Social and Clinical Characteristics of Immigrants with Tuberculosis in South Korea

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Purpose: To determine the social and clinical characteristics of immigrants with tuberculosis (TB) in South Korea.

Materials and Methods: The registered adult TB patients who were diagnosed and treated in Korea Medical Centers from January 2013 to December 2015 were analyzed retrospectively. A total of 105 immigrants with TB were compared to 932 native Korean TB patients.

Results: Among these 105 immigrants with TB, 86 (82%) were Korean-Chinese. The rate of drug-susceptible TB were lower in the immigrants group than in the native Korean group [odds ratio (OR): 0.46; 95% confidence interval (CI): 0.22−0.96, p=0.035]. Cure rate was higher in the immigrant group than in the native Korean group (OR: 2.03; 95% CI: 1.26−3.28, p=0.003). Treatment completion rate was lower in the immigrant group than in the native Korean group (OR: 0.50; 95% CI: 0.33−0.74, p=0.001). However, treatment success rate showed no significant difference between two groups (p=0.141). Lost to follow up (default) rate was higher in the immigrant group than in the native Korean group after adjusting for age and drug resistance (OR: 3.61; 95% CI: 1.36−9.61, p=0.010). There was no difference between defaulter and non-defaulter in clinical characteristics or types of visa among these immigrants (null p value). However, 43 TB patients with recent immigration were diagnosed as TB even though they had been screened as normal at the time of immigration.

Conclusion: Endeavor to reduce the default rate of immigrants with TB and reinforce TB screening during the immigration process must be performed for TB infection control in South Korea.

Key Words: Immigrants, tuberculosis, microbial sensitivity tests, medication adherence, mass screening

INTRODUCTION

One third of the world's population is infected by tuberculosis (TB). TB burden in South Korea is intermediate, with annual incidence of 86/100000 in 2014.[1] Keeping pace with Sustainable Development Goals for 2030 proposed by World Health Organization (WHO) to end TB epidemic by 2030, the Korean Centers for Disease Control and Prevention have launched a comprehensive plan for TB control since 2013. Representative policies included the implementation of public-private mix (PPM) program, subsidy of medical expenses, and reinforcement of outbreak investigations such as latent tuberculosis infection (LTBI) control program.[2]

The PPM program provides rigorous follow-up monitoring by nurses trained exclusively for TB patient management. It has resulted in lower follow up loss rate (6.6%) (treatment default rate) for PPM enrolled patients than that for controls (22.9%), resulting in better treatment outcomes (91.6% vs. 71.8%).[3,4] However, there has been no report about treatment behaviors of immi-

grants in South Korea, including the effectiveness of PPM for these immigrants from the viewpoint of treatment outcome.

Theoretically, major TB control strategy in low TB-burden countries is to screen for active TB and LTBI in TB contacts and select high-risk groups, including migrants who are vulnerable and hard-to-reach.[5] In the same context, main candidates for LTBI treatment in low TB-burden countries can be immigrants from TB-endemic areas depending on the situation.[6] The number of immigrants with TB is increasing every year in Korea. The number of notified TB cases and that of sputum smear-positive TB cases among foreigners are 1944 and 398, respectively.[7] The common race of TB patients among these foreigners is Chinese, accounting for 50% of total TB patients. More than half of these Chinese TB patients are Korean-Chinese from northeastern China, including the Yanbian Korean Autonomous Prefecture.[8]

The objective of this study was to determine the characteristics of TB patients among immigrants and defaulters who stopped TB medication arbitrarily compared to native Korean TB patients. Results of this study will help administrative procedure for visa in emigration and immigration process for TB infection control.

MATERIALS AND METHODS

Study population and oversight
Notified and registered TB patients who were diagnosed and treated at Korea University Ansan Hospital and Korea University Guro Hospital from January 2013 to December 2015 were analyzed retrospectively in this study. In these hospitals, well-trained TB nurses are working in collaboration with PPM. Subjects used for final analysis were adult TB patients who were foreign-born residents or native Koreans above 20 years old. They completed TB treatment by December 2015. The Korea University Ansan Hospital is a tertiary hospital located in Ansan city where one tenth of 700000 residents are foreigners. Korea University Guro Hospital is a tertiary hospital located near the biggest Korean-Chinese towns.

