (17.7%) patients had at least one comorbid condition. Of these comorbidities, RVI was found to be the most frequently reported comorbid condition (11.9%) followed by severe acute malnutrition (SAM) (3.1%).

Table 3: Comorbid conditions among the reported cases, December 2021-December 2023, N=293.

Comorbid conditions	n (%)
Yes	52 (17.7)
No	241 (82.3)
Types of comorbid conditions	n (%)
RVI	35 (11.9)
SAM	9 (3.1)
DM	7 (2.4)
Others*	9 (3.1)

*CHF, COPD, DVT, Schizophrenia, CKD, Thyroid disorder, MAM.

4.5 Types of ADRs Reported

Since December 2021, EFDA received 293 ADR reports related to DR-TB treatment throughout the country. From these reports, a total of 333 valid¹ ADRs were identified which gives an average number of 1.14 ADRs per patient. Among the reported 333 ADRs, the three most common were peripheral neuropathy 60 (18.0%), nausea and vomiting 49 (14.7%), and optic neuritis 32 (9.6%). (table 4).

Table 4: Reported ADEs among DR-TB patients, December 2021-December 2023, N=293.

Types of ADRs reported	n (%)
Peripheral neuropathy	60 (18.0)
Nausea and vomiting	49 (14.7)
Optic neuritis	32 (9.6)
Gastritis/dyspepsia	25 (7.5)

¹ Valid ADE report means in this report, an ADE report that at least contains the adverse event description or name or code regardless of other data completeness.

Drug induced liver injury (DILI)	20 (6.0)
Arthralgia/arthritis	24 (7.2)
Anemia	18 (5.4)
Myelosuppression	4 (1.2)
Skin reaction	16 (4.8)
Skin pigmentation	8 (2.4)
Psychotic symptoms	10 (3.0)
Depression	6 (1.8)
Headache	6 (1.8)
Insomnia	6 (1.8)
QT prolongation	5 (1.5)
Fatigue	4 (1.2)
Renal toxicity	3 (0.9)
Hearing impairment	2 (0.6)
Death	12 (3.6)
Others*	21 (6.3)

* Acne vulgaris; confusion; Darkening of stool; Dryness of mouth; Hypo calcemic tetani; Hypokalemia; Anorexia; loss of smell and taste; Emphysema; Oral thrush; persistent dry cough; Pregnancy; Tendinitis; urine discoloration; yellow discoloration of the eye; Syncope; fast breathing; SOB; Diarrhea

Among the ADR reports, which were categorized based on body-system, close to half of the reports were comprised of GI (70, 24.3%) and neurologic (65, 22.6%) related problems. Ototoxicity and respiratory problems were reported in only two and four of the cases, respectively (Table 3).

Table 5: System Based Classification of ADRs among DR-TB patients, N=333

S. No	ADRs category	Frequency	Percentage
1	GI problems (Nausea & Vomiting, Diarrhea, Darkening of stool and Epigastric)	76	22.9
2	Neurological problems (Peripheral neuropathy, Numbness, Paresthesia, Headache & Burning sensation)	66	19.8

3	Dermatologic problems (Skin rash, Itching, Allergic reaction, Skin discoloration, Skin dryness)	25	7.5
4	Psychiatric problems (Depression, Insomnia, Mood disturbance, & Confusion)	23	6.9
5	Ophthalmologic problems (Vision problem, Blurred vision, Optic neuritis, Burning sensation in eye, erythema in eye)	32	9.6
6	Musculoskeletal (Arthralgia, Myalgia, Joint and limb swelling, Tendinitis, Joint pain, Shoulder pain, Hypocalcemic tetani)	26	7.8
7	Ototoxicity (Hearing loss, Tinnitus)	2	0.6
8	Renal problems and electrolyte disturbance (Nephrotoxicity, Hypokalemia, Urine discoloration)	5	1.5
9	Respiratory problems (Shortness of breath, Tachypnea, Cough, and Emphysema)	4	1.2
10	Myelosuppression (Anemia, thrombocytopenia, or Neutropenia)	22	6.6
11	Liver problem (Drug induced liver injury, Liver enzyme elevation,)	20	6.0
12	Others (Pregnancy, Death, QT Prolongation, Loss of appetite, Xerostomia, Syncope, Oral thrush, Loss of smell and taste, Yellow discoloration Of the Eye, and Fatigue)	32	9.6

