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Short Communication

Socioeconomic disparities and multidrug-resistant tuberculosis in South Korea: Focus on immigrants and income levels

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Received 16 May 2022; received in revised form 24 July 2022; accepted 21 August 2022

Available online 7 September 2022

KEYWORDS

Tuberculosis;
Multidrug-resistant
tuberculosis;
Socioeconomic;
Predictors;
Disparities

Abstract Risk factors of MDR-TB remain unclear in South Korea, despite being an important public health issue. Findings from this study, which included $\geq 50,000$ patients with TB from South Korea, suggests that immigrants and patients with lower income levels were strong predictors of MDR-TB in a high-income, high TB incidence country.

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Introduction

Tuberculosis (TB) remains an important public health issue in South Korea, by ranking first in TB incidence amongst 38 Organization for Economic Co-operation and Development

(OECD) member countries.¹ With the dramatic increase from 1.5 million immigrants in 2013 to 2.4 million in 2018, South Korea is projected to become a multi-ethnic country (immigrant proportion $>5\%$) by 2024. Meanwhile, income inequality is also substantial in South Korea (Gini coefficient 0.345 versus 0.316 [OECD average]),² placing it ninth among OECD member countries. Despite these emerging challenges in socioeconomically vulnerable or immigrant populations, risk factors of multidrug-resistant TB (MDR-TB) remain yet to be fully understood, which warrant a comprehensive description of MDR-TB predictors. Hence, we aimed to identify demographic, socioeconomic, and

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clinical predictors associated with MDR-TB development among patients with TB in South Korea.

Methods

We used, to our knowledge, the largest nationwide TB database available by linking approximately 0.1 million patients in the TB registry of the Korea Disease Control and Prevention Agency (KCDA) to insurance claims and health examination records for 50 million Korean residents of the Health Insurance Review and Assessment Service (HIRA) and the National Health Insurance Service (NHIS), respectively. We identified all patients newly diagnosed with TB between 2013 and 2018, and defined cohort entry as the first date of diagnosis. Patient characteristics were classified into four categories (data source with respective variable): demographic (HIRA/KCDA), socioeconomic (NHIS), and clinical (KCDA/HIRA/NHIS) data. We described baseline patients' characteristics as counts with proportions for categorical variables and mean with standard deviations for continuous variables. We then conducted univariable and multivariable logistic regression analyses to estimate unadjusted and adjusted odds ratios (OR) with 95% confidence intervals (CIs) for predictors associated with MDR-TB, respectively.

All analyses were done using SAS Enterprise, version 7.1 (SAS Institute Inc, NC, USA). The study protocol was approved by the Institutional Review Board of Sungkyunkwan University (SKKU 2019-10-030-001) and obtaining informed consent was waived by the board.

Results

Of 63,241 patients with TB identified from the large-scale, linked, nationwide TB database, 1309 (2.1%) developed MDR-TB. The mean age of the cohort of patients with TB was 54.7 years (standard deviation 19.7 years), with the majority being male (60.9%), Korean (98.5%), and national health insurance beneficiaries (89.5%). Among patients with TB, those who developed were generally younger (mean age 49.8 years [standard deviation 18.4 years] versus 54.8 years [19.7]) and more male sex (66.0% versus 60.8%) (Table 1).

In the multivariable regression analysis, immigrants (or foreign-born persons) were identified as the strongest predictor of developing MDR-TB among patients with TB by having the largest positive association (OR 2.38, 95% CI 1.78–3.18) when compared with Koreans, followed by low (Q1; OR 1.48, 95% CI 1.22–1.79) and lower-middle (Q2; OR 1.54, 95% CI 1.29–1.84) income levels compared to the high-income level, TB reported from public health centers versus clinics (OR 1.46, 95% CI 1.16–1.85), and history of type 2 diabetes (T2D) versus no T2D history (OR 1.38, 95% CI 1.16–1.64) (Fig. 1). Meanwhile, patients who were aged more than 65 years of age, as compared with those aged less than 25 years, were found to be inversely associated with MDR-TB onset (OR 0.58, 95% CI 0.46–0.72). Only associations between patient characteristics and risk of developing MDR-TB that were statistically significant are presented in the Figure.

