High Prevalence of Adverse-drug-effects of Multi-drug-resistant Tuberculosis Treatment in Two Referral Hospitals in Uganda

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Abstract

Background

Multi-drug resistant tuberculosis (MDR-TB) treatment involves toxic drugs that cause adverse-drug-effects (ADEs), which are life threatening and may lead to death if not well managed. In Uganda, the prevalence of MDR-TB is increasingly high and about 95% of the patients are on treatment. However, little is known about the prevalence of ADEs among the patients on MDR-TB medicines. We therefore estimated the prevalence of ADEs of MDR-TB drugs and factors associated with ADEs in two health facilities in Uganda.

Methods

Between March and November 2021, we conducted a retrospective cohort study of MDR-TB patients enrolled at Mulago national referral and Mbarara regional referral hospitals in Uganda. We reviewed files of MDR-TB patients enrolled between January 2015 and December 2020. We extracted data on ADEs, defined as irritative reactions to MDR-TB drugs. We conducted descriptive analysis and modified Poisson regression analysis to determine factors associated with ADEs.

Results

A total of 856 files were reviewed. Overall, 369 (43.1%) of 856 patients had ADEs and 145 (17%) of 856 suffered from more than one. The most recorded effects were: joint pain (244/369 (66%)); hearing loss (75/369(20%)); and vomiting (58/369(16%)). Patients started on the 24 months regimen (adjusted prevalence ratio (adj.PR=1.4, 95%; 1.07, 1.76) and individualized regimens (adj.PR=1.5, 95%; 1.11, 1.93) were more likely to suffer from ADEs. Lack of transport for clinical monitoring (adj.PR=1.9, 95%; 1.21, 3.11); alcohol consumption (adj.PR=1.2, 95%; 1.05, 1.43), and receipt of directly-observed-therapy from peripheral health facilities (adj.PR=1.6, 95%; 1.10, 2.41) were significantly associated with experiencing ADEs. However, patients who received food supplies (adj.PR=0.61, 95%; 0.51, 0.71) were less likely to suffer from ADEs.

Conclusion

Adverse-drug-effects were high among MDR-TB patients and joint-pains was the commonest effect. Interventions such as provision of food supplies, transport and consistent counselling on alcohol consumption to patients at initiation treatment facilities may reduce ADEs

Background

Globally, 4.1% and 19% of new and retreatment tuberculosis (TB) cases respectively (1) were estimated to have rifampicin resistance and started on second line anti-TB treatment (2, 3). The treatment lasts for 18 to 24 months, 6 months of injectable and the other months the patient will receive orals (4), though they are newer oral regimens. The treatment involves toxic drugs that cause adverse-drug-effects (ADEs),

which are life threatening and may lead to death if not well managed (1). Studies have estimated the prevalence of adverse drug effects of second-line anti TB to be between 30%- 90% (5–7). A study conducted in Ethiopia found that 89.9% of the MDR-TB on treatment had ADEs (8).

In 2019, an estimated 88,000 people fell ill with TB in Uganda, and an estimated 15,600 people died (9). Furthermore, in 2019, of the estimated 1,500 drug-resistant TB (DR-TB) cases, only 559 were diagnosed, started on treatment and 96% of the patients who started treatment in 2017 completed treatment (10). It's was also estimated that 57% of the patients that were started on second-line anti-TB treatment during 2016 had adverse drug effects (4). This may have been responsible for the poorer treatment success rates, prolonged periods of morbidity and higher mortality. The multi-drug tuberculosis (MDR-TB) guidelines where developed and they state that monthly clinical check-ups are done for all patients started on treatment (4). This is to monitor adverse drug effects that are caused by the second-line drugs.

Management of ADEs of MDR-TB treatment

MDR-TB patients are started on second-line anti-TB treatment that lasts for 18 to 24 months or 9–12 months. The treatment regimen may include: 18–24 months; 6km, lfx, eto, csz/18lfx, eto, csz, or the short-term regimen will last for 9–12 months; 4–6 Km-Mfx-Pto-Cfz-Z-H_{high}-dose-E/5Mfx-Cfz-Z-E. (Km = Kanamycin; Mfx = Moxifloxacin; Pto = Prothionamide; Cfz = Clofazimine; Z = Pyrazinamide; Hhigh-dose = high-dose Isoniazid; E = Ethambutol) (4, 11, 12). These drugs are taken for longer periods, they are also highly toxic and cause adverse drug effects if patients are not monitored and well managed (13).

