Effect of Temperature and Altitude Difference on Tuberculosis Notification: A Systematic Review

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Abstract

Background: Ecological factors are important indicators for tuberculosis (TB) notification. However, consolidation of evidence on the effect of altitude and temperature on TB notification rate has not yet been done. The aim of this review is to illustrate the effect of altitude and temperature on TB notification rate. **Methods:** Electronic searches were undertaken from PubMed, EMBASE, and Scopus databases. Hand searches of bibliographies of retrieved papers provided additional references. A review was performed using the Meta-analysis Of Observational Studies in Epidemiology guideline. **Results:** Nine articles from various geographic regions were included in the study. Five out of nine studies showed the effect of altitude and four articles identified temperature effects. Results showed that TB notification rates were lower at higher altitude and higher at a higher temperature. **Conclusion:** This review provides qualitative evidence that TB notification rates increase with temperature and decrease with altitude. The findings of this review will encourage policymakers and program managers to consider seasonality and altitude differences in the design and implementation of TB prevention and control strategies.

Keywords: Altitude, notification, systematic review, temperature, tuberculosis

Introduction

Globally, over past decades, considerable effort has been undertaken in an attempt to control tuberculosis (TB).[1] However, TB remains a significant public health problem: in 2015, an estimated 10.4 million TB cases occurred, and 1.8 million people died with or from the disease (including 0.4 million among people with HIV).[2] The risk of transmission differs markedly by geographical area with noticeable heterogeneity within and among continents.[2,3] The notification rate is higher in poorer and remote areas, with the highest rate reported from the Southeast Asia region (61% of new cases), followed by Africa (26% of new cases).[2]

Socioeconomic and individual factors associated with TB such as ethnicity, place of residence, drug use, alcohol consumption, homelessness, human immunodeficiency virus infection/acquired immune deficiency syndrome, age, and sex have been investigated in numerous studies.[4-6]

Climate change plays an important role in the seasonality and geographical heterogeneity of TB notifications, although it is likely to be distally related to TB incidence.[7] Although published literature suggests there are no specific favorable or unfavorable climate conditions for TB incidence, transmission could be enhanced via poor ventilation and overcrowding.[8]

Variation in TB notifications associated with altitude and temperature, particularly for pulmonary TB, has been widely assumed.[9-13] The causative agent replicates more readily at higher temperatures. Furthermore, airflow is often high in hot conditions providing an environment conducive to the spread of TB.[13,14]

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Epidemiological studies suggest that high altitude is associated with lower TB notification and mortality. However, the biological mechanisms underlining this apparent effect are poorly understood.[15-17] Furthermore, the effects of these factors have not been well studied and have not taken into account common confounding factors.[18]

Systematically summarizing the role of these factors on TB notification may help to provide relevant information to support TB control and prevention. Therefore, the aim of this review is to survey existing evidence on the altitude and temperature effects on TB notifications.

Methods

We searched the PubMed, EMBASE, and Scopus for all studies of the association between altitude and temperature and TB disease. We also hand searched bibliographies of retrieved papers for additional references. Data filtering used keywords, title, abstracts, and full-text reviews. EndNote was used to eliminate duplicated articles. The full search strategy is available as Supplement 1.

Our searches were limited to human studies. Studies were included if quantitative effect estimates of the relationship between temperature or altitude and TB (regardless of the clinical diagnosis and measure of morbidity) were presented or could be calculated from the data provided. Articles with any of the following: case reports, anonymous reports, studies on biomedical aspects of TB, and bovine TB were excluded from the study. Furthermore, studies conducted to assess risk factors other than temperature and altitude factors were not included in the study [Figure 1].

For all included studies, location/country of the study, study period, study population, exposure temperature or altitude, outcome, TB notification (prevalence or incidence of TB), confounders adjusted for, and effect estimates such as mean, correlation, path coefficient, beta coefficient, relative risk (RR), and odds ratio (OR) were extracted by two independent reviewers (Y. G and W. Y) using a standard data extraction format. We used the following definition to standardize the data extraction process.

Tuberculosis notifications

TB cases (all forms of TB) were diagnosed biologically or clinically and confirmed cases registered and reported. Included papers defined TB morbidity as incidence, prevalence, or notification of TB. Nevertheless, to harmonize this, we defined notification as diagnosed and reported TB incidence/prevalence. The term notification will be used to encompass both incidence and prevalence in the present paper.

Temperature

Temperature measured in °C was obtained from the meteorology agency/Bureau of the appropriate country. It was defined as monthly or yearly average calculated from the daily/weekly/monthly records.

