



## Secondary Attack Rate (SAR) of Tuberculosis in Hamedan Province, 2005 - 2013

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### Abstract

This cross-sectional study was conducted on all registered smear-positive Tuberculosis (TB) patients during a time period of eight years (2005 - 2013); patients with records in the Hamadan provincial surveillance database were studied, in order to find secondary attack rate of TB. The contact investigation in 510 clusters resulted in secondary attack rate (SAR) of 18.75 per 1000 (95% confidence interval: 1.3 - 38.7) children below the age of 15; SAR of 6.7 per 1000 (95% confidence interval: 2.1 - 11.3) adults; and overall SAR of 8.14 per 1000 contacts (95% confidence interval: 3.4 - 12.8). we concluded that age and household size had a significant impact on the transmission of TB to household contacts.

**Keywords:** Household Contacts, Tuberculosis, Hamden Province

### 1. Background

Tuberculosis (TB) is a curable and preventable disease, yet still poses a menace to the community, especially in developing countries (1).

The importance of TB control in social and economic development has been acknowledged in the millennium development goals. In this context, the world health organization (WHO) stop TB partnership has set two targets: 1, to reduce prevalence and deaths by 50% by 2015, relative to 1990 levels; and 2, to eliminate TB as a public health problem by 2050 (2).

Contact investigation includes systematic evaluation of contacts of a confirmed TB patient in order to identify active disease or latent TB infection (LTBI). It is one of the active case-finding strategies to increase case detection (3-5).

Being at higher risk of exposure to causative organism and therefore higher risk of acquiring the disease, makes the active case-finding in contacts of a TB patient worthwhile (5, 6).

Moreover, assessment of people, who have been exposed to *Mycobacterium tuberculosis* is important in the light of progressing to active tuberculosis generally within

one to two years after infection has occurred (7). However, despite the higher degree of risk among close contacts, the number of people at risk might be limited (8).

One previous meta-analysis examined data from 41 household contact investigation studies in low to middle-income countries up to 2005 and showed that the pooled prevalence of TB infection among household contacts was 45% for all active tuberculosis, 2.3% for confirmed tuberculosis, and 51.4% for LTBI (5).

Several factors related to the source case (drug abuse, unsanitary residence, and delayed diagnosis), organism, environment, closeness of contact, and duration of exposure determine whether transmission and a new infection will occur (5, 9). The risk of a contact becoming infected relates to the infectiousness of the TB patient (particularly smear-positive TB patients), the duration, proximity, and susceptibility of the contact (10-13).

Previous studies have suggested similar patient characteristics associated with a profile of patients more likely to be involved in recent transmission (13-15).

Contact investigation involving clinical assessment, chest radiography, microbiological evaluation of sputum, tuberculin skin test (TST) and an interferon- $\gamma$  release assay is currently a standard practice in low incidence areas (16).

There has been a growing interest in contact investigation in resource-limited settings as national programs seek new methods for improving case detection. Recently, the WHO has also launched the first international standards for the investigation of contacts of patients with infectious TB (17).

In addition, identification of high-risk groups and early detection of TB transmission allows timely implementation of focused control measures (13).

## 2. Objectives

In this report, we estimate the risk of developing tuberculosis after household exposure and assess related factors.

## 3. Methods

This cross-sectional study was conducted on tuberculosis patients with records at the Hamadan provincial surveillance database. All registered smear-positive TB patients during a time period of eight years (2005 - 2013) in Hamadan Province were retrieved from national TB Program (NTP) database.

Because of low chance of infections in patients with sputum smear-negative TB (12, 18), clusters with this type of patients were excluded from the analysis. Moreover, extra-pulmonary TB patients were also excluded because of no chance of transmission. Due to the retrospective nature of the gathered data, no ethical approval was needed.

The inclusion criteria for a confirmed TB index case (19) were as follows: age of  $\geq 15$  years, sputum smear-positive, typical tuberculosis chest radiograph, first tuberculosis case identified in a household, at least one household contact (20), and being resident of the Hamadan province. In addition, we used the following criterion for the identification of household contacts: aged of  $\geq 6$  months, living at the same property as the respective index case most of the time, sharing meals, and identifying a common household head (20).

Data were extracted using a checklist of items including gender, age group (< 15, 15 - 29, 30 - 49, and > 50 years), residency (urban/rural), household size (less than/equal or more than five members), laboratory results before treatment (1-9 Basil, 1+, 2+, 3+), treatment delay by patient recall (< 30, 30 - 90 and more than 90 days).

For computation of TB secondary attack rate (SAR), we defined a secondary case as a person diagnosed after at least three months from the commencement of diagnosis in the index case (20, 21). The formula used for SAR was defined as follows (22):

Equation 1.

$$SAR = \frac{\text{Number of cases among contacts of index cases}}{\text{Total number of contacts}} \times 10^n \tag{1}$$

In addition, chi-square test was used for data analysis at the 5% significance level ( $P < 0.05$ ). All statistical analysis was done with Stata computer software version 12 (StataCorp LP, College Station, TX, USA).