Adverse drug effects can be managed through constant monitoring of the patient and minimum modification in the treatment regimen (14). Studies have shown that Km is the most substituted drug in the regimen (15). Guidelines state that MDR-TB patients should receive MDR-TB treatment under the directly observed therapy (DOT) (4). Where patients are admitted on start of treatment for a period of 2 weeks to a month or when the culture convert and discharged to the community where they continue to receive treatment under DOT from a lower facility near their home of their choice.

2% of MDR-TB patients stopped treatment and 30% required removal of the suspected drugs in the regimen due to ADEs because they were monitored daily while taking their treatment (16). If the patients are mismanaged, it can easily cost them their life or permanent disabilities like hearing loss. It is important to understand and know the number of people affected with ADEs of second-line anti -TB treatment. However, there is relatively limited research about prevalence and incidence of ADEs related to MDR –TB treatment most of the studies have focused on the factors associated with the ADEs. Therefore, this study determined and described the prevalence of the ADEs of the second-line drugs and factors associated with them.

Methods

Aim of the study

To determine the prevalence and factors associated with advance drug effects of MDR-TB treatment using secondary data in Mulago national referral hospital and Mbarara regional referral hospital, Uganda.

Study Design:

The study was a retrospective cohort study that employed quantitative research methods among MDR-TB patients receiving or who received second line anti-TB drugs. This involved reviewing records of MDR-TB patients enrolled on second line TB drugs. Such records included: drug-resistant management information system (DR-TB MIS) that has most of the patient information, and the patients' files which are kept at the initiation facilities in locked cabinets.

Study Setting

The study was conducted in Mulago national referral hospital (NRH) (TB ward i.e. wards 5 and 6) and Mbarara regional referral hospital (RRH) (TB ward) in Uganda. Mulago NRH is the largest public hospital in Uganda. It's located on Mulago Hill the northern part of Kampala, less than five km from Kampala's central business district. The MDR-TB site in Mulago NRH serves the central region that includes districts such as Mpigi, Luwero, Kayunga, Buikwe, Kampala divisions, and Wakiso. It leads the national MDR-TB panel and has the greatest number of patients initiated on treatment. Mbarara RRH is located in Mbarara district, Ankole sub-region within the central business district. It is located approximately 268 km south west of Kampala the capital city of Uganda by road. The hospital has an MDR-TB site that serves districts such as Mbarara, Isingiro, Bushenyi, Kiruhura, Ibanda, Ntugamo, Sheema, and Mitooma. The hospital serves a population of over four million people and has a bed capacity of over 350 beds. Both facilities are responsible for coordinating and training follow up facilities (FUFs) in administering DOTs to the MDR-TB patients in their regions respectively. Both Mulago NRH and Mbarara RRH were selected because of the great numbers of MDR_TB patients that are seen at these two facilities. They also had updated records of their MDR-TB patients compared to other MDR-TB facilities.

Study Population

The study population comprised of all confirmed MDR-TB patients who were started on second line anti TB treatment during the period of 1st Jan, 2016 and 31st Dec, 2020. These patients included; those documented that were started on treatment and completed, and those that were still on treatment. This period was chosen because the MDR-TB program had fully been initiated in these two facilities. The study excluded all patients that were transferred into Mulago NRH-TB and Mbarara RRH. This was because review of these patients' records is done at their former initiation site which may have caused double counting. Patients who were identified as rifampicin resistant and started on second line anti-TB treatment and then later returned to first line if any, were included for only the period they had the treatment.

Data Management And Analysis

Data collection/ Extraction - Procedure

Data was extracted from the MDR-TB MIS a DHIS 2 platform; by downloading it into Ms-excel. In case of any missing data, data was extracted from the patients' files so that it would fill the missing gaps in the data in order to have a complete data set in Ms-excel. The data was then exported to Stata v14 where data cleaning was done. This was done by identifying the duplicates and transfer ins from other sites which were dropped from the data set.

