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Short Communication

Malnutrition is a risk factor for tuberculosis disease among household contacts: A case-control study in Uganda

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ABSTRACT

Objective: Household contacts (HHCs) of persons with tuberculosis (TB) including rifampicin-resistant or multi-drug-resistant TB (RR/MDR-TB) are at risk for TB infection. We investigated whether index patient-level clinical and socio-demographic factors of persons with MDR-TB are associated with TB disease among their HHCs in Uganda.

Methods: We designed an unmatched case-control study. Cases were HHCs of persons with MDR-TB that had TB disease while controls were a random sample of HHCs of persons with MDR-TB that had no TB disease. The case-to-control ratio was 1:3. We identified the factors that significantly differed between the cases and controls in a multivariable binary logistic regression analysis and reported the odds ratio (OR) and 95% confidence interval (CI).

Results: We found similar demographic and clinical characteristics among the 11 cases and 33 controls. In a multivariable analysis, malnutrition was significantly associated with being a case than a control (adjusted OR 5.01; 95% CI 1.18-24.83).

Conclusion: Therefore, TB Control Programs should focus on identifying malnutrition among persons with MDR-TB and providing nutritional counseling and support to improve recovery, and potentially reduce household TB transmission and optimize treatment success. Additionally, rapid screening for TB and preventive therapy should be prioritized to reduce transmission.

Background

In sub-Saharan Africa, about 4% of household contacts (HHCs) of persons with tuberculosis (TB) have TB disease according to a meta-analysis of data from 14 countries [1]. Multi-drug-resistant TB (MDR-TB) is more transmissible than drug-susceptible TB, with a significant proportion of HHCs progressing to develop MDR-TB within 2 years of exposure [2]. The cumulative incidence of TB infection among HHCs of persons with TB is around 21.6% and that for TB disease is 2.3% [2]. Transmission of MDR-TB to HHCs occurs more easily than in the general population since >50% of MDR-TB families (54.5%) have identical genotypes [3]. Transmission is exacerbated if HHCs interact closely with index patients, for example via shared bedrooms and living rooms and when the index patient is not on anti-TB treatment.

Agent-based simulation models show that 75-95% of household TB infections occur before the diagnosis of TB disease in the index case, with 1.5-3% of the households progressing to develop TB disease [4]. However, there is limited information regarding the risk factors for TB disease among HHCs of persons with MDR-TB in Uganda. We, therefore, assessed the index patient-level clinical and socio-demographic factors associated with TB disease among HHCs of persons with MDR-TB who had received care at Mubende Regional Referral Hospital in Uganda.

Methods and materials

Setting and data source

We abstracted medical records for persons with MDR-TB treated between January 2012 and October 2023 at Mubende Regional Referral Hospital in central Uganda.

Data were abstracted from the Health Management Information System TB 016 drug-resistant TB register. We excluded persons with MDR-TB with no treatment outcome evaluation like those transferred to other health facilities and those with unknown treatment outcomes to the reporting TB Unit. Ethical approval was from the Clarke International University Research Ethics Committee (CLARKE-2023-870). Informed consent was waived by the Ethics Committee given the analysis involved secondary anonymous data. Socio-demographic data included age, sex, residence, and risk groups. Clinical data included the past TB treatment history; nutrition status measured using color-coded mid-upper

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Table 1
Participant characteristics.

