Drug Resistant TB in Migrant and Refugee Populations

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Overview

- United Nations High Commissioner for Refugees (UNHCR): A Refugee as “Person who owing to a well-founded fear if being persecuted for reasons of race, religion, nationality, membership of a particular social group or political opinion, is outside the country of his nationality, and is unable to, or owing to such fear, is unwilling to avail himself the protection of that country”.

- Internally displaced person (IDP): Persons sharing the characteristics of refugees but displaced within the boundaries of their own country.

- UNHCR estimates that in 2006, there are more than 32 million refugees, IDP or other people of concern.
History of Major Refugee Movements in Asia

- Afghanistan: Since 1979, nearly 6 million Afghan refugees have moved in and out of Pakistan and Iran.
- 1947 Partition of India and Pakistan created the largest human movement in history – 15 million.
- Bangladeshi Liberation War in 1971.
- 1975 Vietnam War.
- 1959 Himalayan Refugees – Tibetan Refugees in India, Nepal and Bhutan.

Refugee Status – A driver of Tuberculosis: Overcrowding

Displacement

Scarcity of Shelter

Overcrowding

Spread of Infections including Tuberculosis
Refugee Status – A Driver of Tuberculosis: Delayed Diagnosis

Refugees → Hardships and Challenges → Increased Mental and Physical Tolerance

Increased Spread in the Community ↔ Delayed Diagnosis of Tuberculosis ↔ Reluctance to visit doctor unless urgent
Refugee Status – A Driver of Tuberculosis: Other Possible factors

- Language and Culture Barrier
- Nutritional Deficiencies
- Lack of Health Education
- New Environment
Refugee Status – A Driver of Tuberculosis: Migration

- No sustained Financial Source
- Unemployment
- Stateless
- No Permanent Home

Migration
Refugee Status – A Driver of Tuberculosis: Migration

- Increased Risk of HIV
- Challenge to Implement DOTS
- Poor Treatment Adherence and Defaulters
- Emergence of Drug Resistant Strains
Tibetan Refugees

In 1959, thousands of Tibetans followed His Holiness the Dalai Lama into exile. Government of India continues to provide asylum to Tibetans who continue to flee across the Himalayas into exile in India.

Tibetans began to be resettled in various settlements throughout India through Govt. of India resettlement project for the Tibetan refugees.

Tibetan Government in Exile (TGIE) seated at Dharamshala, H.P., India continues to look after the exile Tibetans with support from the host country.

In the early exiled days (1960’s), large number of Tibetans had died due to Tuberculosis. Department of Health of TGIE estimates the TB prevalence at that time to be around 30% of the entire exile population.
Distribution of Tibetan Refugees

- Total Population of 150,000 in India, Nepal and Bhutan
- Largest Number in India

Tibetan Population Distribution in India - Tibetan Demographic Survey 2009

- Total Population: 109,015
- Males: 60,599
- Females: 40,443
Challenges of TB Control in the Tibetan Population

- Highly Migrant Population: Tibetans are an extremely mobile population characterized by a number of Tibetans coming into India and returning back to Tibet annually.

- Lot of fluid movement across India, Nepal and Tibet making individual case management a challenging task.

- Lot of cross-border and within-border migration.

- Social structure of Tibetans is such that a large number of people live in closed and congregate settings such as dormitories in school, in monasteries, nunneries, reception centers of newly arrived refugees …etc making community transmission easy and delayed diagnosis very costly.
Reasons for migration among Tibetans in India, Nepal and Bhutan (TDS – 2009)

- Displaced: 8871
- Marriage: 3584
- Education: 16758
- Work: 3578
- Family Moved: 6653
- Religion: 8129
- Resettlement: 7859
- Business: 1199
- Service: 1348
- Other: 3264
Future Trend of Migration Among Tibetans in India and Nepal

<table>
<thead>
<tr>
<th>Country</th>
<th>Intending to Migrate</th>
<th>Migrating Within</th>
<th>Migrating Abroad</th>
<th>Total Pop.</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Male</td>
<td>Female</td>
<td>Total</td>
<td>Male</td>
</tr>
<tr>
<td>India</td>
<td>16841</td>
<td>11,153</td>
<td>27,994</td>
<td>3638</td>
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<tr>
<td>Nepal</td>
<td>2549</td>
<td>2388</td>
<td>4937</td>
<td>218</td>
</tr>
</tbody>
</table>

Source: TDS 09

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SUMMARY

OBJECTIVE: To determine tuberculosis (TB) incidence, independent risk factors for TB, and predictors of adverse outcomes.
DESIGN: Data from a house-to-house census/demographic survey were merged with TB patient data. Separate multivariable models for each birthplace were developed for outcomes of interest.
RESULTS: From 1994 to 1996, 47,491 Tibetans were surveyed and 1,197 TB cases confirmed (incidence 835/100,000). Risk factors for TB in separate multivariable models differed by place of birth. Independent predictors of second-line therapy and no improvement at the end of treatment. No significant risk factors for default were identified for Tibet-born refugees, while region of residence and the absence of a BCG scar were independent predictors among those born in India. Predictors of receipt of second-line therapy among Tibet-born refugees included region, years in camps, and prior TB, while among those born in India they were region, age ≥20 years, sputum-positive at diagnosis, and previous TB.
CONCLUSIONS: TB incidence in Tibetan refugee settlements exceeds the highest national TB rates, and country of birth determines risk factors. TB control efforts in
Tuberculosis Among Tibetan Immigrants From India and Nepal in Minnesota, 1992-1995

