

# Incidence of Tuberculosis after Transplantation: A Nationwide Cohort Study in South Korea, 2008-2020

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## Background

Tuberculosis (TB) is one of the leading causes of morbidity and mortality among transplant recipient. The purpose of this study is to evaluate the standard incidence ratios (SIRs) of TB in all transplant recipient and to compare which is more risk by transplant type.

## Methods

We conducted a nationwide population-based retrospective study using data retrieved from the Health Insurance Review and Assessment Service. Active TB case were studied, and SIRs was calculated based on the most recent year, 2019. SIRs were computed as the ratio of observed to expected numbers of TB, based on national age and sex. All analyses were conducted by transplant type and age group.

## Results

From 2008 to 2020, a total of 57,103 patients who underwent transplantation were included. 830 cases were confirmed with TB (1.45%) and median time to develop TB was 1.74 year following transplantation. When analyzing the cumulative incidence by transplant group, it was in the order of allogenic hematopoietic stem cell transplantation (HSCT), solid organ transplantation (SOT), and autologous HSCT ( $P < 0.001$ ). In SOT, liver transplantation had the highest incidence of TB, followed by lung, heart, and kidney ( $P < 0.001$ ). The cumulative incidence for the age group increased with age ( $P < 0.001$ ). Incidence of TB was markedly increased among transplant recipients compared with general population (SIR: 3.53, Confidence interval (CI): 3.38-3.67). SIR varied according to age group: age under 20 years (SIR: 4.98 CI: 3.16-7.47), age between 20 and 40 years (SIR: 5.83 CI: 5.22-6.49), age between 40 and 60 years (SIR: 4.66 CI: 4.42-4.92), age over 60 years (SIR: 2.05 CI: 1.89-2.21). Based on a multivariate analysis, male sex (hazard ratio (HR) = 1.398;  $P < 0.001$ ), previous TB history (HR = 1.515;  $P = 0.014$ ) were the common independent risk factors for TB after transplantation.

Table 1. Baseline characteristics of the study population

	All transplantation			p-value
	Total (n=57,103)	TB group (n=830)	Non-TB group (n=56,273)	
<b>Age at transplant</b>				
0 to 19 years	4,851 (8.50)	30 (3.61)	4,821 (8.57)	<0.001
20 to 39 years	9,884 (17.31)	128 (15.42)	9,756 (17.34)	
40 to 59 years	31,783 (55.66)	474 (57.11)	31,309 (55.64)	
over 60 years	10,585 (18.54)	198 (20.56)	10,387 (18.46)	
<b>Sex</b>				
Male	35,123 (61.51)	575 (69.28)	34,548 (61.39)	<0.001
Female	21,980 (38.49)	255 (30.72)	21,725 (38.61)	
<b>Duration of follow-up, year</b>	5.29 ± 3.54	1.74 ± 2.03	5.35 ± 3.53	<0.001
<b>Comorbidities</b>				
Diabetes mellitus	23,028 (40.33)	377 (45.42)	22,651 (40.25)	0.003
Hypertension	32,726 (57.31)	485 (58.43)	32,241 (57.29)	0.051
Asthma	7,841 (13.73)	107 (12.89)	7,734 (13.74)	0.479
COPD	3,186 (5.58)	42 (5.06)	3,144 (5.59)	0.512
Liver Cirrhosis	12,019 (21.05)	198 (23.86)	11,821 (21.01)	0.046
Chronic kidney disease	21,930 (38.4)	319 (38.43)	21,611 (38.40)	0.986
Solid cancer	12,696 (22.23)	200 (24.10)	12,496 (22.21)	0.194
Hematologic malignancy	12,547 (21.97)	174 (20.96)	12,373 (21.99)	0.479
Autoimmune disease	309 (0.54)	1 (0.12)	308 (0.55)	0.144
<b>Charlson comorbidity index</b>	5.48 ± 2.85	5.88 ± 2.95	5.48 ± 2.85	<0.001
<b>Risk factors</b>				
Previous TB History	1,741 (3.05)	37 (4.46)	1,704 (3.03)	0.017
Pulmonary TB	965 (1.69)	27 (3.25)	938 (1.67)	<0.001
Extrapulmonary TB	1,024 (1.79)	15 (1.84)	1,009 (1.79)	0.976
<b>Type of Transplant</b>				
SOT	36,626 (64.14)	554 (66.75)	36,072 (64.1)	0.003
Allogenic HSCT	11,202 (19.61)	188 (22.65)	11,014 (19.57)	0.027
Autologous HSCT	9,275 (16.24)	88 (10.60)	9,187 (16.33)	<0.001
<b>Transplant site of SOT</b>				
Kidney*	20,904 (36.61)	296 (35.66)	20,608 (36.62)	0.569
Heart	1,373 (2.40)	19 (2.29)	1,354 (2.41)	0.827
Liver	13,568 (23.76)	224 (26.99)	13,344 (23.71)	0.028
Lung	600 (1.05)	11 (1.33)	589 (1.05)	0.435
Others †	181 (0.32)	4 (0.48)	177 (0.31)	0.394
<b>Outcome</b>				
Death	9,739 (17.06)	224 (26.99)	9,515 (16.91)	<0.001

## Conclusion

The incidence of TB in transplant recipient is at least three times higher than the general population in South Korea. Regardless of the type of transplant, TB should be considered as a complication within 1 years of transplantation and special attention should be paid to patients with a history of previous TB history.