Data analysis

Descriptive, Bivariate and Multi-variable analysis

Quantitative data was analyzed using Stata v.14 software; data was described first using frequencies, percentages, median and standard deviation for the demographic and clinical factors. This determined prevalence of ADEs. To determine the factors associated with ADEs of taking second line anti-TB drugs, modified poison regression that provides prevalence ratio was used. Prevalence ratios were used because they don't overestimate the prevalence unlike the odds ratios if the prevalence of the outcome is above 10%. This was used to identify the variables to be included in multivariable analysis providing prevalence ratios and p-values too. Variables with a p value less than 0.20 were selected for multi-variable analysis.

Multi-collinearity was done and there were no variables removed due to multi-collinearity, since they had a p-value less than 0.40. Then these variables selected had their prevalence ratios adjusted for multivariable analysis. Forward and backward elimination was used to select the variables after considering the p-value of less than 0.05 to come up with a perfect model.

Results

Descriptive statistics

A total of 856 MDR-TB patients' data was extracted with 369 (43.1%) patients with ADEs. Most MDR-TB patients were male 543 (63.4%), with most of the patients aged 25–34 291 (34%) where the mean age was 34 years (SD of 12.4years), majority of the patients had a weight of 46-55.9kg 320 (37.4%) with the mean weight of 48.3kg (SD of 25.12kg). Most of the patients were single 354 (41.4%), working 633 (73.9%) in informal employment 589 (92.9%). The details are shown in Table 1 below.

Most of the MDR-TB patients were new cases 454 (53%) and mostly co-infected with HIV 489 (57.7%). Majority of the patients were started on long term regimen (LTR) 457 (53.4%) where most of them received their treatment from follow-up facilities (FUFs) 744 (86.9%). Most of them had attended their clinical visits 505 (59%) and received food supplies 690 (80.6%) and transport 767 (89.6%). Most of them

adhered to treatment 565 (66%) and few of them took alcohol while on treatment 287 (33.5%). As seen in Table 1.

Table 1
Social –demographic factors for the MDR-TB patients in Mulago NRH and Mbarara RRH

Characteristics	Frequency (Percentage)
	(n = 856)
Age	
0–14	39 (4.6%)
15–24	133 (15.5%)
25–34	291 (34%)
35–44	230 (26.9%)
45–54	114 (13.3%)
55+	49 (5.7%)
Weight	
1-29.9 kg	77 (9%)
30-35.9kg	27 (3.1%)
36-45.9kg	189 (22.0%)
46-55.9kg	320 (37.4%)
56-69.9kg	201 (23.5%)
70kg+	42 (4.9%)
Sex	
Male	543 (63.4%)
Female	313 (36.6%)
Marital Status	
Single	354 (41.4%)
Married	350 (40.9%)
Separated	152 (17.8%)
Occupation	
Working	633 (73.9%)
Not working	223 (26.1%)
Form of employment	

Characteristics	Frequency (Percentage)
Formal	45 (7.1%)
Informal	589 (92.9%)
Health facilities	
Mulago NRH	684 (79.9%)
Mbarara RRH	172 (20.1%)
Year of treatment	
2015	114 (13%)
2016	166 (19%)
2017	136 (16%)
2018	166 (19%)
2019	182 (21%)
2020	92 (11%)
Co-Infected with HIV	
No	367 (42.9%)
Yes	489 (57.1%)
Regimen	
Short Term Regimen	117 (20.7%)
Long Term Regimen	457 (53.4%)
Individualised regimen	162 (18.9%)
modified Short Term Regimen/ Standard regimen	60 (7.0%)
TB Registration Group	
New	454 (53.0%)
Retreatment	402 (47.0%)
Place of Directly Observed Treatment	
Initiation Facility based	112 (13.1%)
Follow Up Facility	744 (86.9%)
Received Food Supplies	
No	166 (19.4%)

Characteristics	Frequency (Percentage)
Yes	690 (80.6%)
Received Transport	
No	89 (10.4%)
Yes	767 (89.6%)
Taking alcohol	
No	569 (66.5%)
Yes	287 (33.5%)
Adherence to treatment	
Missed dozes	291 (34%)
All dozes taken	565 (66%)
Clinical Visits made	
Missed	351 (41%)
All Attend	505 (59%)

Prevalence of ADEs among MDR-TB patients on second line anti TB treatment.