Dung H. Truong, MPH; Linda L. Hedemark, MD; James K. Mickman, MD; Laura B. Mosher, MS; Stephen E. Dietrich, MS; Philip W. Lowry, MD

Objective.—To study screening outcomes among a group of Tibetan immigrants at high risk for developing active tuberculosis (TB) after arrival in Minnesota.

Design.—Retrospective cohort study.

Participants.—A total of 191 Tibetan immigrants undergoing medical screening.

Main Outcome Measures.—Occurrence and treatment outcomes of active TB.

Setting.—A health maintenance organization and a public TB clinic in Minneapolis, Minn.

Results.—Positive (induration, ≥10 mm) tuberculin skin test results were documented in 98% of Tibetans, compared with 44% of Vietnamese, 10% of Hmong, and 51% of Russian refugees in Minnesota (P<.001 for each group). Sixteen active cases (8.4%) were confirmed by isolation of Mycobacterium tuberculosis; however, 5 (31%) were culture-negative on initial screening in Minnesota. Seven (41%) cases were detected during follow-up screening efforts and 8 cases (58%) were discovered in 15 US cities, including Minneapolis–St Paul, Minn. Among this first group of Tibetans relocating in the United States, 191 Tibetans settled in Minnesota and underwent screening and follow-up for TB. Because Tibetans emigrated from a region in northern India with one of the highest documented rates of TB in the world, we conducted a study to determine their risk of developing active disease compared with non-Tibetan refugee groups settling in Minnesota during the same period.

Source: JAMA March 5 – 1997 Vol 277
Tuberculosis Among Tibetan Refugee Claimants in Toronto*

1998 to 2000

Theodore K. Marras, MD; Jean Wilson, BScN, MHSc; Elaine E. L. Wang, MD; Monica Avendano, MD, FCCP; and Jae Won Yang, MD, FCCP

Background and objectives: Between 1998 and 2000, approximately 525 Tibetan people previously living in the United States claimed refugee status in Canada, many of whom were referred to our centers for completion of tuberculosis (TB) screening. We reviewed TB-related outcomes in this cohort, to compare our experience with previously published work, and to assess follow-up after a stay in a low-incidence region.

Methods: We performed a retrospective study of all patients of Tibetan origin assessed at our centers (St. Michael's Hospital and West Park Healthcare Centre, both in Toronto) for completion of TB screening, referred because of abnormal chest radiographic findings or positive tuberculin skin test (TST) result. We compared rates of active and drug-resistant TB in our cohort with local and national rates, as well as those previously published in similar groups.

Results: One hundred eighty-nine individuals were referred to us for assessment, and 181 records were available for review. The mean duration of stay in Canada prior to presentation was 2.6 months, after having spent a mean of 11 months in the United States. Thirty-two percent of patients gave a history of previous TB, and 97% were TST positive. Culture-positive TB was diagnosed in 24 patients (13%, 4,571 per 100,000), 12 patients had at least one drug resistance (20% of cases); other patients were investigated in the United States and/or China.

Source: Chest 2003

Total Population: 47,326
NO. OF TB PATIENTS DURING THE YEAR 2006

- STANDARD
- M.D.R.
NO. OF T.B. PATIENTS DURING THE YEAR 2007

INDEX
- STANDARD
- MDR

Jan 2007: 1
Feb 2007: 1
Mar 2007: 1
Apr 2007: 2
May 2007: 8
Jun 2007: 7
Jul 2007: 3
Aug 2007: 2
Sep 2007: 2
Oct 2007: 2
Nov 2007: 1
Dec 2007: 1
Jan 2008: 1
Feb 2008: 1
Mar 2008: 16
MONTHLYWISE TUBERCULOSIS CASES 2010-11

INDEX
- 2009-10
- CAT I
- CAT II
- CAT III
- CAT IV

2009-10
- April: 10
- May: 9
- June: 8
- July: 7
- Aug: 6
- Sept: 5
- Oct: 4
- Nov: 3
- Dec: 2
- Jan: 1
- Feb: 1

2010
- April: 5
- May: 5
- June: 1
- July: 1
- Aug: 1
- Sept: 1
- Oct: 0
- Nov: 0
- Dec: 0
- Jan: 0
- Feb: 0
Village wise TB case distribution in Kollegal Dhondenling Tibetan Settlement - 2011

Number of TB cases

Name of Village

Red = MDR
Blue = Standard
Five Year TB Data in Kollegal Tibetan Settlement

<table>
<thead>
<tr>
<th>Year</th>
<th>Number of cases</th>
</tr>
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<tbody>
<tr>
<td>2006</td>
<td>11</td>
</tr>
<tr>
<td>2007</td>
<td>2</td>
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<tr>
<td>2008</td>
<td>0</td>
</tr>
<tr>
<td>2009</td>
<td>0</td>
</tr>
<tr>
<td>2010</td>
<td>12</td>
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</tbody>
</table>

