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Risk factors for drug-resistant tuberculosis in the cattle-corridor region of south-western Uganda: a case-control study

Mathias Ngobi Bogere

ngobikb@yahoo.com

Busitema University

Maxwell Otim Onapa

Busitema University

Jimmy Patrick Alunyo

Busitema University

Sarah Rachael Akello

Busitema University

Grace Nabaggala Ssanyu

Busitema University

Patience Birungi

Busitema University

Micheal Madenje

Busitema University

Benard Charles Okalebo

Busitema University

Sydney Nsubuga

Busitema University

Deborah Aujo

Busitema University

Benon Wanume

Busitema University

Alex Mulindwa

National TB and Leprosy Programme

Amanya Geoffrey

National TB and Leprosy Programme

Mpagi Luwaga Joseph

Busitema University

Peter Olupot-Olupot

Busitema University

Joseph KB Matovu

Busitema University

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Abstract

Background

Drug-resistant tuberculosis remains a major threat to tuberculosis control in high-burden settings. In Uganda, the Ankole region of south-western Uganda lies within a cattle corridor characterised by rural livelihoods, close human–animal interaction, and variable access to tuberculosis services. Despite persistent notification of drug-resistant tuberculosis in the region, context-specific evidence on individual, social, community, and health-system risk factors remains scarce. We aimed to identify factors associated with drug-resistant tuberculosis among adults diagnosed with tuberculosis in the Ankole region.

Methods

We did a 1:3 individually matched case-control study among adults aged 18 years or older diagnosed with tuberculosis in public health facilities in Ankole region between Jan 1, 2023, and Sept 30, 2024. Cases were all eligible participants with drug-resistant tuberculosis confirmed using WHO-recommended molecular tests. For each case, up to three controls with drug-susceptible tuberculosis were systematically sampled from facility tuberculosis registers and matched by health facility, sub-county, sex, and age within ± 2 years. Data were collected using a structured questionnaire. We used generalised linear models with a log link to estimate adjusted prevalence ratios.

Results

We enrolled 131 participants: 34 cases and 97 controls. Drug-resistant tuberculosis was associated with previous tuberculosis treatment (adjusted prevalence ratio [aPR] 2·0, 95% CI 1·3–3.0; p = 0.001), chronic medical conditions (aPR 1.8, 95% CI 1.2–2.6; p = 0.001), daily alcohol consumption (aPR 2.3, 95% CI 1.7–3.0; p < 0.001), and low-income affecting access to tuberculosis care (aPR 1.5, 95% CI 1.1–2·0; p = 0.004). Tobacco smoking was inversely associated with drug-resistant tuberculosis (aPR 0.2, 95% CI 0.1–0.8; p = 0.019).

Discussion

Drug-resistant tuberculosis in Ankole was associated with previous treatment exposure, chronic illness, daily alcohol use, and financial barriers. Tuberculosis control in cattle-corridor settings should integrate retreatment follow-up, chronic disease care, alcohol-use interventions, and social protection.

Background

Tuberculosis remains one of the world's leading infectious causes of death, and its control is increasingly threatened by antimicrobial resistance. Despite advances in prevention, molecular diagnosis, and treatment, the global burden of tuberculosis has risen since 2021, with about 10 million people developing tuberculosis each year and approximately 1·5 million deaths annually (WHO, 2024a). Drug-resistant tuberculosis (DR-TB), particularly multidrug-resistant and rifampicin-resistant tuberculosis (MDR/RR-TB), is a major public health threat because it requires longer, more complex, and more costly care, and is associated with poorer treatment outcomes than drug-susceptible tuberculosis [1], [2].

The emergence of DR-TB reflects failures across the tuberculosis care pathway. Resistance may arise from inadequate treatment, suboptimal dosing, interrupted therapy, poor adherence, and incomplete treatment, but transmission of already resistant strains is also increasingly recognised as an important driver[1][3]. In 2022, an estimated 410,000 people developed MDR/RR-TB globally, yet only 175,650 were diagnosed and started on treatment, leaving a large gap between need and access to effective care [1]. These gaps are particularly concerning settings where diagnostic coverage, treatment support, and follow-up systems remain limited.

The burden of tuberculosis and DR-TB is disproportionately concentrated in Africa. Although the WHO African Region accounts for a smaller proportion of the global population, it carries a substantial share of tuberculosis disease and mortality, including thousands of people with DR-TB each year [1], [4]. Uganda is among the high HIV/TB burden countries, with an estimated 96,000 people developing tuberculosis annually and about two in every 100 people with tuberculosis having drug-resistant disease[5][1]. However, national estimates may obscure local variation, particularly in rural and underserved settings where access to rapid drug-susceptibility testing is incomplete.

The Ankole region of south-western Uganda is one such setting. Situated within Uganda's cattle corridor, Ankole has consistently been reported among regions with a high burden of DR-TB. In the 2023/2024 programme period, 83 people with DR-TB were estimated in the region, but only 52 were diagnosed, despite GeneXpert access of 69.1% among people with presumptive tuberculosis [5], [6]. This diagnostic gap suggests that people with DR-TB may be missed or diagnosed late, with implications for ongoing transmission, delayed initiation of effective treatment, and poor outcomes.