Discussion

This study, which included $\geq 50,000$ patients with TB from South Korea, is likely generalizable and comprehensive by being nationwide and having explored diverse factors associated with MDR-TB onset, respectively. Especially, immigrants and lower income levels were strong predictors of MDR-TB among the range of characteristics examined, with immigrants having a 2.38-fold increased risk of MDR-TB compared with Koreans.

There was high heterogeneity in the patient characteristics assessed from existing literature and thus, a direct comparison with our findings was difficult. Nevertheless, our findings were largely consistent with systematic reviews from Europe (high-income, low TB incidence) and China (upper/middle-income, high TB incidence) that identified MDR-TB predictors as foreign-born (OR 2.46, 95% CI 1.86–3.24) and male (OR 1.38, 95% CI 1.16–1.65),³ and migrant populations (OR 1.96, 95% CI 1.50–2.57) and low family income (OR 2.23, 95% CI 1.74–2.85),⁴ respectively. Furthermore, 97.5% of MDR-TB cases ($n = 196$) in the United States (high-income, low TB incidence) were foreign-born patients.⁵ Moreover, the non-linear association observed between the risk of MDR-TB and the level of income may be due to the majority of patients included in this study having received substantial financial support from the government for their TB-related medical expenses.⁶ Hence, our findings add to the evidence that immigrants and low-income levels are predictors of MDR-TB in a high-income, high TB incidence country, transcending a country's economic level or incidence TB.

Although management of TB among immigrants after their entry into South Korea remains difficult, those diagnosed with TB or MDR-TB are eligible to receive any necessary treatment at TB-centered hospitals at no costs, given that all TB-related healthcare services (including new high-priced MDR-TB treatments) are covered entirely by the domestic health insurance program since 2011. Hence, immigrants and Korean nationals are given equal healthcare access, with regard to TB. However, immigrants that are non-compliant with treatment or have entered Korea for treatment purposes will be deported and restricted reentry upon treatment completion under quarantine. Meanwhile, the Korean government has implemented foreigner-specific TB and latent TB screening pilot programs starting in 2018 to specifically address these often neglected, but vulnerable populations and to eventually achieve a systematic and early TB detection strategy. As for immigrants seeking long-term residency or work from high-risk countries (e.g., China, Vietnam), it is currently mandatory that they undergo TB screening upon arrival, where if tested positive, visa issuance will be delayed until further proof of full recovery. Nevertheless, the Korean government is making persistent efforts given the raised awareness of the importance of immigrants in effectively managing TB.⁶

Unfortunately, global TB efforts have been catastrophically impacted due to the coronavirus disease 2019 (COVID-19),^{7,8} raising concerns on the already fragile health systems of and populations with TB. Moreover, indirect inferences to TB or MDR-TB could also be made on the basis of previous studies on COVID-19 which also showed that migrants in

Table 1 Baseline characteristics of patients with tuberculosis overall and stratified by the development of multidrug-resistant tuberculosis in South Korea, 2013–2018.