Out of the different types of ADRs reported, eight types of adverse events of special interest (AESI) were identified. Of which, peripheral neuropathy (60), optic neuritis (32) and myelosuppression (22) constitute more than three-fourth of the total AESI encountered. Only a single report has indicated the presence of hypokalemia among DR-TB patients.

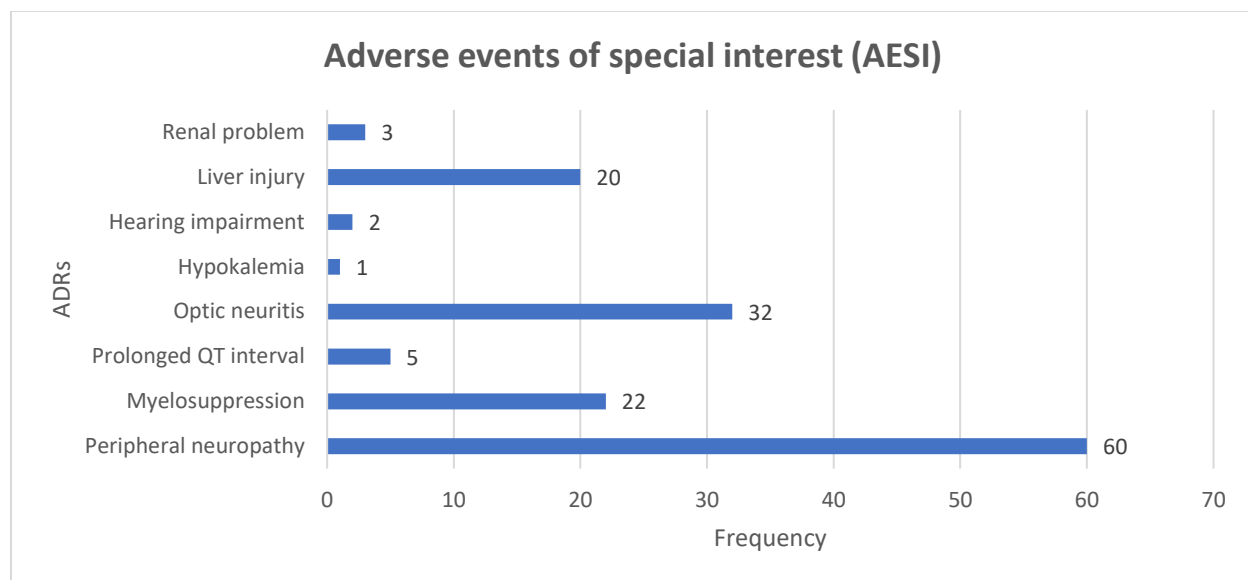


Figure 2: Adverse events of special interest (AESI), December 2021-December 2023, N=293.

4.6 Suspected drugs/regimens related with ADRs

As depicted in table 6, Linezolid was the most commonly suspected medicine accounting for 87 (29.7%) of the ADRs reported, followed by cycloserine 23 (7.8%) and long-term regimen (LTR) 21 (7.2%).

Table 6: Suspected medications implicated in ADR, December 2021-December 2023, N=293.