Sputum smear was examined after Ziehl-Nelsen Acid Fast Bacilli stain. Sputum samples were cultured in solid mycobacterial culture medium (Ogawa medium) and liquid broth medium (MGIT tube; Becton-Dickinsonand Co., Sparks, MD, USA).

Visa types of immigrants were reviewed to investigate their relationships with interruption of TB drugs. Based on previous reports, common types of visa for these immigrants were F-4 (overseas Korean, 17.1%), H-2 (working visit, 15.9%), E-9 (non-professional employment, 14.8%), F-5 (permanent resident,

Table 1. Clinical Characteristics of all TB Patients

Variable	Total (n=1037)	Immigrants (n=105)	Korean (n=932)	p value	OR	95% CI
Sex						
Male	562 (54)	53 (50)	509 (55)	0.420	0.85	0.57–1.27
Female	475 (46)	52 (50)	423 (45)		1	
Age						
20–30	141 (13)	31 (30)	110 (12)	0.001	2.33	1.39–3.91
31–50	361 (35)	39 (37)	322 (34)		1	
>50	535 (52)	35 (33)	500 (54)	0.023	0.58	0.36–0.93
Mean age	52±18.1	42.5±13.9	53.5±18.2	0.010		
Classification of TB						
Pul. TB	697 (67)	72 (69)	625 (67)	0.754	1.072	0.69–1.65
Extrapul. TB	340 (33)	33 (31)	307 (33)		1	
Birth place						
China		86 (82)	NA			
East Asia		12 (11)	NA			
Central Asia		5 (5)	NA			
Other region		2 (2)	NA			
Employment						
Unemployed		48 (46)	0		1	
Employed		37 (35)	526 (56)	<0.001	0.42	0.28–0.64
Unknown		20 (19)	406 (44)			
DST result						
All sensitive		34 (76)	344 (87)	0.035	0.46	0.22–0.96
Resistant		11 (24)	51 (13)		1	
≥1 drug						

TB, tuberculosis; Pul, pulmonary; Extrapul, extrapulmonary; DST, drug susceptibility testing; OR, odds ratio; CI, confidence interval.

Table 2. Treatment Outcomes for All TB Patients

Outcome	Total (n=1037)	Immigrants (n=105)	Korean (n=932)	p value	OR	95% CI
Cured	156 (15)	26 (25)	130 (14)	0.003	2.03	1.26–3.28
Treatment completed	644 (62)	49 (47)	595 (64)	0.001	0.50	0.33–0.74
Treatment failed	1 (<1)	1 (1)	0			
Died	50 (5)	4 (4)	46 (5)	0.610	0.76	0.27–2.16
Lost to follow-up (default)	70 (7)	20 (19)	50 (5)	<0.001	4.15	2.36–7.30
Not evaluated (transferred out)	116 (11)	5 (5)	111 (12)	0.028	0.37	0.15–0.93
Treatment success	800 (77)	75 (71)	725 (78)	0.141	0.71	0.46–1.12

TB, tuberculosis; OR, odds ratio; CI, confidence interval.

6.4%), D-2 (student, 3.9%), and F-2 (resident, 2.0%) in 2015.[9] Immigration procedure for overseas Korean including F4 type visa has been relieved since 2013. F4 type visa can be acquired now after certain period of H2 type visa.[10]

The definition of treatment outcome was categorized based on 2013 WHO revised definition.[11] The visa type was the initial visa status of immigrants on entrance to South Korea. The study protocol was approved by the Institutional Review Board (IRB) of Korea University Ansan (KUAS15157-001) and Guro Hospital (KUGH15328-001). Informed consent for this study was waived by IRB due to its retrospective nature.

Statistical analysis

All analyses were performed using SPSS software, version 20.0 (SPSS Inc., Chicago, IL, USA). χ^2 test and t test were used to determine differences between immigrants and Koreans. All tests for significance were two-sided. Statistical significance was set at $p<0.05$. Associations of treatment outcome with nationality, age, and drug sensitivity were analyzed by binary logistic regression.