## 4. Results

Overall, 510 clusters were identified by definition. The contact investigation in these clusters was done separately for ages below and above 15 years old. There were 160 children within such clusters, all of whom were included in our study. We found three new patients of TB, which yielded an SAR of 18.75 per 1000 (95% confidence interval: 1.3 - 38.7). Computing this process for almost all (92%, 1191 out of 1297) adults with available data yielded eight new cases of TB and SAR of 6.7 per 1000 (95% confidence interval: 2.1- 11.3) (Figure 1). Overall, SAR for the disease among household contacts of TB patients was found to be 8.14 per 1000 contacts (95% confidence interval: 3.4 - 12.8).

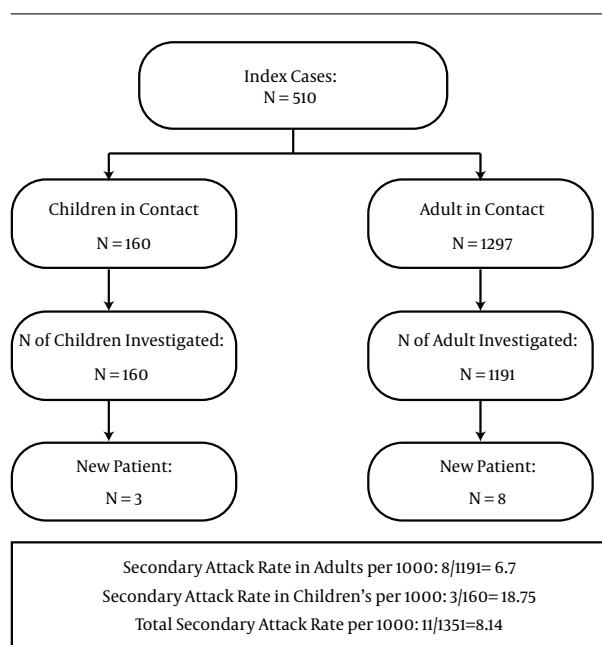


Figure 1. Household Contacts of Tuberculosis Patients in Hamedan Province, 2005 - 2013

Table 1 shows the impact of several factors on the transmission of disease. Results showed that the significant factors related to the transmission of disease included age

and household size. On the other hand, gender, residency, laboratory results and delayed diagnosis were not found to be significant.

The transmission process behaved differently among different age groups so that while 60% of people under 15 years of age significantly ( $P_v < 0.001$ ) had positive diagnosis, this occurred only for 3 to 5% of people above 30 years and no one was diagnosed between ages of 15 and 29 years. The overcrowded households with a TB member had a significant impact ( $P_v: 0.009$ ) on transmission as well. Specifically, nearly 6% of people living in a crowded household (with more than five members) versus 1.4% of people living in an under crowded households were diagnosed positive.

## 5. Discussion

This was a cross-sectional study of eight years follow-up of 510 clusters of TB in Hamedan province.

The SAR of disease in household contacts was found to be 0.814%. This finding is substantially lower compared to African countries like Uganda where SAR was reported as 3% (1). The variation in the SAR for disease could be attributable to both the likelihood of acquiring new infection in the household and to the differing risks for progressive primary disease among newly infected household contacts.

In the household contact instance, the SAR is used as a measure of risk for disease in the household and is estimated as the proportion of household members exposed, who also develop disease within a specified time period (1). However, the validity of SAR depends heavily on the degree of concordance of strain types of *M. tuberculosis* between index and secondary cases. Recent population-based studies from industrialized countries have shown that the strain of *M. tuberculosis* may differ between the index and contact cases in up to 30% of pairs (1).

To convey meaning about risk for disease, considering that TB has a long and variable latent period, the SAR for disease must specify a time frame for the development of disease. In this study, the SAR for disease capture risk for eight years after the diagnosis of the index case.

In the household of an infectious index case, there are several factors making interactions between the contacts and index case complex. The duration and intensity of exposure to the index case depends on familial relationships, traditions about nursing for ill relatives, ability of the index case to cough, and ventilation in the house. Each discrete exposure is associated with an unknown probability of becoming infected. Since it is not feasible to measure the risk of infection for any single exposure to the index case, we used age-specific prevalence as a measure of the cumulative risk over time.

We found that age is an important factor in TB transmission. Specifically, the prevalence of disease in contacts was highest among children below age of 15. This finding is consistent with other studies reporting higher transmission of smear-positive TB in lower age groups (16, 18, 23, 24). In fact, according to the WHO, children under five years are one of the two high-risk groups for contact investigation in low-to-middle income countries (25). The reason for higher transmission rate among children could be explained by immunological reasons like diminished CD4+ T cells responses in response to pathogens compared to adults (26).