Suspected medicine/regimen	n (%)
Lzd	87 (29.7)
Cs	23 (7.8)
LTR	21 (7.2)
Cfz	18 (6.1%)
Eto	16 (5.5)
Cs and Lzd	15 (5.1)
Pto	15 (5.1)
Z	13 (4.4)
Lfx	11 (3.8)
STR	11 (3.8)

INH and Z	9 (3.1)
INH	7 (2.4)
Others*	31 (10.6)
Missing	16 (5.5)

*Bdq;Bdq&Cfz;Bdq&Lzd;Z-flx-Cs-Cfz-Bdq;Bdq%INH;Cfz&Pto;Cs-Lfx-Lzd;Dlm;E;E&Lzd;Eto&Lfx;Eto-E-Z-Cfz;INH-Bdq;Lfx-Bdq;Lfx-Z;Lzd-Clf-Cs;Lzd-AZT; Mflx; Pretomanid

4.7 Severity and Seriousness of ADRs reported

4.7.1. Severity of ADRs

Regarding the severity of ADRs reported, majority of the reported cases were mild (135, 46.1%) while only 3 (1.0%) of the cases were reported as life threatening. The details of ADRs grading is indicated in figure 3.

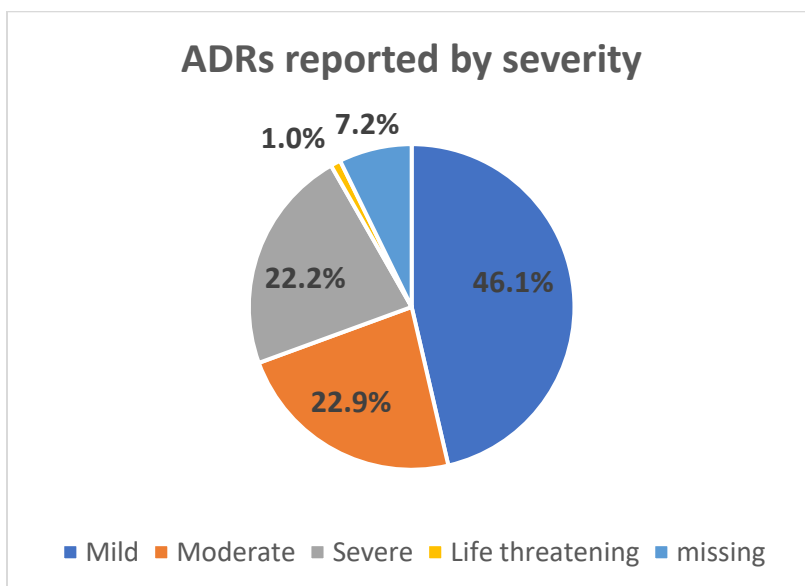


Figure 3: Grading of ADRs by severity, December 2021-December 2023, N=293.

4.7.2. Seriousness of ADRs

Of the total ADRs reported, only 21 of them were classified as serious. Of these, 12 cases were death, four were hospitalization, four were other medically important condition and one was life threatening.