Cattle-corridor settings present distinctive epidemiological and social conditions that may shape DR-TB risk. These settings are characterised by cattle keeping, rural livelihoods, close human animal interaction, household crowding, long working hours, movement for grazing or income, and variable access to health services. Previous work in pastoral communities like Karamoja in North Eastern Uganda has suggested that mobility, delayed health seeking, treatment interruption, and barriers to continuous care may increase vulnerability to tuberculosis and DR-TB [7]. However, evidence from predominantly nomadic settings such as Karamoja may not be directly generalisable to Ankole, where many cattle-keeping communities are more sedentary and differ in livelihood patterns, culture, environment, and access to services.

DR-TB is therefore not only a microbiological or clinical problem; it is also a social and health-system problem. The risk of developing, transmitting, and surviving tuberculosis is shaped by the conditions in which people live, work, seek care, and receive treatment [8]–[10]. Individual factors such as previous tuberculosis treatment, chronic illness, alcohol use, and adherence challenges may interact with social and community factors, including poverty, stigma, inadequate household support, mobility, and community perceptions. These risks may be further amplified by health-system barriers such as delayed diagnosis, limited access to drug-susceptibility testing, weak patient monitoring, transport barriers, inadequate follow-up, drug stockouts and limited staffing.

Despite persistent DR-TB notification in Ankole, context-specific evidence on the individual, social, community, and health-system factors associated with DR-TB in this cattle-corridor region remains scarce. The last national survey on DR-TB prevalence and associated factors in Uganda was conducted in 2010 and did not specifically characterise risk factors in cattle-corridor communities [11]. Without local evidence, tuberculosis control programmes risk applying generic interventions to a setting where poverty, chronic disease, alcohol use, mobility, stigma, and health-system constraints may intersect in distinct ways.

We therefore conducted this study to identify risk factors for DR-TB in the Ankole cattle-corridor region of south-western Uganda. Specifically, we aimed to identify individual risk factors, assess social and community risk factors, examine health-system risk factors, and generate evidence to guide context-specific interventions for DR-TB control in Ankole and similar rural cattle-corridor settings.

Methods

Study design

We conducted a retrospective case-control study to assess risk factors for drug-resistant tuberculosis among adults with tuberculosis in the Ankole region of south-western Uganda. This paper reports on the case-control study conducted. The section is structured to reflect key reporting elements for observational case-control studies, including study design, setting, participants, case and control definitions, sampling, matching, bias control, study size, data collection, statistical analysis, and ethics.

Study setting

The study was conducted in public health facilities in Ankole, a predominantly cattle-keeping region within Uganda's cattle corridor. Communities in this region combine livestock keeping with crop farming, and cattle keepers often spend long hours grazing animals.

Tuberculosis services in the region are provided mainly through public health facilities, including Health Centre IIIs, Health Centre IVs, district hospitals, and the regional referral hospital. Sputum samples collected at lower-level facilities are commonly transported to Health Centre IVs or hospitals for testing using WHO-recommended molecular diagnostic platforms, including Xpert MTB/RIF and Truenat.

Patients diagnosed with drug-resistant tuberculosis are referred to the multidrug-resistant tuberculosis clinic at the regional referral hospital, whereas patients with drug-susceptible tuberculosis are generally managed at primary health-care facilities.

We included public health facilities that had diagnosed at least one person with drug-resistant tuberculosis between Jan 1, 2023, and Sept 30, 2024, in Kazo, Kiruhura, Isingiro, Ntungamo, Buhweju, Ibanda, Sheema, Mbarara City, and Rwampara districts. These facilities used standard National Unit Tuberculosis registers to record all tuberculosis diagnoses before entry into the District Health Information System.

Study participants

The source population comprised adults aged 18 years or older who had been diagnosed with tuberculosis using WHO-recommended molecular diagnostic tests and were recorded in tuberculosis registers at selected public health facilities in Ankole region between Jan 1, 2023, and Sept 30, 2024.

A case was defined as an adult with bacteriologically confirmed drug-resistant tuberculosis, including rifampicin-resistant or isoniazid-resistant tuberculosis, diagnosed using Xpert MTB/RIF, Truenat, culture and drug-susceptibility testing, or another WHO-recommended molecular assay during the study period.

A control was defined as an adult with bacteriologically confirmed drug-susceptible tuberculosis diagnosed using the same diagnostic platforms during the same period and selected from the same health facility and community catchment area as the corresponding case.

Participants were eligible if they were aged 18 years or older, had a documented diagnosis of drug-resistant or drug-susceptible tuberculosis during the study period, and were recorded in the facility tuberculosis register. Individuals were excluded if they declined informed consent or had died before data collection.

Case ascertainment and control selection

We reviewed the District Health Information System and facility tuberculosis registers to identify all public health facilities that had diagnosed people with drug-resistant tuberculosis during the study period. At each eligible facility, all eligible people with drug-resistant tuberculosis were selected as cases.

For each case, up to three controls with drug-susceptible tuberculosis were selected from the same facility tuberculosis register. Controls were individually matched to cases by health facility, sub-county of residence, sex, and age within ±2 years. Systematic sampling was used to select controls from the list of eligible drug-susceptible tuberculosis patients diagnosed during the same period.