Out of 856 MDR-TB patients, 369/856 (43.1%) had ADEs out of these 145/856 (16.9%) suffered from more than one ADE; where 106/856 (12.4%) suffered from two ADEs, 27/856 (3.2%) suffered from three ADEs and 12/856 (1.4%) suffered from more than three ADEs.

Most of the patients 244/856 (29%) suffered from arthralgia; 204/244 (83.6%) where mild, 38/244 (15.6%) where moderate and only 2/244 (0.8%) were severe. 75/856 (9%) of the patients suffered from ototoxicity; 19/75 (25.3%) where mild, 18/75 (24%) where moderate, 24/75 (32%) where severe and 14/75(18.7%) where life threatening. Patients that suffered from Peripheral neuropathy (29/856 (3%)), dermatologic (36/856 (4%)), nausea/ Vomiting (58/856 (7%)), Psychiatric/ psychosis (15/856 (2%)), Vision change (17/856 (2%)) and gastrointestinal (37/856 (4%)) where mild, moderate and severe. Patients that suffered from gynecomastia (7/856 (3%)) where mild and moderate. Patients that suffered from Hypothyroidism and Hepatotoxicity had only moderate effects as seen in the Table 2.

Table 2
A table showing percentages of adverse drug effects for the MDR-TB patients on second line anti-TB drugs.

ADE	Mild	Moderate	Severe	Life threatening	Total
Arthralgia	204 (83.6%)	38 (15.57%)	2 (0.8%)		(29%) 244/856
Peripheral Neuropathy	22 (75.9%)	6 (20.7%)	1 (3.4%)		(3%) 29/856
Gynecomastia	5 (71.4%)	2 (28.6%)			(1%) 7/856
Dermatologic	12 (33.3%)	22 (61.1%)	2 (5.5%)		(4%) 36/856
Ototoxicity	19 (25.3%)	18 (24%)	24 (32%)	14 (18.7%)	(9%) 75/856
Gastrointestinal	14 (37.8%)	22 (59.4%)	1 (2.7%)		(4%) 37/856
Hypothyroidism		6 (100%)			(1%) 6/856
Hepatotoxicity		1 (100%)			(0.1%) 1/856
Nausea / Vomiting	17 (29.3%)	37 (63.8%)	4 (6.9%)		(7%) 58/856
Psychiatric / psychosis	5 (33.3%)	4 (26.7%)	6 (40%)		(2%) 15/856
Vision change	14 (82.3%)	2 (11.8%)	1 (5.8%)		(2%) 17/856

To determine the factors associated with ADEs of DR-TB treatment among DR-TB patients in Mulago national and Mbarara regional referral hospitals in Uganda.

From the Table 3 below; patients that received adherence enablers were 39% less likely to suffer from ADEs compared to those that did not get the enablers at Adj PR 0.39; 95% CI (0.51–0.71). Patients that did not received transport to attend their monthly clinical visits were 90% more likely to suffer from ADEs compared to those receiving the transport Adj PR 1.9; 95% CI (1.36-3.00). The patients that abused drugs 20% of them were more likely to suffer from ADEs compared to those that did not at Adj PR 1.2; 95% CI (1.05–1.43).

Patients that received their treatment from follow up facilities were 60% more likely to suffer from ADEs compared to those that received their daily treatment from the initiation facilities at Adj PR 1.6; 95% CI (1.10–2.41). Patients who received the 24 months' regimen were 40% more likely to suffer from ADEs compared to those that were on the short-term regimen at Adj PR 1.4; 95% CI (1.07–1.76) controlling for other factors. Patients that received an individualized regimen were 50% more likely to suffer from ADEs compared to those that were on the short-term regimen at Adj PR 1.5; 95% CI (1.11–1.93) controlling for other factors.