	Patients with TB		Developed MDR-TB		Did not Develop MDR-TB	
Total (n, %)	63,241	100.0	1309	100.0	61,932	100.0
Demographic variables						
Age (years; mean \pm SD)	54.7 \pm 19.7		49.8 \pm 18.4		54.8 \pm 19.7	
Age group (years; n, %)						
<25	6633	10.5	152	11.6	6481	10.5
25–44	12,227	19.3	352	26.9	11,875	19.2
45–64	21,309	33.7	495	37.8	20,814	33.6
\geq 65	23,072	36.5	310	23.7	22,762	36.8
Sex (n, %)						
Male	38,506	60.9	864	66.0	37,642	60.8
Female	24,735	39.1	445	34.0	24,290	39.2
Region of residence (n, %)						
Urban	43,335	68.5	912	69.7	42,423	68.5
Rural	19,906	31.5	397	30.3	19,509	31.5
Nationality (n, %)						
Korean	62,291	98.5	1257	96.0	61,034	98.6
Immigrant ^b	950	1.5	52	4.0	898	1.5
TB-reporting institute (n, %)						
Public health center	2540	4.0	83	6.3	2457	4.0
Clinic	60,701	96.0	1226	93.7	59,475	96.0
Socioeconomic variables						
Health insurance (n, %)						
NHI	56,605	89.5	1146	87.6	55,459	89.6
Medical aid	6636	10.5	163	12.5	6473	10.5
Income level^a (n, %)						
Q1 (most deprived)	15,126	23.9	204	15.6	14,922	24.1
Q2	15,927	25.2	316	24.1	15,611	25.2
Q3	14,981	23.7	377	28.8	14,604	23.6
Q4 (most affluent)	17,207	27.2	412	31.5	16,795	27.1
Clinical variables^c (n, %)						
History of cardiovascular disease						
Yes	8494	13.4	114	8.7	8380	13.5
No	54,747	86.6	1195	91.3	53,552	86.5
History of chronic kidney disease						
Yes	1849	2.9	36	2.8	1813	2.9
No	61,392	97.1	1273	97.3	60,119	97.1
History of asthma						
Yes	14,614	23.1	254	19.4	14,360	23.2
No	48,627	76.9	1055	80.6	47,572	76.8
History of COPD						
Yes	13,637	21.6	225	17.2	13,412	21.7
No	49,604	78.4	1084	82.8	48,520	78.3
History of type 2 diabetes						
Yes	16,326	25.8	348	26.6	15,978	25.8
No	46,915	74.2	961	73.4	45,954	74.2
History of chronic liver disease						
Yes	2547	4.0	62	4.7	2485	4.0
No	60,694	96.0	1247	95.3	59,447	96.0
CCI score						
0	20,043	31.7	505	38.6	19,538	31.6
1–2	18,707	29.6	370	28.3	18,337	29.6
3+	24,491	38.7	434	33.2	24,057	38.8
Past insulin use						
Yes	4243	6.7	106	8.1	4137	6.7
No	58,998	93.3	1203	91.9	57,795	93.3

Table 1 (continued)

	Patients with TB		Developed MDR-TB		Did not Develop MDR-TB	
Past systemic steroid use						
Yes	30,710	48.6	599	45.8	30,111	48.6
No	32,531	51.4	710	54.2	31,821	51.4
Past immunosuppressant use						
Yes	2244	3.6	42	3.2	2202	3.6
No	60,997	96.5	1267	96.8	59,730	96.4
Health care utilization						
Admission history						
0	22,022	34.8	466	35.6	21,556	34.8
1–2	28,874	45.7	583	44.5	28,291	45.7
≥3	12,345	19.5	260	19.9	12,085	19.5
Physician visits						
0–2	4628	7.3	150	11.5	4478	7.2
3–5	3818	6.0	101	7.7	3717	6.0
≥6	24,491	38.7	434	33.2	24,057	38.8

^a Income levels classified into 11 groups from 0 to 10, according to the type of health insurance. 10 of the groups are for employee and district subscribers while, group 0 indicates medical aid. Low (Q1, groups 0–2), Lower-Middle (Q2, groups 3–5), Upper-Middle (Q3, groups 6–8), High (Q4, groups 9–10).

^b Defined as a non-Korean (e.g., immigrants). Of 960 immigrant patients with TB, the top 3 nationalities were China (n = 665 [69.3%]), Vietnam (n = 73 [7.6%]), and Philippines (n = 25 [2.6%]). Immigrant patients with TB from Russia had the highest incidence of MDR-TB (27.3%), followed by Uzbekistan (25.0%) and China (6.0%).

^c Assessed within 365 days prior to cohort entry (date of diagnosis with TB).

CCI, Charlson comorbidity index; COPD, chronic obstructive pulmonary disease; MDR-TB, multidrug-resistant tuberculosis; NHI, national health insurance; TB, tuberculosis.