The sampling interval was calculated by dividing the total number of eligible controls in the register by the number of controls required. After a random starting point was selected, every kth eligible control

was approached. If a selected control had migrated, died, or could not be contacted, the next eligible control in the register was selected.

Study size

The sample size was calculated using OpenEpi version 3 for case-control studies. We assumed a 95% confidence level, 80% power, 30% exposure prevalence among controls, 60% exposure prevalence among cases, and a minimum detectable odds ratio of 3.5, based on previous evidence [12].

Because drug-resistant tuberculosis was uncommon, a 1:3 case-to-control ratio was selected to improve statistical precision. Increasing the number of controls per case improves statistical power when cases are few, although the gain becomes limited beyond about four controls per case [13], [14].

Three sample-size estimates were generated using the Kelsey, Fleiss, and Fleiss with continuity correction methods. The largest estimate, from the Fleiss method with continuity correction, required 127 participants, comprising 32 cases and 95 controls. We enrolled 131 participants, including 34 cases and 97 controls.

Variables

The outcome was tuberculosis resistance status, coded as drug-resistant tuberculosis for cases and drug-susceptible tuberculosis for controls.

Explanatory variables were selected according to the study objectives, biological plausibility, previous evidence, and the social determinants of health framework. Individual-level variables included age, sex, education level, previous tuberculosis diagnosis or treatment, chronic medical conditions, HIV status, tobacco smoking, alcohol consumption, healthcare seeking, and treatment-related history.

Social and community variables included household size, housing conditions, number of meals per day as a proxy for food access, family and community support, tuberculosis contact history, cattle ownership or caregiving, and raw milk consumption. Health-system variables included access to health facilities, previous visits to tuberculosis treatment facilities, income-related barriers to tuberculosis care, and reported challenges experienced at health facilities.

Data sources and measurement

Data were obtained through register review and face-to-face interviews. Facility tuberculosis registers and District Health Information System records were used to identify eligible cases and controls, confirm tuberculosis resistance status, determine dates of diagnosis, and extract available demographic and clinical information, including sex, age, HIV status, previous tuberculosis treatment history, and village of residence.

Participant-level data were collected using a structured questionnaire. Because no validated questionnaire specific to the study objectives was available, the tool was developed for this study (*see*

appendix I in supplementary file) and reviewed for content validity by two epidemiologists with tuberculosis programme experience, including one from the National Tuberculosis and Leprosy Control Programme and one from the USAID Tuberculosis Activity. The questionnaire was pretested in a non-study facility and revised before data collection.

The final questionnaire collected information on sociodemographic characteristics, previous tuberculosis treatment, chronic medical conditions, HIV status, alcohol use, tobacco smoking, housing conditions, household size, number of meals per day, social and community support, tuberculosis contact history, cattle ownership or caregiving, raw milk consumption, access to health facilities, income-related barriers to tuberculosis care, and perceived family, community, and health-facility challenges.

Bias

We used several procedures to reduce selection, information, and recall bias. Cases and controls were selected from the same health facilities and community catchment areas. Controls were individually matched to cases by health facility, sub-county, sex, and age within ±2 years, reducing confounding by facility access, geography, sex, and age.

Controls were systematically sampled from facility tuberculosis registers to minimise investigator discretion in selection. Tuberculosis resistance status was based on documented results from WHO-recommended molecular diagnostic tests rather than self-report. Trained research assistants used structured interviews and standardised probing to improve consistency and reduce recall error. Register data were used where available to confirm key clinical information.

Data quality and management

Research assistants were selected on the basis of Runyankore-Rukiga language proficiency, familiarity with the study area, and communication skills. They were trained in the study protocol, informed consent, confidentiality, human-subject protection, interviewing techniques, and electronic data capture.

The questionnaire was programmed in Kobo Toolbox. Data were reviewed centrally for completeness, consistency, and range errors during data collection. Routine supervision and debriefing meetings were used to identify and resolve data-quality issues. After data collection, the dataset was exported to Microsoft Excel for cleaning and then to Stata version 17 for analysis. Personal identifiers were not included in the analytical dataset.

Statistical analysis

We summarised participant characteristics using frequencies and percentages for categorical variables. Characteristics of cases and controls were compared using χ^2 tests or Fisher's exact tests when expected cell counts were small.

The primary outcome was drug-resistant tuberculosis status. We estimated crude and adjusted prevalence ratios using generalised linear models with a binomial family and log link. This approach was used because drug-resistant tuberculosis accounted for more than 10% of the analytical sample, and prevalence ratios were considered more interpretable for the study objective than odds ratios.

The adjusted model included variables selected a priori on the basis of biological plausibility, previous evidence, and relevance to the study objectives. These variables included previous tuberculosis diagnosis or treatment, chronic medical conditions, tobacco smoking, frequency of alcohol consumption, prior visits to tuberculosis treatment facilities, income level affecting access to tuberculosis treatment, and cattle ownership or caregiving.

Because controls were individually matched to cases at selection, matching factors were accounted for by design and considered in the analytical approach. Health facility, sub-county, sex, and age were assessed as matching factors to minimise residual confounding. Associations are presented as prevalence ratios with 95% confidence intervals and p values. Statistical significance was assessed at a two-sided α level of 0.05.