Table 3
A table showing unadjusted and adjusted prevalence ratios for factors associated with adverse drug effects for the MDR-TB patients on second line anti-TB drugs.

Variables	No ADEs	ADEs	Unadjusted		Adjusted PR	
			PR	95% CI	PR	95% CI
Number of Patients	487 (56.9%)	369 (43.1%)				
Age						
0–14	29 (5.9%)	10 (2.7%)	1			
15–24	78 (16%)	55 (14.9%)	1.6	(0.91–2.85)		
25–34	162 (33.3%)	129 (34.9%)	1.7	(0.99–2.99)		
35–44	128 (26.3%)	102 (27.6%)	1.7	(0.99–3.01)		
45–54	61 (12.5%)	53 (14.3%)	1.8	(1.02–3.21)		
55+	29 (5.9%)	20 (5.4%)	1.5	(0.84–2.99)		
Weight						
1-29.9 kg	54 (11.1%)	23 (6.2%)	1			
30-35.9kg	18 (3.7%)	9 (2.4%)	1.1	(0.59–2.11)		
36-45.9kg	103 (21.1%)	86 (23.3%)	1.5	(1.04–2.21)		
46-55.9kg	171 (35.1%)	149 (40.4%)	1.5	(1.08–2.23)		
56-69.9kg	117 (24.0%)	84 (22.7%)	1.3	(0.95–2.04)		
70kg+	24 (4.9%)	42 (4.9%)	1.4	(0.88–2.34)		
Sex						
Male	316 (64.9%)	227 (61.5%)	1			
Female	171 (35.1%)	142 (38.5%)	1.1	(0.92–1.27)		
Marital Status						

Variables	No ADEs	ADEs	Unadjusted		Adjusted PR	
			PR	95% CI	PR	95% CI
Single	201 (41.3%)	153 (41.5%)	1			
Married	199 (40.9%)	151 (41%)	0.9	(0.84–1.18)		
Separated	87 (17.9%)	65 (17.6%)	0.98	(0.79–1.23)		
Occupation						
Working	360 (73.9%)	273 (73.9%)	1			
Not working	127 (26.1%)	96 (26.1%)	0.9	(0.83–1.18)		
Form of employment						
Formal	22 (6.1%)	23 (8.4%)	1			
Informal	339 (93.1%)	250 (91.6%)	0.8	(0.61–1.12)		
Received Food supplies						
No	74 (15.2%)	92 (24.9%)	1		1	
Yes	413 (84.8%)	277 (75.1%)	0.7	(0.61–0.85)	0.61	(0.51–0.71) ***
Received Transport						
Yes	69 (14.2%)	20 (5.4%)	1		1	
No	418 (85.8%)	349 (94.6%)	2	(1.36-3.00)	1.9	(1.21–3.11) ***
Drug Abuse (Alcohol)						
No	350 (71.9%)	219 (59.4%)	1		1	
Yes	137 (28.1%)	150 (40.6%)	1.3	(1.16–1.58)	1.2	(1.05–1.43) **
Co-Infected with HIV						
No	211 (43.3%)	156 (42.2%)	1			
Yes	276 (56.7%)	213 (57.7%)	1.02	(1.07–1.19)		

Variables	No ADEs	ADEs	Unadjusted		Adjusted PR	
			PR	95% CI	PR	95% CI
Regimen						
STR	121 (24.8%)	56 (15.2%)	1		1	
LTR	236 (48.6%)	221 (59.9%)	1.5	(1.20–1.93)	1.4	(1.07–1.76) *
IND	89 (18.2%)	73 (19.8%)	1.4	(1.08–1.87)	1.5	(1.11–1.93) **
m STR/STD	41 (8.4%)	19 (5.1%)	1.001	(0.65–1.53)	1.1	(0.69–1.64)
Adherence to treatment						
Missed dozes	179 (36.8%)	112 (30.3%)	1			
All dozes taken	308 (62.2%)	257 (69.7%)	1.2	(0.99–1.40)		
Clinical Visits made						
Missed	192 (39.4%)	159 (43.1%)	1			
All Attend	295 (60.6%)	210 (56.9%)	0.9	(0.78–1.07)		
Place of DOT						
Initiation Site	85 (17.4%)	27 (7.3%)	1		1	
Follow Up Facility	402 (82.6%)	342 (92.7%)	1.9	(1.36–2.67)	1.6	(1.10–2.41) *
TB Reg Group						
New	255 (52.4%)	199 (53.9%)	1			
Retreatment	232 (47.6%)	170 (46.1%)	0.9	(0.82–1.12)		