Variables	Levels	Cases (n = 11)	Controls (n = 33)	*P*-value
Age groups (years)	15-34	6 (54.5)	15 (45.5)	0.812
	35-44	2 (18.2)	9 (27.3)	
	45-78	3 (27.3)	9 (27.3)	
	mean (SD)	35.9 (14.1)	35.2 (19.1)	0.912
Sex	Female	5 (45.5)	8 (24.2)	0.340
	Male	6 (54.5)	25 (75.8)	
Residence	Rural	8 (72.7)	29 (87.9)	0.475
	Urban	3 (27.3)	4 (12.1)	
Type of TB	New	7 (63.6)	20 (60.6)	1.000
	Previously treated with first or second-line treatment	4 (36.4)	13 (39.4)	
Risk category	Diabetic patient	2 (18.2)	0 (0.0)	0.071
	HIV infected	0 (0.0)	2 (6.1)	
	Miner	0 (0.0)	3 (9.1)	
	Others	6 (54.5)	23 (69.7)	
	TB contact	3 (27.3)	5 (15.2)	
Anti-TB regimen type	Individualized regimen	0 (0.0)	5 (15.2)	0.068
	Modified second-line treatment regimen	7 (63.6)	9 (27.3)	
	Second-line treatment regimen	4 (36.4)	19 (57.6)	
Nutritional status	Well-nourished	4 (36.4)	24 (72.7)	0.070
	Malnourished	7 (63.6)	9 (27.3)	
Treatment supporter type	Family member	3 (27.3)	8 (24.2)	0.663
	Health workers	2 (18.2)	3 (9.1)	
	None	6 (54.5)	22 (66.7)	
Treatment supporter availability	No	6 (54.5)	22 (66.7)	0.717
	Yes	5 (45.5)	11 (33.3)	
HIV serostatus	Negative	6 (54.5)	24 (72.7)	0.455
	Positive	5 (45.5)	9 (27.3)	

TB, tuberculosis.

arm circumference tapes marked green (12.5-26.5 cm), yellow (11.5-12.49 cm), and red color (<11.5 cm) to denote no, moderate, and severe malnutrition, respectively; diagnostic method; treatment model; treatment support; HIV serostatus; diabetes mellitus; sputum smear/culture grade; type of drug resistance; and, adherence to treatment and other comorbidities. Mid-upper arm circumference is simpler to perform and utilize compared to body mass index hence is preferred in routine care, and has been widely used to study undernutrition among persons with TB, and the measures are highly correlated to body mass index [5]. We combined moderate and severe malnourished categories of persons with MDR-TB to form the malnourished group and compared it with the well-nourished group. Household level data include the number of persons in the household, the number of HHCs screened for TB disease, and the number found with TB disease.

Study design and measurements

We designed an unmatched case-control study. Cases were HHCs of persons with MDR-TB that had TB disease while controls were a random sample of HHCs of persons with MDR-TB that had no TB disease. For one case, we selected three controls.

Baseline socio-demographic and clinical factors were considered as the exposures of interest, with the outcome as TB disease among ≥1 HHCs of persons with MDR-TB, measured on a binary scale (yes vs no).

Statistical methods

We hypothesized that TB disease will more likely occur among HHCs that had a malnourished person with MDR-TB compared to HHCs with a well-nourished person with MDR-TB. No sample size was determined *a priori* as we used all the available data. Numerical data were summarized as mean and standard deviation. Categorical data were summarized as frequencies and percentages. Bivariate analysis for categorical data was performed using the chi-square test for cell counts ≥5 otherwise the Fisher exact test was used. For numerical data, the *t* test was used as the data were normally distributed. Variables with $P < 0.25$ were considered statistically significant in the bivariate analysis. Factors associated with being a case were modeled using a binary logistic regression, adjusted for clinically relevant factors and factors with $P < 0.25$ in the bivariate analysis. Our final model was parsimonious—had the lowest Akaike Information Criteria. We reported the odds ratio (OR) and 95% confidence interval (CI).

Results

Of 111 records retrieved, 13 were excluded with reasons: seven returned on first-line treatment and six had no TB treatment outcome evaluated. Of the 98 persons with MDR-TB, household TB screening was conducted among 71, and 11 of them had ≥1 HHCs with TB disease (cases).

Of the 60 persons with MDR-TB who had no HHCs with TB disease, 33 were randomly selected as controls. Table 1 shows the distribution of characteristics between cases and controls. Table 2 shows that malnutrition was significantly associated with being a case than control at both the unadjusted (OR 4.67, 95% CI 1.14-21.73) and adjusted analyses (OR 5.01, 95 CI 1.18-24.83).