Results

Participant characteristics

We enrolled 131 adults with tuberculosis, including 34 participants with drug-resistant tuberculosis and 97 with drug-susceptible tuberculosis. Overall, 81 participants (61.8%) were male, 86 (65.6%) were married, and 90 (68.7%) lived in rural areas. Most participants identified as Anglican (59 [45.0%]) or Catholic (46 [35.1%]). Seventy-two participants (55.0%) had previously been treated for tuberculosis, and 59 (45.0%) were new tuberculosis patients. Household size varied, with households of three members being the most common (28 [21.4%]), followed by four members (23 [17.6%]) and seven or more members (22 [16.8%]; Table 1).

Table 1: Socio-demographic characteristics of the study participants

Variables	Frequency	Percentage
Gender	(N=131)	
Male	81	61.80
Female	50	38.20
Marital status		
Not married	45	34.40
Married	86	65.60
Religion		
Catholics	46	35.10
Born again	14	10.7
Anglican	59	45.00
Moslem	12	9.20
Residence		
Rural	90	68.70
Urban	41	31.30
Category of patient		
New	59	45.00
Previous TB patient	72	55.00
Number of household members		
1	16	12.20
2	13	9.90
3	28	21.40
4	23	17.60
5	19	14.50
6	10	7.60
7+	22	16.80

Sociodemographic characteristics by tuberculosis resistance status

Sociodemographic characteristics were broadly similar between participants with drug-resistant and drug-susceptible tuberculosis. The proportion of males was lower among cases than controls (18

[52·9%] of 34 vs 63 [64·9%] of 97), although this difference was not statistically significant. Most cases and controls were married, and rural residence was common in both groups (25 [73·5%] of 34 cases vs 65 [67·0%] of 97 controls). Previous tuberculosis treatment was slightly more frequent among cases than controls (20 [58·8%] vs 52 [53·6%]), but this difference was not significant in bivariable analysis. Household size also did not differ significantly by tuberculosis resistance status, although households with seven or more members were more common among cases than controls (8 [23·5%] vs 14 [14·4%]; Table 2).

Table 2: Comparison of Socio-Demographic Characteristics by TB Status

Variables	TB status		P-value
	Controls	Cases	
	n=97	n=34	
Gender			0.215
Male	63 (64.9)	18 (52.9)	
Female	34 (35.1)	16 (47.1)	
Marital status			0.481
Not married	35 (36.1)	10 (29.4)	
Married	62 (63.9)	24 (70.6)	
Religion			0.538
Catholics	34 (35.1)	12 (35.3)	
Born again	12 (12.4)	2 (5.9)	
Anglican	41 (42.3)	18 (52.9)	
Moslem	10 (10.3)	2 (5.9)	
Residence			0.481
Rural	65 (67.0)	25 (73.5)	
Urban	32 (33.0)	9 (26.5)	
Category of patient			0.599
New	45 (46.4)	14 (41.2)	
Previous TB patient	52 (53.6)	20 (58.8)	
Number of household members			0.588
1	14 (14.4)	2 (5.9)	
2	9 (9.3)	4 (11.8)	
3	19 (19.6)	9 (26.5)	
4	19 (19.6)	4 (11.8)	
5	15 (15.5)	4 (11.8)	
6	7 (7.2)	3 (8.8)	
7+	14 (14.4)	8 (23.5)	

Individual biological and lifestyle factors

Several biological and lifestyle factors differed between cases and controls. Other chronic medical conditions were more frequently reported among cases than controls (6 [17·6%] of 34 vs 6 [6·2%] of 97; p=0·046). HIV-positive status was more common among controls than cases (40 [41·2%] vs 10 [29·4%]), but the difference was not statistically significant.

Tobacco smoking was less common among cases than controls (2 [5·9%] vs 22 [22·7%]; p=0·029). Any alcohol consumption did not differ significantly between groups, but frequency of alcohol use varied by resistance status (p=0·041). Daily alcohol consumption was more frequent among cases than controls (7 [20·6%] vs 14 [14·4%]), whereas weekly alcohol use was more common among controls (23 [23·7%] vs 2 [5·9%]). Among participants who consumed alcohol, missed doses were the most commonly reported way in which alcohol affected tuberculosis treatment adherence. See Table 3.

Table 3: Biological and lifestyle characteristics of participants by TB Status

Variables	TB status		P-value
	Controls	Cases	
	N=97	N=34	
Currently undergoing treatment for TB	19 (19.6)	8 (23.5)	0.625
Ever been in contact with someone known to have TB before	12 (12.4)	6 (17.6)	0.442
HIV status			0.222
Negative	57 (58.8)	24 (70.6)	
Positive	40 (41.2)	10 (29.4)	
Have any other chronic medical conditions	6 (6.2)	6 (17.6)	0.046
Other chronic medical conditions			0.343
(Asthma, dementia, diabetes)	1 (16.7)	2 (33.3)	
Hypertension	5 (83.3)	4 (66.7)	
Smoke tobacco(Yes)	22 (22.7)	2 (5.9)	0.029
Consume alcohol(yes)	38 (39.2)	11 (32.4)	0.479
Frequency of drinking alcohol			0.041
None	59(60.8)	23(67.7)	
Daily	14 (14.4)	7 (20.6)	
Once a week	23 (23.7)	2 (5.9)	
Other	1 (1.0)	2 (5.9)	
Alcohol consumption affects your TB treatment adherence	6 (14.0)	2 (18.2)	0.725
How alcohol consumption affect one’s treatment			0.537
Missed doses	5 (83.3)	2 (100.0)	
Stopped taking medicine altogether	1 (16.7)	0 (0.0)	
Use any other substances	1 (1.0)	1 (2.9)	0.434