*** - p < 0.05 ** - p < 0.01 *** - p < 0.001**

Discussion

Summary of the results

The study determined the prevalence of adverse drug effects in two referral hospitals where 369/856 (43.1%) MDR-TB patients had ADEs and 145/856 (16.9%) suffered from more than one ADE. Furthermore, the study determined the factors associated with ADEs and these included; patients started on the 24 months regimen (LTR) and individualized regimens were more likely to suffer from ADEs. Lack of transport for clinical monitoring; alcohol consumption, and receipt of directly-observed-therapy from peripheral health facilities were significantly associated with experiencing ADEs. However, patients who received food supplies were less likely to suffer from ADEs.

Prevalence Of Ades

The purpose of the study was to determine the prevalence and factors associated with ADEs of MDR-TB treatment in Mulago NRH and Mbarara RRH among MDR-TB patients. The above results showed that out of 856, 369 (43.1%) of the MDR-TB patients suffered from ADEs; and 16.9% suffered from more than 2 adverse drug effects. Compared to the prevalence of ADEs of MDR-TB treatment in India of 57.6%, this is higher than that of 43.1% found in this study because of the high prevalence of MDR-TB patients in India. (17).

In this study, it was found that patients that were co-infected especially with HIV (57.7%) suffered ADEs from MDR-TB treatment. This may be because of the high pill burden that the patient has and also drug interaction of the two diseases. The study showed that 57.7% of the patients were HIV/MDR-TB patients having ADEs, these results were lower compared to the finding of a systematic review that showed 83.7% of the HIV/MDR-TB patients suffering from ADEs (18).

In this study, most patients had mild forms of ADEs (83.6%) and the most suffered ADEs were joint pains (arthralgia) and hearing loss (ototoxicity) which were mainly caused by injectable drugs such as kanamycin. Furthermore, hearing loss caused life threatening forms of ADE to 14 patients in the study. This was because Kanamycin normally affects the ears. These results are similar to a study (19) that showed patients on second line anti-TBs mostly suffered from joint pains (arthralgia). Ototoxicity was the most severe ADE with 32% of the patients having it these results are higher than a study that showed that 44% of them having ototoxicity and 14% had to change treatment because of the severity (20).

Factors Associated With Ades

In this study, age was not statistically significant to ADEs which was contrary to the findings that showed age was significant especially those that were 40 years above (21). This because it was case-control study and it had a higher sample size compared to this one. The most affected age groups were (25–34, 35–44) with a mean of 34 years and 12.4 SD with about 61.5% being males with ADEs. The reason for this, is because these are the most economically active age groups that strive hard to make ends meet. Therefore, the chances of exposure are high since they interact with individuals that smoke, work in

mines which are risk groups for TB. Uganda is named among the TB/HIV high burdened countries according to WHO (9).

Provision of food to patients on second-line anti-TB treatment helps reduce the risk of ADEs. This is because taking MDR-TB drugs after a meal or food reduces ADEs such as nausea and vomiting and irritations in the stomach. Since most MDR-TB patients may not be able to afford a meal daily, it's important to provide food to them to reduce the risk of ADEs from the drugs. The study findings were similar to findings that showed providing adherence enablers especially food was statistically significant to adherence to treatment and good treatment outcome (22).

The findings in this study showed that patients taking alcohol were 20% more likely to suffer from ADEs because the treatment caused them depression and a lot of pain. A study showed that 14% of the patients were likely to have depression and sleeping disturbance as ADEs while on MDR-TB treatment which is similar to the findings in this study (23).

