



Background

- The risk of active tuberculosis (TB) is elevated following solid organ transplantation with an estimated relative risk of 26.6 vs. the general population.¹ Renal transplant recipients have an estimated TB incidence of 1.7-3.9%.²⁻⁶
- The risk of mortality from TB in transplant patients ranges from 10-36%; the attributable risk of mortality from a TB is estimated to be 9.5%.¹
- In BC, solid organ transplant (SOT) donors and recipients have been screened inconsistently. But, individuals testing positive were referred for treatment
- From December 2014 to March 2015, there were two cases of TB among SOT recipients, prompting a review of all TB cases among SOT recipients since 2005.
- The objectives of this study were to describe the epidemiology and clinical outcomes of SOT recipients diagnosed with TB to identify potential missed opportunities for TB prevention.

Methods

- We identified all cases of TB diagnosed in BC between January 2005 and June 2015 who had transplant reported as a risk factor in the provincial electronic database, integrated Public Health Information System. Only cases who received SOT prior to TB diagnosis were included.
- Charts were reviewed to collect and analyze demographic, clinical and laboratory data including genotyping results if available. Contact tracing data was not reviewed.
- 24-locus Mycobacterial Interspersed Repetitive Units Variable Number Tandem Repeats [MIRU-VNTR] results were compared for similarity against a database of all MIRU-VNTR performed in BC (BC Bionumerics database).
- A linkage was performed with BC Transplant to collect transplant information.
- TB diagnosis rate was estimated using the population of SOT recipients followed by BC Transplant for two time-points and extrapolated. There were 4036 and 4233 patients in BC being followed post-transplant in 2015 and 2016, respectively. Thus, we project that there is an increase of about 200 individuals per year living with a transplant in BC. Based on this, we estimated there was 3036 SOT recipients in 2010 (i.e. study period midpoint).

Results

- There were 28 patients diagnosed with active TB with transplantation as a risk factor over the study period. Six were excluded after a chart review (3 were erroneously listed as having a transplant, 3 did not have a SOT), resulting in a final number of 22 patients or an estimated diagnosis rate of 0.7% among SOT recipients.
- Only 8 cases had any record of a TST or IGRA test with half (4/8) completed prior to SOT. Of those with a TST prior to SOT, 2 were <5mm; 1 was 5-10 mm; 1 was >10 mm reaction. Only the last client received latent TB treatment.

Results (cont'd)

Table 1. Characteristics of TB cases among solid organ transplant recipients, 2005-2015

Characteristic		Number (%)
Sex	Male	16 (27%)
	Female	6 (73%)
Transplanted Organ	Kidney	18 (82%)
	Liver	2 (9%)
	Heart	1 (5%)
	Kidney and Pancreas	1 (5%)
Age at time of TB Diagnosis, Median (Range)		59 years (26-80)
Place of Residence in BC	Greater Vancouver Area	18 (82%)
	Outside Greater Vancouver	4 (18%)
Country of Birth, by TB Incidence	> 100 per 100,000	16 (27%)
	10-100 per 100,000	2 (9%)
	< 10 per 100,000	4 (18%)
Transplant to TB Diagnosis Time, Median (Range)		684 days (86-5028)
Year of Transplant	2011-2015	4 (18%)
	2006-2010	8 (36%)
	2001-2005	6 (27%)
	1996-2000	3 (14%)
	1991-1995	1 (5%)
Other Risk Factors (n=number completed)	Chronic Kidney Disease (n=22)	21 (95%)
	Diabetes (n=20)	13 (59%)
	HIV (n=20)	0 (0%)
	Hepatitis B (n=20)	1 (5%)
	Hepatitis C (n=20)	1 (5%)
	Liver Disease (n=20)	4 (25%)
Site of TB disease	Pulmonary	10 (45%)
	Single organ (except pulmonary)	4 (18%)
	Disseminated	8 (36%)

Table 2. Cluster characteristics of TB cases among solid organ transplant recipients with MIRU-VNTR patterns with matches in the BC database

Cluster	Cluster Size	Transplant Case Birth Region	Cluster Cases Birth Region	TB Lineage
012	67	North America	84% North America, 7% Various, 6% Unknown	Euro-American
011	36	South East Asia	94% South East Asia, 3% North America, 3% Unknown	Indo-Oceanic
021	25	South East Asia	96% South East Asia, 4% Unknown	Indo-Oceanic
042	6	South East Asia	50% East Asia, 33% South East Asia, 17% North America	East Asian
076	3	South East Asia	100% South East Asia	Indo-Oceanic
085	3	South East Asia	100% South East Asia	Indo-Oceanic
096	2	South East Asia	100% South East Asia	Indo-Oceanic
115	3	South Central Asia	100% South Central Asia	Euro-American
206	2	North America	50% East Asia, 50% North America	East Asia

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Results (cont'd)

- 13 (59%) had a unique MIRU-VNTR pattern with no identical matches found in the BC database suggesting reactivation of latent TB infection. 9 cases (41%) had MIRU-VNTR patterns that matched clusters within the BC database; the majority of cases (8/9) were born in the same subcontinent as the dominant subcontinent in the cluster suggesting infection in country of origin. (Table 2)
- Of 22 clients, 17 were successfully treated for TB, 1 was lost to follow-up, and 4 died prior to completion of TB treatment for a mortality rate of 18%; 5 of 20 (25%) individuals were known to have an adverse reaction to a TB medication requiring a medication change.
- Of the 6 individuals who died or had a graft failure, the median time from TB diagnosis to death or graft failure was 82.5 days (range: -7 [post mortem] to 1852 days).

Discussion

- We identified 22 SOT recipients with active TB over a 10.5 year period, or an estimated diagnosis rate of 0.7%
- The estimated diagnosis rate is lower than that found in the literature while the median time from transplant to TB infection was higher.²⁻⁶ This may be because of the small number of SOT recipients that we identified with TB or may reflect that many of the studies were conducted in countries with a higher incidence of TB than Canada. The mortality rate was similar to that reported in the literature.
- The vast majority of cases with clustered MIRU-VNTR patterns were from TB lineages corresponding to their country of birth, suggesting that these cases were not due to local transmission of TB
- TB screening prior to transplantation is either not done or poorly documented. This certainly suggests a missed opportunity for screening and a need for consistent, evidence-based approaches.
- The Provincial TB Program and BC Transplant are currently collaborating on a systematic approach to screening of living donors, and SOT recipients (preferably pre-transplant) to risk stratify patients and identify those candidates for treatment of LTBI.

Selected References

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