**Examining The Relationship Between History of Detention and MDR-TB in Moldova Between 2008-2009**

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**Introduction**

Multi-drug resistant tuberculosis (MDR-TB) is characterized by WHO as TB with resistance to two common first-line antibiotics: isoniazid and rifampicin. MDR-TB can result from not completing the full course of anti-TB medications, however, MDR-TB can also be transmitted person-to-person via MDR-TB infected airborne droplets.1 Its airborne transmission mechanism allows MDR-TB to spread easily in crowded, poorly ventilated, indoor areas, including prisons.1

Former Soviet countries experience heavy burdens of MDR-TB, including Moldova, in which a 2006 nationwide survey found that 19.4% and 50.8% of new and previously treated TB, respectively, had MDR-TB.2 Former Soviet countries also experience high incarceration rates coinciding with the TB epidemic.1 The relationship between TB and incarceration have been well documented and studied. Proscriptive laws promote the incarceration of populations considered at high risk for TB infection, i.e. people who use substances and/or are unhoused, which inadvertently creates a concentration of risk within prisons.1,3 These facilities then facilitate the spread of TB among the incarcerated population via poor ventilation, overcrowding, and poor nutrition.1,3 Prisons often also do not have efficient and timely diagnostic and control policies in place to facilitate screening, isolation, and treatment.3

MDR-TB puts great strain on health care systems and patients – MDR-TB takes longer to diagnose and treat, costs more money and resources, and has a greater chance of treatment failure.1 Containing the transmission of MDR-TB and engaging incarcerated people in treatment within prisons will not only improve the health and well-being of the incarcerated population, but will also prevent transmission of MDR-TB to surrounding communities since incarcerated people do interact with facility staff, visitors, and other incarcerated people about to be released, all of whom can carry the infection from the facility into the community and general population. Contributing to the literature on the association between MDR-TB and incarceration will help inform policy decisions on where to focus resources when it comes to managing MDR-TB.

Using data about active TB from the Moldova Ministry of Health between 2008 and 2009, we examined the association between detention and risk of MDR-TB.

**Methods**

*Data Source*

We used the Moldovan Ministry of Health’s TB database that monitors all notified TB cases between 2008 and 2009 (11,687 cases). The TB database contains demographic, socioeconomic, and residential information, as well as lab data pertaining to diagnosis, degree of infection, results from drug susceptibility testing (DST), and treatment and outcome data. We excluded cases with missing data for detention, education, occupation, and houselessness (11,098 cases). We also excluded patients who were untested for HIV or had unknown results or were coded with an unknown code (8,718 cases). Our final population for analysis included 8,718 patients.

*Variables*

Detention status was obtained using question P11 in the demographics section on the initial intake form. MDR-TB status was determined using the various DSTs conducted: once at baseline and then one every follow up appointment (2-3 months after treatment initiation; 3-4 months after treatment initiation; 5 months from treatment initiation; and 6-9 months after treatment initiation). If a patient was found to be resistant to both isoniazid and rifampicin at any point, we identified them as an MDR-TB case, therefore, patients with MDR-TB at baseline were included in our analysis.

We identified and tested additional risk factors and covariates, including: previous TB case, concurrent HIV infection, sex, houselessness, occupation, residence, and citizenship.

*Statistical Analysis*

Baseline characteristics were compared across detention status. Cross-tabulation tables were conducted between detention status and covariates mentioned previously to assess potential confounding and effect measure modification. We then ran simple logistic regression models predicting the likelihood of MDR-TB using detention and all covariates in order to: calculate the crude model and unadjusted odds ratio (OR) of the relationship between detention and MDR-TB; to assess potential confounding from all covariates; and to determine which covariates to retain in our model. We ran a full multivariable logistic regression on the relationship between MDR-TB and detention, adjusting for confounders and other covariates to estimate the adjusted OR. All analyses were carried out in SAS Studio, version 3.82 (SAS Institute, Inc., Cary, NC, USA).

**Results**

*Patient Characteristics*

Between 2008-2009, more than one-fifth of notified TB cases in the Moldovan database were MDR-TB cases (21.21%; Table 1). Among TB patients in Moldova without a history of detention, 17.97% had MDR-TB, while among patients with a history of detention, more than one-third had MDR-TB (39.80%). In terms of detention history, 14.84% of notified TB patients in this database had a history of dentation. Most covariates were found to be significantly associated with detention status at an alpha level of 0.001, except for housing status, which was significantly associated with detention status at an alpha level of 0.01, and citizenship was not found to be associated with detention status at all. This indicates that there are large demographic differences between our sample with a history of detention and out sample without a history of detention. Our sample of patients with a history of detention generally had a larger proportion of males, urban residence, unhoused, having had previous TB treatment, and having concurrent HIV when compared to our sample of patients with no history of detention.