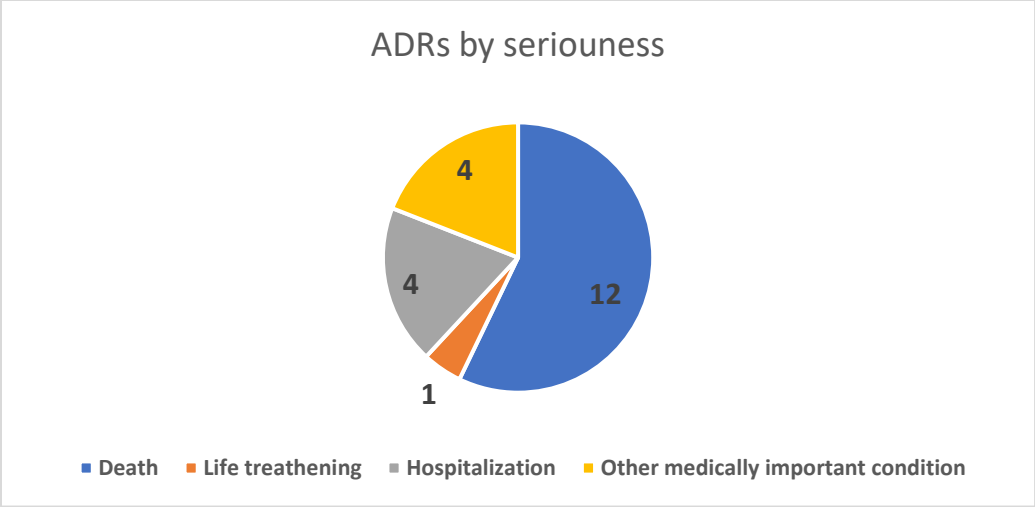


Figure 4: Grading of ADRs by seriousness, December 2021-December 2023, N=293.

4.8 Causality assessment of ADRs by TICs

Of the total ADRs reported, causality assessment by the TICs was made only to 169 ADRs. Of these, 74 (25.3%) were classified as probable/Likely, followed by possible (48, 16.4%) and certain (28, 9.6%) (table 7).

Table 7: Causality assessment classification by TICs, December 2021-December 2023, N=169.

Causality assessment by TICs	n (%)
Probable/Likely	74
Possible	48
Certain	28
Conditional/Unclassified	16
Unlikely	3

4.9 Causality assessment by EFDA

Of the reported 21 serious ADRs by the TICs, EFDA has conducted SAE investigation for 13 of the cases. In addition, of the investigated 13 cases, EFDA through its national pharmacovigilance Advisory Committee has conducted causality assessment and classification for 9 of the cases. However, due to information incompleteness, six of them were classified. Accordingly, three cases were classified as possible, two were classified as unassessible/unclassifiable, and one was classified as conditional/unclassified.

4.10 Outcomes of ADRs

As illustrated in Figure 5 below, almost half of the reported ADRs 145 (49.5%) were resolved, whereas it was unknown in 49 (16.7%) of the cases and 35 (11.9%) of the ADRs were resolving.

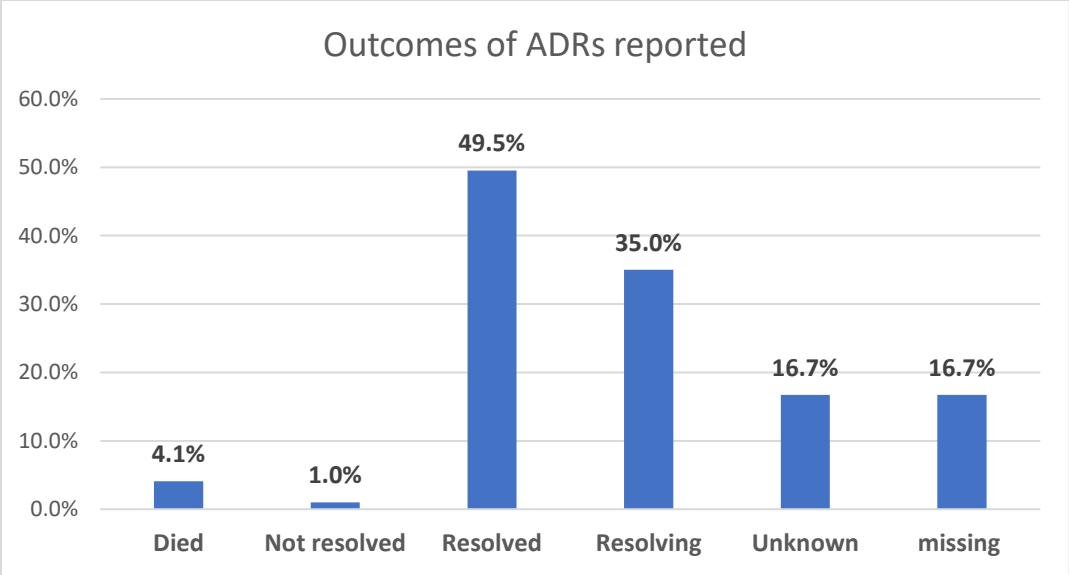


Figure 6: Outcome of reported ADRs, December 2021-December 2023, N=293.