RESULTS

Clinical characteristics

Of a total of 1087 patients, 1037 patients who met the inclusion criteria were finally analyzed in this study (Table 1). The mean ages of patients in the immigrant group and the native Korean groups were 42.5±13.9 years and 53.5±18.2 years ($p=0.010$), respectively. A total of 53 patients (51%) in the immigrant group and 509 patients (55%) in the native Korean groups were males. One hundred-five patients were immigrants from 9 countries: China (82%), East Asia (11%), Central Asia (5%), and other regions (2%). A total of 72 patients (69%) in the immigrant group and 625 patients (67%) in the native Korean group were confirmed as pulmonary TB, whereas a total of 33 patients (31%) in the immigrant group and 307 patients (33%) in the native Korean group were confirmed as extra-pulmonary TB. Less patients were in employed state in the immigrant group compared to those in the native Korean group [37 (35%) vs. 526 (56%), odds ratio (OR): 0.42, 95% confidence interval (CI): 0.28–0.64,

Table 3. Difference in Treatment Outcomes between Immigrants and Native Koreans after Adjusting for Age, DST Result, and Employment Status

Outcome	p value	OR	95% CI
Lost to follow-up (default)			
Nationality			
Immigrants	0.010	3.61	1.36–9.61
Korean		1	
Age	0.825	0.997	0.97–1.02
DST result			
Resistant	0.078	2.34	0.91–6.05
All sense		1	
Treatment success			
Nationality			
Immigrants	0.055	0.39	0.15–1.02
Korean		1	
Age	<0.001	1.03	1.01–1.04
DST result			
Resistant	<0.001	0.31	0.17–0.56
All sensitive*		1	
Employment			
Unemployed	0.501	0.61	0.15–2.55
Employed		1	

DST, drug susceptibility testing; OR, odds ratio; CI, confidence interval.
*All sensitive means that cultured *Mycobacterium tuberculosis* was sensitive to all tuberculosis drugs on drug sensitivity test.

$p<0.001$]. The rate of drug-susceptible TB were lower in the immigrants group than in the native Korean group [34 (76%) vs. 344 (87%), OR: 0.46, 95% CI: 0.22–0.96, $p=0.035$].

Treatment outcomes for TB patients

Treatment outcomes for all TB patients are summarized in Table 2. Cure rate was higher in the immigrant group (25%, 26/105) than that in the native Korean group (14%, 130/932) (OR: 2.03, 95% CI: 1.26–3.28, $p=0.003$). Conversely, treatment completion rate was lower in the immigrant group (47%, 49/ 105) than that in the native Korean group (64%, 595/932) (OR: 0.50, 95% CI: 0.33–0.74, $p=0.001$). However, treatment success rate was not significantly different between immigrants (71%, 75/105) and native Koreans (78%, 725/932) (OR: 0.71, 95% CI: 0.46–1.12,

Table 4. Resistance to Individual Anti-Tuberculosis Drugs

Outcome	Immigrants (n=105)	Korean (n=932)	p value
Isoniazid	8 (8.0)	34 (4.0)	0.137
Rifampin	3 (3.0)	17 (2.0)	0.684
Ethambutol	2 (2.0)	12 (1.0)	0.809
Pyrazinamide	2 (2.0)	7 (1.0)	0.406
Rifabutin	1 (1.0)	10 (1.0)	1.000
Kanamycin	0 (0.0)	1 (0.1)	0.926
Amikacin	0 (0.0)	1 (0.1)	0.926
Streptomycin	12 (1.0)	5 (5.0)	0.050
Levofloxacin	5 (5.0)	3 (0.3)	0.001
Moxifloxacin	5 (5.0)	4 (0.4)	0.001
Ofloxacin	5 (5.0)	4 (0.4)	0.001
Prothionamide	0 (0.0)	5 (0.5)	0.951
Cycloserine	0 (0.0)	1 (0.1)	0.926
Para-aminosalicylic acid	1 (1.0)	3 (0.3)	0.486
Linezolid	0 (0.0)	1 (0.1)	0.926
Clofazimine	0 (0.0)	1 (0.1)	0.926

p=0.141), even though there was one treatment failure in the immigrant group. Default (lost to follow-up) rate was significantly higher in the immigrant (19%, 20/105) than that in the native Korean group (5%, 50/932) (OR: 4.15, 95% CI: 2.36–7.30, p<0.001). Transfer-out (not evaluated) rate was significantly lower in the immigrant group (5%, 5/105) than that in the native Korean group (12%, 111/932) (OR: 0.37, 95% CI: 0.15–0.93, p=0.028). However, default (lost to follow-up) rate was not significantly different between Korea University Ansan Hospital and Guro Hospital (OR: 1.61, 95% CI: 0.60–4.34, null p value).