**Table 1.** Patient characteristics across detention status.

|  |  |  |  |
| --- | --- | --- | --- |
|  | History of detention (N=1294) | No history of detention (N=7424) | Total  (N=8718) |
| **MDR-TB\*\*\***  Yes  No  **Sex**\*\*\* | 515 (39.80)  779 (60.20) | 1334 (17.97)  6090 (82.03) | 1849 (21.21)  6689 (78.79) |
| Male  Female | 1245 (96.21)  49 (3.79) | 5174 (69.69)  2250 (30.31) | 6419 (73.63)  2299 (26.37) |
| **Residence**\*\*\* |  |  |  |
| Urban  Rural | 786 (60.74)  508 (39.26) | 3599 (48.48)  3825 (51.52) | 4385 (50.30)  4333 (49.70) |
| **Citizenship** |  |  |  |
| Moldovan  Other | 1287 (99.46)  7 (0.54) | 7391 (99.56)  33 (0.44) | 8678 (99.54)  40 (0.46) |
| **Education**\*\*\* |  |  |  |
| Primary  Secondary  Specialized secondary  Higher  None | 301 (23.26)  837 (64.68)  134 (10.36)  9 (0.70)  13 (1.00) | 1636 (22.04)  4192 (56.47)  1080 (14.55)  319 (4.30)  197 (2.65) | 1937 (22.22)  5029 (57.59)  1214 (13.93)  328 (3.76)  210 (2.41) |
| **Occupation**\*\*\* |  |  |  |
| Employed  Unemployed  Retired  Student  Disabled | 70 (5.41)  1106 (85.47)  15 (1.16)  41 (3.17)  62 (4.79) | 1482 (19.96)  4259 (57.37)  590 (7.95)  358 (4.82)  735 (9.90) | 1552 (17.80)  5365 (61.54)  605 (6.94)  399 (4.58)  797 (9.14) |
| **Unhoused**\*\* |  |  |  |
| Yes  No | 92 (7.11)  1202 (92.89) | 382 (5.15)  7042 (94.85) | 474 (5.44)  8244 (94.56) |
| **Had previous TB treatment**\*\*\* |  |  |  |
| Yes  No | 706 (54.56)  588 (45.44) | 2073 (27.92)  5351 (72.08) | 2779 (31.88)  5939 (68.12) |
| **Concurrent HIV**\*\*\* |  |  |  |
| Yes  No | 205 (15.84)  1089 (84.16) | 321 (4.32)  7103 (95.68) | 526 (6.03)  8192 (93.97) |

\*significant at p ≤ 0.05

\*\*significant at p ≤ 0.01

\*\*\*significant at p ≤ 0.001

*Confounders*

All our remaining covariates - previous TB treatment, concurrent HIV, sex, residence, occupation, education, and being unhoused – were also found to be individually associated with MDR-TB. Upon testing a model with all these confounders, we retained all but education due to its loss of significance in the presence of other factors and its negligible effect on the overall models’ fit, if not slight improvement with its removal. Our final model predicting MDR-TB included detention adjusting for previous TB treatment, concurrent HIV, sex, residence, occupation, and being unhoused.

*Detention and MDR-TB*

Our crude model estimates that patients with a history of detention have 3.108 times the odds of developing MDR-TB compared to patients without a history of detention (Table 2). Our adjusted model found that patients with a history of detention have 1.877 times the odds of developing MDR-TB, adjusted for previous TB treatment, concurrent HIV, sex, residence, occupation, and being unhoused, compared to patients without a history of detention.