4.11 Measures taken when the ADRS happened

As per the reports, the most common measures taken when ADRs happened were treatment of ADRs by giving medications 78 (26.6%) followed by discontinuing the suspected medication 44 (15.0%) and holding/adjusting the dose of the suspected medication and treatment of the ADR 36 (12.3%).

Table 7: Measures taken when ADRs happened, December 2021-December 2023, N=293.

Measures taken	n (%)
Hold regimen	1 (0.3)
Change regimen	4 (1.4)
Regimen discontinued	3 (1.0)
Hold suspected medication	16 (5.5)
Discontinue suspected medication	44 (15.0)
Change suspected medication	18 (6.1)
Treatment of ADR	78 (26.6)
Change suspected medication and treat ADR	8 (2.7)
Hold/adjust dose of suspected medication and treat ADR	36 (12.3)
Dose adjustment	13 (4.4)
Referral	3 (1.0)

Reassurance/Counselling	28 (9.6)
Reassurance and treat ADR	16 (5.5)
Missing	25 (8.5)

4.12 ADR reporters' information by TIC, Region, and Profession

Out of the total 67 TICs, 37 (55%) TICs/health facilities sent at least one ADR report in the past two years (Dec 2021-Dec 2023). Of these TICs, only three hospitals, namely ALERT Hospital (73 reports), St.Peter Hospital (51 reports) and Geda TIC (Adama Hospital) (29 reports), contributed more than half of the total reports 153 (52.2%) (Annex 1). In addition, Shenen Gibe Hospital, Dilla Teaching Hospital, and Gondar University Specialized Hospital reported 19 (6.5%), 12 (4.1%) and 11 (3.8%), respectively.

When we see the regional distribution of the reporting TICs, Addis Ababa was the top reporter where a total of 124 (42.3%) ADR reports were sent from its two TICs (ALERT and St. Peter hospitals) followed by Oromia 85 (29.0%), Amhara 28 (9.6%) and South Ethiopia 24 (8.2%) (table 8).

Table 8: Regional distribution of ADR reporting TICs, December 2021-December 2023, N=293.

Region/city administration	n (%)
Addis Ababa	124 (42.3)
South Ethiopia	24 (8.2)
Tigray	3 (1.0)
Afar	3 (1.0)
Amhara	28 (9.6)
Central Ethiopia	4 (1.4)
Diredawa	7 (2.4)
Harari	3 (1.0)
Oromia	85 (29.0)
Sidama	9 (3.1)
Somali	3 (1.0)

Regarding reporters profession, nurses were the top ADR reporters which accounts for 170 (58.0%), followed by physicians (103, 35.2%), pharamcists (16, 5.5%) and public health experts (4, 1.4%).

4.13 Comparison between the 2021 and 2023 ADR analysis reports

About the common types of ADRs reported, nausea and vomiting, gastritis and peripheral neuropathy were the top three ADRs in the 2021 report. But, in the 2023 report, peripheral neuropathy, nausea and vomiting and optic neuritis were the top three ADRs reported.

With respect to suspected medicine/regimen, Linezolid followed by cycloserine and all medicines in the regimen continued to be on the top in both the 2021 and 2023 analysis reports.

Regarding severity of the ADRs, most of the ADRs reported were mild (48% in 2021 and 46.1% in 2023) and the percentage remains comparable between the 2021 and 2023 analysis reports. Similarly, only 6.1% of the reported cases were labeled as serious in 2021 and 7.1% in the 2023 analysis report, and the percentage remains almost comparable.

About the outcome/consequence of the ADRs reported, it was resolved in 36.5% of the cases in 2021 report while 49.5% in the 2023 analysis report. Death remains comparable between the 2021 and 2023 reports, 3.8% and 4.1%, respectively.