The study findings further showed that patients that were taking long term regimen (18–24 months) and individualized regimens for MDR-TB were significantly associated with ADEs. This is contrary to the study findings that showed MDR-TB treatment regimens weren't associated to ADEs (24). Though similar results of patients taking kanamycin which is being used in the long term regimen were 98% more likely to suffer from ototoxicity (19).

Study Limitations

There were no major issues with missing data because in-case information was missing from the system patient files were checked-up and the missing data was then filled. Missing data would reduce the statistical power of the study and it would lead to bias in the study results, skewing estimates away from the true parameter values.

The study used secondary data which may not have included some independent variables of interest such as wealth index as compared to using a questionnaire. A questionnaire would have captured extra variables on the factors associated with ADEs of MDR-TB treatment. The data were collected at a point in time hence casual inference cannot be assured.

The study interviewed patients on their experience of taking MDR-TB drugs where they may have been issues of recall bias. This was solved by probing during the in-depth interviews that helped the patients to recall some of the scenarios they went through.

The study didn't put into consideration the levels of care for the different health facility since only referral hospitals were used. This created selection bias were if the other levels such as hospitals were included in the study the results may have been different.

It may be difficult to attribute all the recorded ADEs to second-line anti-TB drugs. The study did not assess ADEs that were; due to other drugs e.g., ARVS, due to TB itself or due to other diseases or due to the nocebo effect. Therefore, further studies should be conducted to assess which ADEs are due to ARVs, TB, other diseases and nocebo effect. Furthermore, the study didn't know look at the pharmaceutics of the drugs used in second line anti-TB treatment. This would have enabled us to understand which drugs are associated with the ADEs.

Recommendation

To reduce the prevalence of acquiring ADEs while on MDR-TB treatment, emphasis should be put to provision of transport and nutritious food to all MDR-TB patients. This encourages patients to adhere to treatment because the MDR-TB drugs are taken after having a meal which allows easy absorption of the drugs into the body. The patient centered care (PCC) approach should be fully emphasized because it helps patients especially those with ADEs to stay on treatment and cure. Therefore, the government should train the health-workers in the PCC approach in order to help patients with ADEs adhere to treatment.

Conclusion

The overall prevalence of adverse drug effects among MDR-TB patients is high at 43.1% with about 17% having more than one ADE. Provision of food supplies and transport to patients where statistically associated with ADEs where patients who received them were less likely to get ADEs. Patients taking alcohol while on treatment had high chances of getting ADEs.

Declarations

Ethics Approval and consent

The study protocol was submitted to the institution review board (IRB) of Makerere University School of Public Health Higher Degrees Research and Ethics Committee (HDREC) whose clearance letter (IRB letter of approval) has been attached in the supplementary materials that cleared the study. The study involved review of records without involving patient interaction, so individual patient consent was deemed unnecessary according to national regulations and HDREC. Then administrative permission to access MDR-TB patients' data was sought from the Mbarara RR and Mulago NR hospital administrators. All methods were carried out in accordance to the study protocol and within the relevant guidelines and regulations provided by the IRB and national council for research.

Use of MDR-TB identification numbers was done to ensure confidentiality of the patients' information during data extraction. Therefore, the names of the patients were not extracted but only the MDR-TB number of that file. The data extracted was password protected and also backed up on an external hard drive that was also password protected and the password was known to only the researcher.

Consent for publication

Not applicable

Availability of data and materials

The dataset extracted and analyzed during the study are not publicly available due to restricted access of patient data from the MDR-TB database from ministry of health Uganda/ national TB and leprosy program but the data is available from the corresponding author on reasonable request.

Competing interests

The authors declare that they have no competing interests.

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Authors' contributions

PM conceived, led the design and development of the study proposal. He supervised data collection, led the data analysis and drafted the manuscript.

CN and AK participated in data extraction of MDR-TB patients from the DR-TB MIS and patients files that made up the data set for analysis.

MM, RN, PK, SK, NK made substantial contributions to the conceptualization and design of the study, data interpretations, and writing the manuscript. All authors read and approved the final version of the manuscript.

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