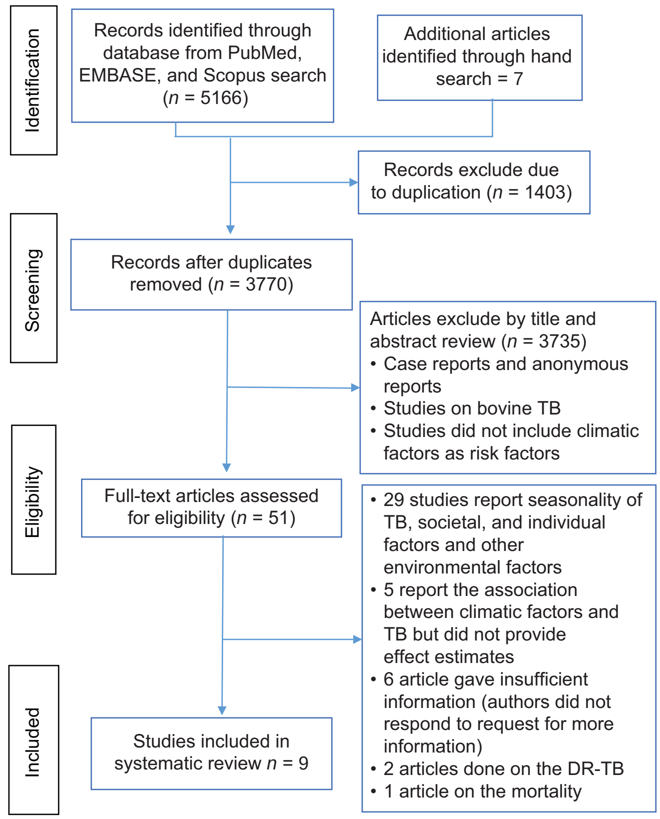

Figure 1: Flow diagram of literature search strategy for the effect of temperature and altitude difference on tuberculosis notification

Altitude

The mean height above sea level, measured in meters (m), was obtained from geo-coordinates of the geographical location.

The reporting of this review follows the guidelines for the Meta-Analyses and Systematic Reviews of Observational Studies (MOOSE).[19]

The Newcastle–Ottawa Scale for cross-sectional studies was used to assess the quality of the included papers [Supplement 2].[20] Each article was rated for quality based on the three elements such as selection, comparability, and outcome and is presented in Supplement 3. All items in the three elements were evaluated irrespective of reporting.

A narrative review and a descriptive summary are given because of the variability in measures of temperature and analytical approaches, as well as in the definitions of control groups. Adjusted effects from studies on the association between altitude and TB notification were pooled with random effects. Heterogeneity was assessed using the I^2 statistic, which describes the percentage of variation between studies compared to that within studies. Data were analyzed using MetaXL version 5.2 (EpiGear International).

Results

Overall, 5166 references were first retrieved via the electronic database search: 956 articles from PubMed, 2866 from

EMBASE, and 1344 from Scopus, and hand searching other literature sources yielded 7 studies. After removing duplicates, 3770 titles were screened. Finally, 9 studies from 5 countries were relevant for inclusion.[21-29]

Of the 9 included articles, 7 were carried out in Asia, 1 in South America, and 1 in Africa. All eligible studies used clinical record linkage of governmental reports for the assessment of TB notification. In the included studies, a diagnosis of TB was made based on a combined evaluation of clinical, radiological, and laboratory features of the patients in line with the National TB Prevention and Control Programs. Four articles did not describe diagnostic methods.[21,23,26,28]

The identified articles were quite variable, reporting different effect estimates (eta correlation, RR, OR, path coefficient, and mean), different exposure scales, as well as different TB reporting (prevalence of TB, the incidence of TB, and TB notification).

Various statistical methods were used to examine the research questions relating to altitude and temperature and TB notification. Effect estimates included correlation coefficient methods (Pearson and eta correlation coefficients) and regression models (partial path coefficients, normal regression beta coefficients, and Bayesian models). Some articles used more than one method. None of the eligible studies adequately justified the sample size.

The measurement of temperature and altitude differed in different studies. The temperature in °C as monthly or annual averages and altitude in meter (m) were defined as categorical or continuous. Results of this review are presented as a qualitative summary of temperature and altitude factors on TB notification.

The five studies examining the association between altitude and notified TB cases were conducted in the following four countries: China, Turkey, Mexico, and Kenya.[22,23,26-28,30] Details are presented in Table 1.

The studies conducted in China in 2014 and 2015 reported that altitude is associated with TB notifications. A 2014 study showed that TB notifications increased in high-altitude regions (path coefficient = 0.5953), whereas in a 2015 study, the notifications decreased (path coefficient = −0.595).[22,26]

The retrospective study conducted from 1999 to 2005 in 56 randomly selected Turkish cities involving 378 patients showed that the mean number of TB notifications decreased in high altitude ($r = -0.58$, 95% confidence interval [CI]: −0.73, −0.38): TB notifications were higher in cities at altitudes below 750 m than for cities located above 750 m (OR = 3.28, 95% CI: 1.83, 5.88, $P = 0.001$).[27]

The Mexico study found that altitude above sea level was correlated with low TB notifications in 2014 ($r = -0.74$, 95% CI: −0.87, −0.53, $P = 0.001$).[28] The Kenya study also reported that TB notifications were lower at higher altitudes ($r = -0.071$, 95% CI: −0.51, −0.83, $P = 0.001$).[23]

Although five studies reported the relationship between altitude and TB incidence, three articles were eligible for meta-analysis, since two articles did not report effect estimates. We report the pooled estimates correlation between altitude and TB incidence for these studies. All the three studies found a negative association between altitude and TB notification [Figure 2]. The pooled correlation between altitude and TB notifications was $r = -0.67$ (95% CI: −0.75, −0.55).