Treatment success rate was not significantly different either between immigrants and native Koreans after adjusting for age, drug resistance result, and employment status (OR: 0.39, 95% CI: 0.15–1.02, p=0.055) (Table 3). However, default (lost to follow-up) rate was significantly higher in the immigrant group than that in the native Korean group after adjusting for age, drug resistance result, and employment status (OR: 3.61, 95% CI: 1.36–9.61, p=0.010) (Table 3). In addition, resistances to quinolones were more prevalent in immigrants than in native Koreans (p=0.001) (Table 4).

Table 5. Characteristics of Immigrants with TB

Variable	Total (n=105)	Defaulter (n=20)	Non defaulter (n=85)	p value	OR	95% CI
Sex						
Male	53 (51)	13 (65)	40 (47)	0.149	2.09	0.76–5.75
Female	52 (49)	7 (35)	45 (53)		1	
Age						
20–30	31 (30)	6 (30)	25 (30)	0.456	1.63	0.45–5.95
31–50	39 (37)	5 (25)	34 (39)		1	
>50	35 (33)	9 (45)	26 (31)	0.157	2.35	0.70–7.87
Diagnosis						
Pul. TB	70 (67)	13 (65)	57 (67)	0.861	0.91	0.33–2.54
Extrapul. TB	35 (33)	7 (35)	28 (33)		1	
Birth place						
China	86 (82)	16 (80)	70 (82)	1.0	0.81	0.25–2.93
East asia	12 (11)	2 (10)	10 (12)	1.0	0.83	0.17–4.14
Central Asia	5 (5)	1 (5)	4 (5)	1.0	0.96	0.11–10.09
Other region	2 (2)	1 (5)	1 (1)	0.346	4.42	0.27–73.89
DST						
All sensitive	34 (76)	4 (57)	30 (79)	0.337	0.36	0.07–1.92
1≥drug resistant	11 (24)	3 (43)	8 (21)	0.337	1	
Immigration screening						
Visa without health screening	50 (54)	10 (56)	40 (53)	0.865	1.09	0.39–3.08
Visa with health screening	43 (46)	8 (44)	35 (47)	0.865	1	
Stay duration						
Short stay visa	3 (4)	0	3 (4)			
Long stay visa	90 (96)	18 (100)	72 (96)			
Insurance						
Coverage	97 (91)	16 (80)	79 (93)	0.094	0.30	0.08–1.20
No coverage	10 (9)	4 (20)	6 (7)		1	

TB, tuberculosis; Pul, pulmonary; Extrapul, extrapulmonary; DST, drug susceptibility testing; OR, odds ratio; CI, confidence interval.

Default rate and visa types of immigrants with TB

Characteristics of immigrants with TB are summarized in Table 5. There were no differences between defaulter and non-defaulter in sex, age, TB types, or drug resistant TB. Moreover, birthplace, immigration screening, stay duration, or insurance coverage did not significantly differ between defaulter and non-defaulter in immigrant TB patients (null *p* value).

As shown in Table 6, the most common visa types among immigrants were H-2 (working visit), F-4 (overseas Korean), and F-5 (permanent resident) (at 39.8, 22.6, and 14.0%, respectively). However, three TB patients (4.4%) were found among immigrants with short stay visas such as C-3 (short-term visit), C-4 (short-term employment), and H-1 (working holiday) that were valid less than three months. Moreover, 43 TB patients (46%) who recently immigrated less than 3 months ago (E-9: 6 immigrants, H-2: 37 immigrants) were diagnosed as TB, even though they had been screened as normal at the time of immigration.

DISCUSSION

Default rate of immigrants with TB in South Korea was higher than that in native Koreans. Some immigrants were not screened for active pulmonary TB during the first immigration process. In addition, the proportion of drug resistant strains was relatively higher in immigrants than that in native Koreans.

The mean age of TB patients was younger in immigrants than that in native Koreans (42.5±13.9 years vs. 53.5±18.2 years, *p*=0.010). Half of the immigrants were unemployed. The major ethnic group in immigrants was Korean-Chinese (Chosun Race) who had immigrated from northeastern China for economic goal.[12] The rates of TB cases with mullti-drug resistant (MDR)-TB among new cases and retreatment cases have been reported to be 8.6 and 23.2%, respectively, which are considerably higher than those (2.7, and 14%) in South Koreans.[1] Therefore, the finding that patients with resistant TB strain were more frequent in immigrants than those in native Koreans suggest that more restrictive TB infection control, including expansion of TB sc-reen for immigrants, is necessary to achieve 2030 TB eradication project.