However, since the prevalence of clinically-diagnosed TB among contacts is substantially higher than that confirmed microbiologically (27); the prevalence of disease found in this study was probably overestimated. The overestimation was more likely for children from whom obtaining specimens is difficult (5).

Although several studies have shown that gender differences in TB transmission resulted in twice as many reported cases of TB among males than among females (28), the male: female ratio of transmission in our study was 0.38, which was not significant.

Moreover, our results revealed that intensity of index case of TB had no significant impact on the probability of transmission. This finding is inconsistent with other reports, which displayed evidence that intensity of index case indeed has an incremental impact on household infections (24).

It has been shown that the likelihood of transmission of TB is more in overcrowding households (24). Accordingly, we also found that the prevalence of transmission is higher among contacts that live with a household more than five members.

Based on the results of the current study, we suggest active contact investigation as a means of improving case detection and interrupting the transmission of drug-resistant organisms.

Active case finding is often limited to low and middle-income countries, therefore, it might be logical to assume that all or practically all index cases were identified by passive case finding. Since contact investigation will miss more than three-quarters of transmission leading to active tuberculosis, its public-health impact is expected to be substantially lower than that of passive case finding (8, 29).

Household contact investigation focuses on examination during a short period of time while the incubation period of TB varies widely. Additionally, most infected hosts may not develop disease. Thus, in low to middle income countries, improving accessibility of a patient-friendly health-care services and increasing public awareness of TB, may be more cost-effective. The feasibility of achieving a case detection target of 70% by passive case

**Table 1.** Factors Associated With Diagnosis of Tuberculosis in Household Contact of Smear-Positive Tuberculosis Patients<sup>a</sup>

Variable	Transmitted to Household Member		Not Transmitted to Household Member		Total	P Value
	Number	Percent	Number	Percent		
<b>Gender</b>						0.095
Male	3	1.13	263	98.87	266	
Female	8	3.28	236	96.72	244	
<b>Age groups, y</b>						<0.001
< 15	3	60	2	40	5	
15 - 29	0	0	77	100	77	
30 - 49	3	3	98	97	101	
> 50	5	1.5	322	98.5	327	
<b>Residency</b>						0.82
Urban	7	2.3	301	97.7	308	
Rural	4	2	198	98	202	
<b>L. Results*</b>						0.34
1 - 9 Basil and 1+	2	1.25	158	98.75	160	
2+ and 3+	9	2.57	341	97.43	350	
<b>Household size</b>						0.009
5 and Less	6	1.4	420	98.6	426	
More than 5	5	5.95	79	94.05	84	
<b>Delayed Diagnosis, day</b>						0.7
< 30	1	1.2	84	98.8	85	
30 - 90	5	2.75	176	97.25	181	
> 90	90 day	5	2.05	239	97.95	244

<sup>a</sup>Result of pre-treatment laboratory sputum smear.

finding has been substantiated by early studies in India, which showed that 70% of people with smear-positive tuberculosis had symptoms and sought health care (30).

Sputum smear is the routine diagnosis for TB cases and was used in our study as well. Although it has been shown that more than 95% of sputum smear-positive tuberculosis cases can be expected to have radiographic changes typical of tuberculosis (20), using radiography is also advisable.

Several limitations of our study need to be acknowledged. First, the study was limited to its cross-sectional nature, so temporality arguments (cause-and-effect relationship) cannot be made. Second, the first subject from a given household registered for treatment at the NTP was assumed to be the index case. We are, however, uncertain whether this was indeed the first person to be infected or whether they were a secondary contact of another infected member in the household, who exhibited disease earlier. Third, because of unavailability of the exact dates of diagnosis of *M. tuberculosis* infection in most of the index cases, the duration of contacts for each household mem-

ber could not be ascertained. Fourth, we were not able to evaluate whether or not index patients were suffering from multidrug-resistant TB.

**5.1. Conclusion**

We recommend an awareness program for household contacts about the possibility of acquiring *M. tuberculosis* infection from a sputum smear-positive pulmonary TB case. In low- prevalence settings like Hamden province, integrating modern molecular epidemiology to conventional contact tracing methods could be useful for clarifying accurate measures of disease transmission.

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## Footnote

**Authors' Contribution:** Study concept and design, Salman Khazaei, Abdollah Mohamadian- Hafshejani and Hamid Salehiniya; acquisition of data, Ali Zahiri and Salman Khazaei. Analysis and interpretation of data, Salman Khazaei, Abdollah Mohamadian- Hafshejani and Shahrzad Nematollahi; drafting of the manuscript, Shahrzad Nematollahi; critical revision of the manuscript for important intellectual content: Salman Khazaei; statistical analysis, Salman Khazaei and Shahrzad Nematollahi; administrative, technical, and material support: Ali Zahiri; study supervision, Salman Khazaei.

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