Regarding the number of ADR reporting TICs, there is an increment from 13 TICs (19.4%) in 2021 to 37 TICs (55%). The top reporting TICs continued to be ALERT and St. Peter hospitals. However their contribution to the total reports reduced from 77.8% to 42.6% as other the number of reporting TICs increased and other TICs such as Geda, Shenen Gibe, Dilla and Gondar university hospitals contributed a good number.

5. Challenges/Limitations

- Poor data quality including incompleteness and accuracy
- Use of different versions of monthly AE line listing forms (e.g. some versions have weight others do not).
- Use of non-uniform format to write date, month and year
- Repetition of reports in two or more months
- Invalid reports (ADR reports without at least the ADR description)
- Delay in reporting ADRs
- Not reporting minor ADRs
- Less attention by the hospital management on aDSM implementation

6. Conclusion and Recommendation

6.1. Conclusion

Of the total patients who were reported to have ADRs, the most common ADRs were peripheral neuropathy, nausea and vomiting, optic neuritis, Gastritis/dyspepsia, Drug induced liver injury (DILI), and Arthralgia/arthritis. Based on system affected, close to half of the ADR reports were GI and neurologic related problems. Linezolid was the most suspected medicine for the ADRs reported followed by cycloserine and long-term regimen (LTR). The majority of the reported cases were mild cases. Of the total ADRs having causality classification by the TICs, a quarter of it were classified as probable/Likely followed by possible and certain. Regarding the outcome of ADRs, almost half of the reported ADRs were resolved.

6.2. Recommendations

Based on the findings, the following recommendations were forwarded.

- The implementation of aDSM program should be strengthened at TICs throughout the country to better ensure patient safety on DR-TB treatment.
- Continuous training and supervision of professionals working in TICs should be conducted to increase reporting rate and quality of reports.
- EFDA should revise and distribute uniform AE line listing form to TICs for consistency and data quality.
- Data handling system should be strengthened at EFDA and reporting TICs including digitization.
- EFDA should improve feedback mechanism to reporting professionals and TICs.

References

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4. WHO Active tuberculosis drug-safety monitoring and management (aDSM), Framework for implementation, 2015, Geneva.
5. WHO, Companion handbook to the WHO guidelines for the programmatic management of drug-resistant tuberculosis, 2014, Geneva.

Annex 1: ADR reporter TICs

TICs	Frequency	Percent
Adigirat TIC	2	.7
Bule Hora University Teaching Hospital	4	1.4
Butajira Hospital	4	1.4
Chiro General Hospital	2	.7
Debarik Hospital	6	2.0
Debre Tabor Hospital	2	.7
Debre Birhan Hospital	2	.7
Dembi Dolo University Hospital	3	1.0
Dil Chora Hospital	7	2.4
Dilla Teaching Hospital	12	4.1
Dubti Hospital	3	1.0
Akisita	1	.3
Fiche General Hospital	2	.7
Gara Muleta General Hospital	1	.3
Geda TIC	29	9.9
Gimbi Hospital	1	.3
Gode General Hospital	3	1.0
Gondar University Specialized Hospital	11	3.8
Jegol MDR/TB center	2	.7
Jinka Hospital	4	1.4
Limmu Kossa	4	1.4
Nejo General Hospital	1	.3
Alert Hospital	73	24.9
Robe Didea General Hospital	6	2.0
Shenen Gibe General Hospital	19	6.5
Shashemene Health center	1	.3
St.Peter Hospital	51	17.4
Teferra Hailu Memorial Hospital	1	.3
Tulu Bolo TIC	2	.7
Woldiya Hospital	3	1.0
Yirgalem General Hospital	9	3.1
Ambo general Hospital	4	1.4
Aribaminch Hospital	8	2.7
Ataye Hospital	2	.7
Axum St.Marry TIC	1	.3
Bale Goba TIC	1	.3
Bishofitu General Hospital	6	2.0