Living and working conditions

Housing characteristics, household crowding, ventilation, tuberculosis contact history, travel outside the home for work or animal care, and number of meals before tuberculosis illness did not differ significantly between cases and controls. Most participants reported access to health-care services, and distance to the nearest health facility was similar between groups.

Transport barriers were more frequently reported by cases than controls (8 [23·5%] vs 15 [15·5%]), although this difference was not statistically significant. Among those reporting transport-related barriers, missed clinic appointments were the most common consequences. A higher proportion of cases than controls reported that low income affected their ability to access tuberculosis treatment (10 [29·4%] vs 12 [12·4%]). Cattle ownership or caregiving was more common among cases than controls (13 [38·2%] vs 18 [18·6%]; p=0·020), although consumption of raw milk before tuberculosis illness did not differ significantly between groups. See Table 4.

Table 4: Living and working conditions of participants by tuberculosis status

Variables	TB status		P-values
	Controls	Cases	
	N=97	N=34	
Number of rooms in houses			0.503
1	17 (17.5)	6 (17.6)	
2	29 (29.9)	13 (38.2)	
3	33 (34.0)	7 (20.6)	
4+	18 (18.6)	8 (23.5)	
Number of individuals staying in the house			0.819
0	5 (5.2)	1 (2.9)	
1-2	22 (22.7)	6 (17.6)	
3-4	37 (38.1)	13 (38.2)	
5+	33 (34.0)	14 (41.2)	
House have windows	70 (72.2)	26 (76.5)	0.625
Stayed in close contact with a person with TB	14 (14.4)	5 (14.7)	0.969
Travelled outside home for work or care for animals	16 (16.5)	5 (14.7)	0.807
Traveling outside affects one's adherence to TB treatment	3 (18.8)	3 (60.0)	0.115
How traveling outside affects one's adherence to TB treatment			1
Missed doses	1 (33.3)	1 (33.3)	
Stopped taking medicine altogether	1 (33.3)	1 (33.3)	
Others	1 (33.3)	1 (33.3)	
Number of meals per day before you were sick of TB			0.278
Less than two	8 (8.2)	5 (14.7)	
Two and above	89 (91.8)	29 (85.3)	
Reasons for less than 2 meals			1
Lack of money to buy food	2 (50.0)	2 (66.7)	
No garden to get food from	1 (25.0)	1 (33.3)	
Others specify	1 (25.0)	0 (0.0)	

Have access to healthcare services	91 (93.8)	33 (97.1)	0.416
Distance to a health facility (kilometers)			0.51
< 5	54 (59.3)	19 (57.6)	
> 5	37 (40.7)	14 (42.4)	
Transport affect clinic visits for TB medication	15 (15.5)	8 (23.5)	0.287
How transport affect TB medication adherence			0.513
Missed clinic appointment	12 (80.0)	6 (75.0)	
Missed TB medicines	0 (0.0)	1 (12.5)	
Others	3 (20.0)	1 (12.5)	
Ever visited a facility for TB medication before recent/current episode	27 (27.8)	4 (11.8)	0.044
How health workers handle people with TB in the community			
Very supportive	97 (100.0)	34 (100.0)	
Low-income level affected ability to access TB treatment	12 (12.4)	10 (29.4)	
Have cattle or care for cattle	18 (18.6)	13 (38.2)	0.02
Care for cattle affect one's taking of TB medication	1 (5.6)	1 (7.7)	0.671
How caring for cattle affect one's taking of TB medication			0.5
Failure to keep clinic appointment,	1 (100.0)	0 (0.0)	
Delay to find food to accompany my medicine,	0 (0.0)	1 (100.0)	
Was drinking raw milk before one fell sick with TB	14 (14.6)	7 (20.6)	0.414

Social and community factors

Most social and community network variables did not differ significantly by tuberculosis resistance status. However, psychosocial challenges were more common among cases than controls (p=0·020). Social isolation was reported by 13 (38·2%) of 34 cases compared with 18 (18·6%) of 97 controls. Loss of employment was also more frequent among cases than controls (4 [11·8%] vs 1 [1·0%]; p=0·016). Fear of discrimination was common in both groups, reported by 15 (44·1%) cases and 30 (30·9%) controls. Most participants attributed tuberculosis to tuberculosis germs, and few reported knowledge or use of herbs for tuberculosis treatment. See Table 5.