- MDR
- Standard
Delek Hospital Tuberculosis Control Programme
Tibetan Delek Hospital, Dharamshala

- RNTCP Designated Microscopy Center
- Work in close collaboration with the local RNTCP
- Our Patient Populations are:
  - Tibetans Born in Tibet
  - Tibetans Born in India
  - Local Indian Population
- Patients from a number of states including H.P., Uttaranchal, Sikkim, M.P., Delhi, Punjab and Karnataka
- Our patient population represents various sectors of the society including the monastic population, students, unemployed, business, office staff etc.
- A large section of our population is highly migrant.
Delek Hospital TB Cases 2006-2010 (Cases from Tibetans all-over India and Nepal)
Demographic Profile of the MDR TB patients among Tibetans

Occupation of the MDR TB Patients (2006-2010)

- Students: 72
- Monks & Nuns: 14
- Business: 14
- Unemployed: 57
- Others: 35

*Tibetans Delek Hospital Data*
Country of Birth of the MDR TB Patients 2006-2010

- India: 133 cases
- Tibet: 45 cases
- Nepal: 11 cases
- Others: 4 cases
Gender Distribution of MDR TB Patients

Age –wise Distribution of MDR TB Cases 2006-2010

Number of TB Cases

Gender

Males: 81
Females: 103

Age-group

<15: 3
15-40: 169
>40: 23
Drug Resistance Pattern

- As expected universal resistance to Sm
- INH mono-resistance
- INH and Eto resistance
- Variable number of quinolone resistance. Of this, many were resistant to Ofx and sensitive to Mfx.
- Variable resistance to Km, Am, Cm
- XDR TB: Strains are beginning to emerge in our community.
DST Protocol in Resource Limited Setting

- SIRE (Sm INH RIF EMB)
- KEPO (Km, Eto, PAS, Ofx)
- MACC+PZA (Mfx, Am, Cm, Clf)
Drug Resistant TB in Tibet

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Review


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SUMMARY

Objectives: We aimed to investigate trends in the prevalence of multidrug-resistant tuberculosis (MDR-TB) among Chinese people from first report to 2006, and to detect the high prevalence regions in order to guide control efforts.

Materials and methods: The CBM, VIP, CNKI, and MEDLINE databases were searched through both keywords and subject headings. The literature was screened, and two investigators assessed the quality and extracted the data. Trends in MDR-TB prevalence in three groups – primary, acquired, and combined MDR-TB – were examined separately, using the Genstat Armitage trend test. Differences were tested
Review


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**Figure 8.** Comparison of acquired MDR-TB prevalence with national level, 1985–2006.
Review


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Figure 7. Comparison of primary MDR-TB prevalence with national level, 1981–2006.
Figure 9. Comparison of combined MDR-TB prevalence with national level, 1985–2006.
Summary of Epidemiological Risk Factors for Drug Resistant Tuberculosis Among Tibetan Refugees

- High Rate of Migration poses a challenge to strict implementation of DOTS strategy leading to poor treatment adherence and defaults.
- Age group between 15-45 particularly at risk
- Unemployment is another possible contributing factor to Drug Resistant TB
- Living in congregate settings like Schools, Monasteries, Nunneries may contribute to spread of Primary M/XDR strains
- Female population appear to be at greater risk.
- Though Tuberculosis in general appear to be more prevalent among Tibetans born in Tibet, MDR TB cases are more prevalent among Tibetans born in India.
Our Concerns

- Tibetan population size is only 6 million. An M/XDR epidemic in our community will be highly disastrous.

- Tibetan Population is gregarious facilitating easy community transmission.

- Given the highly sensitive, delicate and charged up political situation, non-political issues such as public health problems like Tuberculosis has a tendency to get overlooked/ignored by the young and old.

- M/XDR TB – risk to the entire generation
Measures We Have Taken

- Since June 2010, sputum cultures sent for every new or relapse smear positive case.

- Series of Sputum culture and DSTs are done for every at crucial time points – 0, 3, 6, 12, 18, 24 months and more frequently for those not showing clinical improvement.

- Strict DOT for every TB patient and if unavoidable situation, then appoint treatment supervisor.

- Following standard WHO and RNTCP guidelines in terms of Diagnostic standards, Infection control (use of N-95 mask etc), treatment protocols, and DOTS strategy.
Patient Quotes

MDR TB patient “A” said, “Whenever my drugs stocks are about to finish, my heart goes heavy. I lose my appetite”.

MDR TB patient “B” said, “These drugs make me forget everything. I just hope that when my treatment is completed, I simply do not forget my wife and children”.
Our Sincere Thanks

- Government of India, Ministry of Health, RNTCP for the immense overall support in helping us fight the challenge of Tuberculosis.

- Johns Hopkins Center for Tuberculosis Research and Italian NGO for all the technical support and guidance.
Thank You

STOP TB