Discussion

Our study showed that TB disease is higher among HHCs of malnourished persons with MDR-TB than HHCs of well-nourished persons with MDR-TB. Malnutrition is a risk factor for immunosuppression, leading to vulnerability to infectious diseases. Malnutrition among persons with MDR-TB compromises TB treatment adherence as they are more likely to experience medication-related adverse effects [6], leading to suboptimal drug levels and delayed sputum smear non-conversion—increasing MDR-TB infectivity. Therefore, efforts to diagnose MDR-TB early, treat patients effectively, and screen close contacts for TB disease are crucial in reducing TB disease among HHCs. Our findings have implications for TB control. The findings underscore the significance of implementing TB preventive treatment in reducing TB disease among HHCs of persons with MDR-TB. The World Health Organization recommends 6 months of levofloxacin for individuals exposed to MDR or rifampicin-resistant

Table 2
Unadjusted and adjusted analysis findings.

Variable	Level	Binary logistic regression analysis	
		Univariable analysis (OR, 95% CI)	Multivariable analysis (aOR, 95% CI)
Age groups (years)	15-34	1	
	35-44	0.56 (0.07-3.05)	
	45-78	0.83 (0.15-4.04)	
	1-unit increase	1.00 (0.96-1.04)	
Sex	Female	1	
	Male	0.38 (0.09-1.64)	
Nutritional status	Well-nourished	1	1
	Malnourished	**4.67 (1.14-21.73)**	**5.01 (1.18-24.83)**
Residence	Rural	1	
	Urban	2.72 (0.46-15.02)	
Treatment supporter availability	No	1	
	Yes	1.67 (0.40-6.79)	
HIV serostatus	Negative	1	1
	Positive	2.22 (0.53-9.31)	2.52 (0.52-12.35)

Note: Bolded figures indicate statistically significant results at a 5% level of statistical significance.
aOR, adjusted odds ratio; OR, crude odds ratio.

TB to prevent TB disease [7]. One study that simulated 6-month TB preventive therapy (TPT) showed that TPT prevents up to 72% of incident MDR-TB cases over 2 years [8]. Our findings imply a need to strengthen community involvement in understanding TB disease transmission risk at the household level, including preventing it. Lastly, the findings underscore the significance of adequate nutrition in improving recovery from MDR-TB since undernutrition negatively impacts treatment success and sputum smear conversion among persons with TB [5].

Providing food to persons with MDR-TB will improve their nutritional status, enhance treatment response and treatment outcomes, and reduce the likelihood of adverse events [9]. Providing nutritional support such as food rations to HHCs of persons with bacteriologically confirmed TB reduces the incidence of TB at the household level [10].

Limitations include a lack of data from HHCs and other social determinants of health like housing conditions (inadequate ventilation and overcrowding), access to TB care, DNA testing to link TB disease to the index person with MDR-TB as evidence of transmission, duration of symptoms among HHCs and treatment adherence among others. These unmeasured factors should be investigated in future research and findings should be considered preliminary data.

Conclusion and recommendation

HHCs of malnourished persons with MDR-TB are more likely to have TB disease compared to the HHCs of well-nourished persons with MDR-TB. Therefore, TB Control Programs should focus on identifying malnutrition among persons with MDR-TB and providing nutritional counseling and support to improve recovery, and potentially reduce household TB transmission and optimize treatment success. Additionally, rapid screening for TB and preventive therapy should be prioritized to reduce transmission.

Declarations of competing interest

The authors have no competing interest to declare.

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Ethical approval statement

Ethical approval was from the Clarke International University Research Ethics Committee (CLARKE-2023-870). Informed consent was waived by the Ethics Committee given the analysis involved secondary anonymous data.

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Author contributions

JI and FB: Study conception and design; SE: Acquisition of data; JI and FB: Analysis and interpretation of data; JI: Drafting of the manuscript; JI and FB: Critical revision; JI, ES, and FB: Final approval of the manuscript.

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