Table 5: Contribution of Social and community networks of participants by TB status

Variables	TB status		p-value
	Controls	Cases	
	N=97	N=34	
Where one spends your leisure time			0.413
Bar	30 (30.9)	8 (23.5)	
Home	62 (63.9)	25 (73.5)	0.307
Playing	6 (6.2)	0 (0.0)	0.158
Betting	3 (3.1)	2 (5.9)	0.388
Other	7 (7.2)	1 (2.9)	0.336
People spend leisure time with, support someone with TB	60 (67.4)	20 (62.5)	0.614
Support offered to people with TB from leisure friends			
Transport to health facility	32 (48.5)	10 (45.5)	0.805
Food	35 (53.0)	13 (59.1)	0.621
Remind to take medication	34 (51.5)	12 (54.5)	0.805
Others	1 (1.5)	0 (0.0)	0.561
Reasons for why one does not get support from People spent leisure time with			
Discourage from taking medication	1 (3.4)	0 (0.0)	1
Stigmatize	23 (79.3)	10 (83.3)	
Others	5 (17.2)	2 (16.7)	
Community provide support for TB patients	52 (53.6)	19 (55.9)	0.819
Community support provided for TB patients			
Adherence support	10 (45.5)	6 (60.0)	
Provide food	10 (45.5)	2 (20.0)	0.163

Contribute transport	4 (18.2)	2 (20.0)	0.627
Others	3 (13.6)	1 (10.0)	0.632
One's believe on what caused one to acquire TB			0.552
Evil spirits	1 (1.0)	1 (2.9)	
TB germ	84 (86.6)	30 (88.2)	
Other	12 (12.4)	3 (8.8)	
Know of any herbs that treat TB in the community	5 (5.2)	0 (0.0)	0.217
Used any herbs that treat TB in the community	3 (60.0)	0 (.)	
Challenges faced as a TB patient			0.02
Social isolation	18 (18.6)	13 (38.2)	
Fear of discrimination	30 (30.9)	15 (44.1)	0.163
Self-stigma	55 (56.7)	16 (47.1)	0.332
Misinformation about TB	10 (10.3)	4 (11.8)	0.517
Hesitancy to seek care	13 (13.4)	1 (2.9)	0.076
Loss of job	1 (1.0)	4 (11.8)	0.016
Family or community rejection	8 (8.2)	1 (2.9)	0.268
Others	9 (9.3)	2 (5.9)	0.419
Ever moved away from home while taking TB	10 (10.3)	6 (17.6)	0.261
Movement affects one's TB treatment adherence	4 (26.7)	1 (14.3)	0.477

Factors independently associated with drug-resistant tuberculosis

In the adjusted model, previous tuberculosis treatment, chronic medical conditions, daily alcohol consumption, and low-income affecting access to tuberculosis treatment were independently associated with drug-resistant tuberculosis (table 3). Participants with previous tuberculosis treatment had twice the prevalence of drug-resistant tuberculosis compared with those without previous treatment (adjusted prevalence ratio [aPR] 2·0, 95% CI 1·3–3·0; p=0·001). Participants with other chronic medical

conditions had a higher prevalence of drug-resistant tuberculosis than those without chronic conditions (aPR 1·8, 95% CI 1·2–2·6; p=0·001).

Daily alcohol consumption was strongly associated with drug-resistant tuberculosis (aPR 2·3, 95% CI 1·7–3·0; p<0·001), whereas weekly alcohol consumption was not associated with drug-resistant tuberculosis after adjustment. Low income affecting access to tuberculosis treatment was also independently associated with drug-resistant tuberculosis (aPR 1·5, 95% CI 1·1–2·0; p=0·004). Tobacco smoking was inversely associated with drug-resistant tuberculosis in the adjusted model (aPR 0·2, 95% CI 0·1–0·8; p=0·019). Cattle ownership or caregiving was associated with drug-resistant tuberculosis in bivariable analysis but not after adjustment (aPR 1·1, 95% CI 0·6–1·6; p=0·775). See Table 6.

Table 6: Multivariate analysis of factors independently associated with tuberculosis status

Variables	cPOR(95% CI)	P-value	aPOR(95% CI)	P-value
Ever been treated for tuberculosis (TB) before recent/current episode	Controls		Cases	
No	1		1	
Yes	1.7(0.9, 3.0)	0.083	2.0(1.3, 3.0)	0.001
Have any other chronic medical conditions				
No	1		1	
Yes	2.1(1.1, 4.1)	0.023	1.8(1.2, 2.6)	0.001
Smoke tobacco				
No	1		1	
Yes	0.3(0.1, 1.1)	0.065	0.2(0.1, 0.8)	0.019
Frequency of drinking alcohol				
None	1		1	
Daily	3.5(0.9, 13.8)		2.3(1.7, 3.0)	<0.001
Once a week	4.2(0.9, 17.9)		0.6(0.2, 1.8)	0.355
Ever visited a facility for TB medication before recent/ current episode				
No	1		1	
Yes	0.4(0.2, 1.1)	0.086	0.9(0.3, 1.8)	0.429
Low-income level affected the ability to access TB treatment				
No	1		1	
Yes	2.1(1.2, 3.7)	0.014	1.5(1.1, 2.0)	0.004
Have cattle or care for cattle				
No	1		1	
Yes	2.0(1.1, 3.5)	0.016	1.1(0.6, 1.6)	0.775

Discussion

In this case-control study from Uganda's Ankole cattle-corridor region, drug-resistant tuberculosis was concentrated among people with previous tuberculosis treatment, chronic medical conditions, daily alcohol use, and financial barriers to accessing tuberculosis care. These findings suggest that drug-resistant tuberculosis in this setting is not only a microbiological outcome, but also a marker of repeated exposure to tuberculosis treatment, comorbidity, behavioural vulnerability, and constrained access to care. Cattle ownership or caregiving was associated with drug-resistant tuberculosis in bivariable analysis, but this association was not retained after adjustment. Tobacco smoking showed an inverse association, a finding that should be interpreted cautiously and not as evidence of protection.