**Table 2.** Adjusted multivariable logistic regression model predicting MDR-TB with detention, adjusting for confounders.

|  |  |  |
| --- | --- | --- |
|  | **OR (95% CI)** | **P-value** |
| **Crude Model** | | |
| Model χ2 = 277.5661 (1 df, N=8718), p-value < 0.0001 | | |
| **Detention** |  |  |
| Yes  No | 3.108 (2.661, 3.424)  Reference | P < 0.0001  Reference |
| **Adjusted model** | | |
| Model χ2 = 993.6623 (14 df, N=8718), p-value < 0.0001 | | |
| **Detention** |  |  |
| Yes  No | 1.877 (1.626, 2.167)  Reference | P < 0.0001  Reference |
| **Had previous TB treatment** |  |  |
| Yes  No | 3.880 (3.462, 4.348)  Reference | P < 0.0001  Reference |
| **Concurrent HIV** |  |  |
| Yes  No | 1.551 (1.258, 1.911)  Reference | P < 0.0001  Reference |
| **Sex** |  |  |
| Female  Male | 0.866 (0.754, 0.994)  Reference | P=0.0409  Reference |
| **Residence** |  |  |
| Urban  Rural | 1.271 (1.135, 1.423)  Reference | P < 0.0001  Reference |
| **Occupation** | - | P < 0.0001 |
| Employed  Disabled  Retired  Student  Unemployed | 0.814 (0.691, 0.958)  1.003 (0.836, 1.204)  0.466 (0.351, 0.617)  0.943 (0.706, 1.259)  Reference | P=0.0135  P=0.9726  P < 0.0001  P=0.6889  Reference |
| **Unhoused** |  |  |
| Yes  No | 1.344 (1.080, 1.672)  Reference | P=0.0080  Reference |

**Discussion**

Our study demonstrates that there is a strong and harmful relationship between history of detention and MDR-TB even when adjusted for confounders such as, previous TB treatment, concurrent HIV infection, sex, residence, occupation, and houselessness. In our sample, a staggering one-fifth of TB cases were MDR-TB cases (21.21%), but when we looked at our sample with a history of detention that proportion almost doubles (39.80%).

Our findings contribute to the literature that prisons in post-Soviet countries, including Moldovan prisons, experience a large burden of MDR-TB.1-3 Identifying high risk populations will allow policy makers to better prioritize resources and strengthen TB diagnostics and treatment initiation in populations most in need. Jenkins et al. (2013) suggests that there is a substantial burden of drug resistance in Moldovan prisons and found that the high MDR-TB prevalence in prison can actually disproportionately contribute to local TB rates in the civilian sector. MDR-TB is not confined to prison walls and in order to prevent community transmission of MDR-TB, which is more costly to treat than DS-TB, we must directly address MDR-TB in prisons and improve timely diagnostic, treatment, and control policies, as well access to healthcare overall.3 Ensuring incarcerated people are able to complete the full regimen of treatment before their release back into the community is also vitally important so as to not transmit TB into the community as well as to prevent the development of drug resistance.1,3 Additionally, it is equally important to implement policies to address overcrowding, poor ventilation quality, and malnutrition to curb the transmission on TB within prisons and decrease incidence.1

*Limitations*

This study was a general investigation of MDR-TB cases in Moldova and therefore did not differentiate between newly developed MDR-TB from DS-TB cases and cases that were drug-resistant at onset. As a result, our findings cannot be used to draw conclusions on the level of community transmission of MDR-TB strains, as opposed to MDR-TB cases that developed throughout treatment for DS-TB cases. This distinction between newly developed MDR-TB and MDR-TB at onset would provide further context to the TB epidemic and indicate a more accurate picture of the burden on disease in Moldova. Jenkins et al. (2013), however, did conduct research using similar Moldova data and found that 23.5% of new cases were MDR-TB and concluded that community transmission of drug resistant strains is a main driver of this epidemic between 2007-2010. Additional research in this area would benefit our understanding and management of the epidemic.

Our findings were also limited in our information regarding the nature of patients’ detention history. More detailed data on length of detention, number of individual instances of detention, how far removed was a patients’ last contact with detention facilities, type of facility, etc. would have helped develop a more robust understanding of the impact of detention history on MDR-TB.

**Conclusion**

MDR-TB is a pressing infectious disease public health threat that comes with high costs for human life, in addition to a large economic burden. MDR-TB also sheds light on the inhumane conditions of prisons plagues with overcrowding, malnutrition, and poor ventilation systems that harm human health beyond TB. It is imperative that resources and efforts begin to be diverted to assessing and improving the current state of prisons and the incarceration system, in addition to improving timely and quality TB diagnosis and treatment as a cost-effective way to curb incidence and death due to TB, generally and within prisons, and prevent transmission to local communities. Large economic costs due to unfettered TB proliferation and death can be circumvented in the long-term by investment in early diagnosis and treatment. This study contributes to the literature urging policy makers to focus on this high risk population as a pivotal component of Moldova’s TB control program.

**References**

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