The default rate of immigrants with TB including lost to follow-up in our study was 19%. The default rate in immigrants with TB in other study has been reported to be 11.5%[13] and 19.5%[14] depending on situations. To decrease default rate, political countermeasures such as strengthening emigration and immigration control and intensifying PPM collaboration by tracing TB medications of immigrants or directly observed treatment might be needed.

Treatment success rates in immigrants and native Koreans were 71 and 78%, respectively, in this study, which were relatively lower than the average success rate of 82% in Korea,[1] even though treatment success rate was not different between the two groups. However, cure rate requiring sequential sputum culture result was higher in immigrants compared to that in native Koreans (25% vs. 14%, *p*=0.003). The rate of treatment completion without result of sequential sputum culture was higher in native Koreans than that in immigrants (47% vs. 64%, *p*=0.001), even though microbiologic culture rates on initial diagnosis were not significantly different between the two groups (53% vs. 58%, null *p* value). These results suggest that reinforced case-holding activities based on standardized TB treatment are warranted in private tertiary hospital of S. Korea.[3] Based on similar treatment success rates between immigrants and native Koreans after adjusting for age, drug susceptibility testing results, and employment status, reinforced case-holding strategy including MDR-TB patients is strongly recommend for concentrated residence area of immigrants in South Korea.

There was no difference in clinical characteristics of immigrants between defaulter and non-defaulter, including mean age (43.5±16.6 years vs. 42.3±13.3 years, null *p* value). Insurance coverage of immigrants or long-term visa type did not affect

Table 6. Types of Visa in Immigrants with TB

Types of visa	Duration of stay	screening	n (%)
C-3 (short-term visit)	Short stay	No	1 (1.1)
C-4 (short-term employee)	Short stay	No	1 (1.1)
H-1 (working holiday)	Short stay	No	1 (1.1)
E-7 (designated activities)	Long stay	No	1 (1.1)
F-1 (visiting or joining family)	Long stay	No	1 (1.1)
F-3 (accompanying spouse/child)	Long stay	No	2 (2.2)
F-4 (overseas Korean)	Long stay	No	21 (22.5)
F-5 (permanent resident)	Long stay	No	13 (14.0)
F-6 (marriage to Korean citizen)	Long stay	No	5 (5.4)
G-1 (miscellaneous)	Long stay	No	4 (4.3)
E-9 (non-professional employment)	Long stay	Yes	6 (6.5)
H-2 (working visit)	Long stay	Yes	37 (39.6)
Total			93 (100)

TB, tuberculosis.

the interruption of TB drugs. However, some immigrants with short-term visa not requiring TB screening were confirmed to have active pulmonary TB after immigration. Moreover, 50.7% of immigrants with long-term visa were not screened at all during the immigration process (Table 6) because F type of visa was easily permitted to Koreans abroad for permanent residency. In addition, some immigrants with long-term visa such as H2 and F4 disappeared for visa renewal in their own country without informing changes of personal information. Therefore, health authorities must try to give information about the treatment course of immigrant TB patients who returned back to their own countries to corresponding country for successive TB treatment and get a confirmation report of continued TB treatment before re-entrance to Korea inversely. Furthermore, visa renewal process for immigrants on TB medication must be relieved to complete TB treatment before returning to their own country for visa extension process. In addition, strengthening of emigration and immigration control about TB screening for F type visa must be considered.

This study has several limitations. First, the number of enrolled immigrants was too small to generalize the findings. Secondly, we could not identify the precise reasons why defaulter stopped TB medications. We could not trace the changed personal information either. Thirdly, ethnic groups other than Korean-Chinese were not sufficiently analyzed for treatment behavior. Lastly, we were not certain whether the infected TB strains originated from their own countries without molecular epidemiologic evidences.

Despite these limitations, endeavor to reduce the default rate of immigrants with TB and reinforce TB screening during the immigration process is necessary to decrease TB incidence rate in South Korea.

ACKNOWLEDGMENTS

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