Previous tuberculosis treatment was independently associated with drug-resistant tuberculosis. This finding is consistent with evidence from other high-burden settings showing higher risk of drug-resistant tuberculosis among previously treated patients [15]–[17]. Previous treatment may reflect prior exposure to inadequate regimens, missed doses, incomplete treatment, treatment failure, delayed recognition of resistance, or reinfection with a resistant strain. In programmatic terms, previous tuberculosis treatment is an easily identifiable marker of increased risk. Patients with any history of tuberculosis treatment should therefore receive early drug-susceptibility testing, careful adherence assessment, and intensified follow-up from the start of care. In settings where diagnostic and follow-up capacity is constrained, prioritising previously treated patients could improve early detection and reduce ongoing transmission of resistant disease.

Chronic medical conditions were also independently associated with drug-resistant tuberculosis. Although the number of participants with chronic illnesses was small, the association is biologically and programmatically plausible. Chronic illness can impair host immunity, increase pill burden, complicate treatment, and expose patients to multiple clinic visits and fragmented care. Previous studies have linked diabetes, chronic obstructive pulmonary disease, and other chronic conditions to tuberculosis risk and poorer tuberculosis outcomes [18]–[20]. In rural settings such as Ankole, comorbidity may also increase indirect costs through repeated facility visits, transport expenditure, and competing treatment appointments. These findings support integrated tuberculosis, HIV, and non-communicable disease services, especially after patients are clinically stable and less infectious. Integrated chronic care models could reduce missed appointments, improve medication continuity, and strengthen long-term follow-up for patients with overlapping health needs [18], [21]. However, integration may work well when the community is properly educated to prevent stigma and improve treatment access.

Daily alcohol consumption was strongly associated with drug-resistant tuberculosis. The distinction between any alcohol use and daily use is important. In this study, frequency of drinking, rather than alcohol consumption alone, was the relevant risk signal. Daily alcohol consumption as compared to occasional use may increase vulnerability to drug-resistant tuberculosis through missed doses, poor appointment keeping, reduced treatment adherence, undernutrition, delayed care-seeking, and social instability. This finding is consistent with studies reporting alcohol use as a contributor to poor tuberculosis treatment adherence and drug-resistant tuberculosis risk [22]–[24]. Tuberculosis programmes should therefore move beyond general health education and incorporate routine alcohol-

use screening, brief counselling, adherence planning, and referral for patients with harmful alcohol use. In high-burden rural settings, alcohol-use interventions should be embedded within tuberculosis care rather than treated as a separate behavioural problem.

Low income affecting access to tuberculosis treatment was independently associated with drug-resistant tuberculosis. This finding highlights the central role of poverty in shaping tuberculosis outcomes. Even when tuberculosis medicines are provided free of charge, patients still face indirect costs, including transport, food, lost income, diagnostic visits, and repeated clinic attendance. These costs can delay treatment initiation, interrupt medication refills, and undermine adherence. Previous evidence has identified out-of-pocket expenditure and catastrophic costs as major barriers to tuberculosis care and treatment completion [2], [25]–[29]. Our findings support explicit social protection interventions for all people diagnosed with tuberculosis irrespective of the type, including transport assistance, nutritional support, decentralised refills, community-based follow-up, and differentiated care models that reduce the frequency and cost of facility visits. Such interventions are not merely welfare measures; they are tuberculosis-control interventions.

The inverse association between tobacco smoking and drug-resistant tuberculosis was unexpected. This finding contrasts with established evidence that smoking increases the risk of tuberculosis infection, disease progression, and poor treatment outcomes [22], [23]. The plausible explanation is not biological protection but bias, under-reporting or imprecision. The number of smokers among cases was small, and self-reported smoking could have been affected by under-reporting, social desirability bias, survival bias, or residual confounding. Smokers with severe disease might also have been less likely to be captured if they died, migrated, or did not access diagnostic services. This result should therefore be interpreted as hypothesis-generating and should not weaken tobacco-control messaging within tuberculosis programmes. Future studies with larger sample sizes and more detailed measurement of tobacco exposure are needed to clarify this association.

Cattle ownership or caregiving was more common among cases in bivariable analysis, but the association was no longer evident after adjustment. This pattern suggests that cattle ownership may be a marker of other linked exposures, such as rural residence, livelihood, income patterns, mobility, food access, or health-service access, rather than an independent risk factor in this dataset. Although cattle-corridor settings raise important questions about zoonotic tuberculosis and human–animal interaction, this study did not test for Mycobacterium bovis and could not distinguish zoonotic tuberculosis from human tuberculosis. Raw milk consumption was also not significantly associated with drug-resistant tuberculosis. The cattle-related findings should therefore be interpreted cautiously. They justify further research using laboratory methods capable of differentiating Mycobacterium tuberculosis from Mycobacterium bovis, but they do not establish zoonotic transmission as a pathway to drug-resistant tuberculosis in Ankole [30]–[32].