Table 2. Risk factors associated with the development of TB after transplantation

		Univariate		Multivariate	
		HR (95% CI)	p-value	HR (95% CI)	p-value
<b>Age</b>	0 to 19 years	0.486 (0.327, 0.724)	<0.001	0.436 (0.291, 1.653)	<0.001
	20 to 39 years	1 (ref.)		1 (ref.)	
	40 to 59 years	1.201 (0.988, 1.460)	0.066	1.250 (1.021, 1.531)	0.030
	over 60 years	1.673 (1.339, 2.090)	<0.001	1.764 (1.394, 2.231)	<0.001
	Sex	M	1.419 (1.224, 1.645)	<0.001	1.398 (1.205, 1.623)
	F	1 (ref.)		1 (ref.)	
<b>Diabetes mellitus</b>	Yes	1.247 (1.108, 1.429)	0.002	1.135 (0.981, 1.314)	0.089
	No	1 (ref.)		1 (ref.)	
<b>Hypertension</b>	Yes	1.005 (0.876, 1.154)	0.939	0.984 (0.832, 1.165)	0.857
	No	1 (ref.)		1 (ref.)	
<b>Asthma</b>	Yes	0.975 (0.796, 1.194)	0.809	0.971 (0.786, 1.199)	0.786
	No	1 (ref.)		1 (ref.)	
<b>COPD</b>	Yes	1.06 (0.777, 1.446)	0.711	0.860 (0.623, 1.187)	0.358
	No	1 (ref.)		1 (ref.)	
<b>Liver Cirrhosis</b>	Yes	1.152 (0.982, 1.351)	0.008	0.882 (0.647, 1.202)	0.427
	No	1 (ref.)		1 (ref.)	
<b>Chronic kidney disease</b>	Yes	0.1121 (0.975, 1.289)	0.109	0.641 (0.429, 0.958)	0.030
	No	1 (ref.)		1 (ref.)	
<b>TB history</b>	Yes	1.55 (1.118, 2.163)	0.009	1.515 (1.087, 2.112)	0.014
	No	1 (ref.)		1 (ref.)	
<b>Transplantation</b>	Liver	1.236 (1.039, 1.471)	0.017	1.953 (1.187, 3.215)	0.008
	Kidney	1 (ref.)		1 (ref.)	
	Heart	1.083 (0.681, 1.721)	0.737	1.590 (0.897, 2.831)	0.115
	Lung	1.881 (1.030, 3.435)	0.039	2.683 (1.284, 5.606)	0.009
	Others	1.61 (0.600, 4.317)	0.344	2.805 (0.984, 7.794)	0.054
	Allogenic HSCT	1.46 (1.216, 1.754)	<0.001	2.910 (1.878, 4.510)	<0.001
Autologous HSCT	0.774 (0.610, 0.982)	0.035	1.223 (0.791, 1.890)	0.365	

Figure 2. Age-adjusted standardized incidence ratios

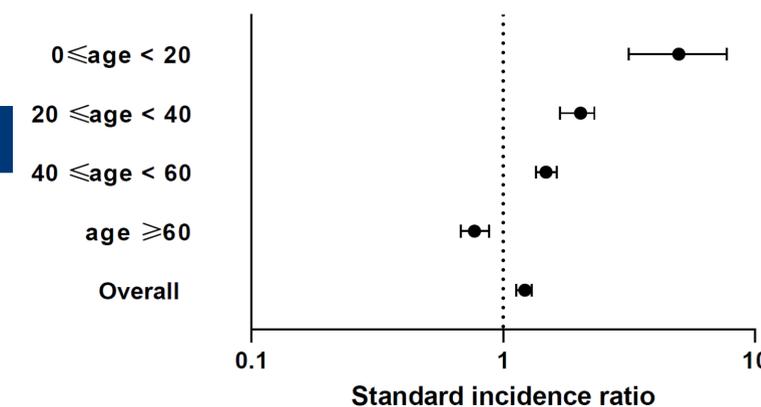


Figure 1. Kaplan-Meier curves for the cumulative incidence of tuberculosis