Predictors (strongest to weakest)	Odds ratio (95% CI)		Adjusted odds ratio (95% CI)
	Crude	Adjusted [†]	
Immigrants <i>versus</i> Korean	2.81 (2.11-3.74)	2.38 (1.78-3.18)	
Income Level [‡] Q2 <i>versus</i> Q4	1.89 (1.59-2.24)	1.54 (1.29-1.84)	
Income Level [‡] Q1 <i>versus</i> Q4	1.79 (1.52-2.13)	1.48 (1.22-1.79)	
Public Health Center (TB report) <i>versus</i> Clinic	1.64 (1.31-2.05)	1.46 (1.16-1.85)	
History [§] of T2D <i>versus</i> No T2D History	1.04 (0.92-1.19)	1.38 (1.16-1.64)	
Income Level [‡] Q3 <i>versus</i> Q4	1.48 (1.24-1.77)	1.30 (1.09-1.56)	
≥3 Hospital Admissions [§] <i>versus</i> No Admissions	1.00 (0.85-1.16)	1.30 (1.09-1.55)	
National Health Insurance <i>versus</i> Medical Aid	1.22 (1.03-1.44)	1.26 (1.03-1.55)	
Male <i>versus</i> Female	1.25 (1.12-1.41)	1.13 (1.00-1.28)	
CCI [§] score 2 <i>versus</i> CCI score 0	0.70 (0.61-0.78)	0.79 (0.65-0.97)	
History [§] of CVD <i>versus</i> No CVD History	0.61 (0.50-0.74)	0.75 (0.61-0.93)	
≥6 Physician Visits [§] <i>versus</i> 0-2 Visits	0.59 (0.49-0.70)	0.71 (0.59-0.86)	
Aged ≥65 years <i>versus</i> <25 years	0.58 (0.48-0.71)	0.58 (0.46-0.72)	

0.4 1.0 3.5
Not Develop MDR-TB Develop MDR-TB

Figure 1. Predictors* of multidrug-resistant tuberculosis development among patients with tuberculosis in South Korea. *Only statistically significant predictors displayed in forest plot; predictors with an OR estimate's 95% CI that included the null (1.0) are not shown. †Adjusted for all baseline characteristics in the multivariable logistic regression model. ‡Income levels classified into 11 groups from 0 to 10, according to the type of health insurance. 10 of the groups are for employee and district subscribers while, group 0 indicates medical aid. Low (Q1, groups 0–2), Lower-Middle (Q2, groups 3–5), Upper-Middle (Q3, groups 6–8), High (Q4, groups 9–10). §Assessed within 365 days prior to cohort entry (date of diagnosis with tuberculosis). CCI, Charlson comorbidity index; CI, confidence interval; CVD, cardiovascular disease; MDR-TB, multidrug-resistant tuberculosis; T2D, type 2 diabetes.

high-income countries were at a higher risk of exposure to, and infection with, COVID-19,⁹ and countries with more immigrants had more COVID-19 cases.¹⁰ Based on these data, the lessons learnt from the ongoing COVID-19 pandemic, for

instance screening and management, could be adapted for future TB measures and complemented with existing measures to eliminate TB to potentially reduce any currently widened gaps in health or socioeconomic disparities.

Eliminating TB and MDR-TB appear particularly challenging in South Korea, despite the persistent efforts and implementations of diverse TB strategies (e.g., expanded insurance coverage, public-private mix models),⁶ which were in accordance with the World Health Organization's END-TB strategy by 2035. This difficulty, in light of our findings and previous evidence, is likely attributable to high-income country-specific characteristics such as the growing influx of immigrants along with widening income inequalities over time. Thus, formal reassessment of current policy and legal frameworks is imperative to accurately address these vulnerable populations with TB where, international collaborative efforts, especially among neighboring countries, may further lower the public health burden from TB.

Funding/support

This work was supported by a grant of the Korea Health Technology R&D Project through the Korea Health Industry Development Institute (KHIDI), funded by the Ministry of Health & Welfare, South Korea (grant number: HI19C1233). The funding source had no role in defining the study objectives, data analysis, interpretation of the results, or the decision to submit the manuscript for publication.

Data availability

The health insurance claims database of the National Health Insurance Service can be accessed at: <https://nhiss.nhis.or.kr/bd/ab/bdaba022eng.do>.

Declaration of competing interest

All authors declare no competing interests.

Acknowledgements

The authors thank the National Health Insurance Service of South Korea for sharing invaluable data (data number: NHIS-2021-6-005), which was linked to the nationwide

tuberculosis notification registry of the Korea Disease Control and Prevention Agency and the Health Insurance Review and Assessment Service.

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