Several bivariable findings, including social isolation, loss of employment, transport barriers, and cattle ownership or caregiving, were more frequent among people with drug-resistant tuberculosis. However,

because they were not all retained as independent factors in the adjusted model, they should be interpreted as markers of vulnerability rather than definitive independent predictors. Their importance lies in showing that drug-resistant tuberculosis occurs within a broader context of social and economic disadvantages. For programme design, this means that clinical risk stratification should be complemented by assessment of financial hardship, treatment access, comorbidity, and adherence risks.

Strengths and limitations

This study has several strengths. Cases and controls were selected from the same health facilities and community catchment areas, reducing differences in diagnostic access and local service context. Controls were individually matched to cases by facility, sub-county, sex, and age, and were systematically sampled from tuberculosis registers. Tuberculosis resistance status was based on documented molecular diagnostic results rather than self-report. The study also assessed clinical, behavioural, socioeconomic, and cattle-corridor-related exposures within one analytical framework, providing context-specific evidence for a region with persistent drug-resistant tuberculosis notification.

The study has limitations. Its retrospective case-control design limits causal inference, and findings should be interpreted as associations rather than proof of causation. Some exposures, including alcohol use, smoking, transport barriers, income-related barriers, and treatment behaviours, were self-reported and may be affected by recall or social desirability bias. The small number of drug-resistant tuberculosis cases limited precision for less common exposures. Excluding patients who had died before data collection could have introduced survival bias. Finally, although the study was conducted in a cattle-corridor region, laboratory testing did not distinguish *Mycobacterium tuberculosis* from *Mycobacterium bovis*; therefore, zoonotic transmission could not be assessed.

Conclusion

Drug-resistant tuberculosis in the Ankole cattle-corridor region was associated with previous tuberculosis treatment, chronic medical conditions, daily alcohol consumption, and financial barriers to accessing tuberculosis care. These findings suggest that people with repeated exposure to tuberculosis treatment, comorbid illness, harmful alcohol use, and limited financial capacity to sustain care represent priority groups for drug-resistant tuberculosis prevention and control. Although tobacco smoking showed an inverse association with drug-resistant tuberculosis, this finding should be interpreted cautiously and should not be regarded as evidence of protection.

Recommendations

Tuberculosis programmes in Ankole and similar rural cattle-corridor settings should strengthen risk stratification at diagnosis, with particular attention to patients who have previously received tuberculosis

treatment. Previously treated patients should be prioritised for early drug-susceptibility testing, adherence assessment, and closer follow-up during treatment.

Tuberculosis services should be integrated with chronic disease care to improve continuity for patients with comorbid conditions. Coordinated appointments, shared clinical reviews, and combined follow-up for tuberculosis, HIV, and non-communicable diseases could reduce missed visits and support treatment completion.

Routine screening for harmful alcohol use should be incorporated into tuberculosis care. Patients reporting daily alcohol consumption should receive targeted adherence counselling, brief behavioural interventions, and referral for additional support where needed.

Financial barriers to tuberculosis care should be addressed through patient-centred support, including transport assistance, nutritional support, decentralised medicine refills, and community-based follow-up. Reducing the cost of accessing care is likely to be essential for improving treatment continuity and preventing drug-resistant tuberculosis in this setting.

Declarations

Ethics approval and consent to participate

The study was conducted in accordance with the declaration of the Helsinki ethical principles involving human subjects. Ethical approval was obtained from the Mbale Regional Referral Hospital Research Ethics Committee (REC) (Approval No. MRRH-2025-617), with administrative clearance from the respective District Health Offices and participating health facilities. All procedures followed ethical standards for research involving human participants. Written informed consent was obtained before enrolment. Participation was voluntary, and participants could decline questions or withdraw at any time without penalty or loss of health services. Confidentiality and privacy were maintained by anonymising data collection tools, excluding personal identifiers from the analytical dataset, training data collectors in confidentiality procedures, and storing study data in password-protected systems accessible only to authorised research team members.

Consent for publication

Not applicable

Availability of data and materials

The datasets used and/or analysed during the current study are available from the corresponding author upon reasonable request.

Competing interests

The authors declare that they have no competing interests.

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Authors' contributions

MNB conceived, designed and led the study, coordinated data collection, conducted the initial analysis, and drafted the manuscript. JPA,AM and AG contributed to study design, data analysis, interpretation of findings, and manuscript writing. JK-BM, P-OO and MOO provided methodological and analytical guidance and critically reviewed the manuscript. SRA, GNS, MNB, PB, MM, CBO, SN, and DA supported field implementation, data acquisition, and manuscript drafting. JK-BM and MOO supervised the study, provided scientific oversight, and contributed substantially to manuscript revision. BW and MLJ supported statistical analysis and data validation. All authors reviewed and approved the final manuscript.

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