Studies of the association between temperature and TB notifications were conducted in three countries such as China, Japan, and Iran.[21,24,25,29] Given the heterogeneity of methods among studies, we did not compute pooled effect estimates. Table 1 shows the individual effect measures for the studies on TB notification; one study found a negative association between temperature and TB notification; with a 10°C increasing monthly average temperature, the monthly notifications of TB decreased by 9% ($\beta = -0.0060$, $t = -5.12$, $P < 0.001$).[25]

Temperature was associated with TB notifications in three studies. The 15-year retrospective review of 46 Japanese prefectures showed that temperature was associated with TB notifications when between 18.0°C and 46.1°C. The 4-year Fukuoka Institute of Health Registry study of 5904 TB cases, carried out three decades later, showed that exposure to extreme heat (RR = 1.20, 95% CI: 1.01–1.43) increased the risk of TB notification.[24] However, effect estimates related to risk were not provided in the article.[29] The study done in mainland China, using a Bayesian model, reported that the risk of a TB notification increased with a one-degree increase in temperature (RR = 1.00324, 95% CI: 1.0015–1.0055).[21]

Discussion

The aim of this review was to examine whether temperature or altitude affected TB notification. Studies found were geographically varied, small, and did not adjust for important confounders. However, regardless of study duration, geographical coverage, and heterogeneity of analytical approaches and effect sizes, this review demonstrated an increasing effect of temperature on TB notification rates, except for one study associated with low notification rates.

Previous studies have demonstrated that TB notification is associated with socioeconomic conditions.[4-6] Our review indicates that TB notification is high in areas where the temperature was high, except for Qinghai province where TB notification decreases exponentially for each 10°C.

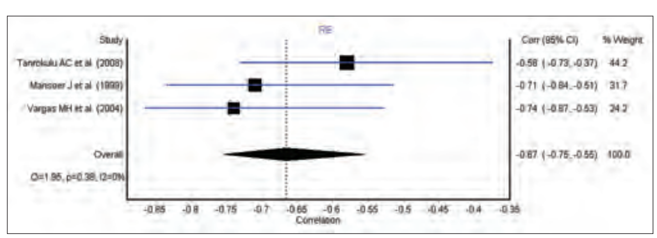

Figure 2: Forest plot of correlation between altitude and tuberculosis

Table 1: Summary of studies included in the systematic review and meta-analysis of effect of climatic factors and altitude on tuberculosis

Study	Country, Population	Study period	Outcome type
24	Japan, all registered TB cases of the Fukuoka Institute of Health	2008-2012	All forms of TB incidence (5904 TB cases)
21	China, all annual reported TB patients in 32 Mainland provinces	2009-2013	TB prevalence
25	Japan, TB patients registered in 46 prefectures Japanese TB registry	1961-1978	TB prevalence determined by clinicians by clinical factors
29	China, all TB patients in randomly selected medical institutions	2009-2013	TB incidence (*n*=27, 655 cases)
27	Turkey, all patients receive treatment in state TB dispensaries from randomly selected 56 cities	1999-2005	All forms of TB (378 TB cases; the mean incidence of TB per 100 k=23.8±9.1 [12.07-47.39])
28	Mexico, all annual PTB notification cases registered obtained from Mexican Health Ministry database	1998, 2002	TB incidence
23	Kenya, all annual TB patient reports in 41 districts of National TB Program	1988-1990	TB prevalence
26	China, all registered TB cases from Chinese center of disease control and prevention management information system	2007	TB prevalence
22	China, all TB patients registered (in 31 provinces) China Health Statistics Yearbook	2001-2010	TB prevalence

Study	Exposure	Adjusted variable	Findings
24	Temperature (29.2°C)	Age, sex	Exposure to extreme heat temperature (RR=1.2, 95% CI: 1.01-1.43)
21	Monthly average temperature	NA	Average annual temperature (RR=1.00324, 95% CI: 1.00150-1.00550)
25	Annual average temperature (°C)	Sunshine hour	The monthly average temperature increase in 10°C TB incidence decrease by 9% (β=−0.0060, *P*<0.001)
27	Monthly average temperature (°C)	Latent variable; TB control programs, population density, income, public assist, past TB control, past epidemic	29.9°C-39.8°C and 18.0°C-46.1°C temperature is associated with TB prevalence and incidence rate, respectively
28	Altitude defined as>750 m and 1-750 m	Green card, annual income, population density, household size, urbanization rate, number of doctors	There is inverse correlation between altitude and mean TB incidence (*r*=−0.58, 95% CI: −0.73-−0.38, *P*=0.000) The incidence higher in cities at an altitude <750 m versus >750 m (OR=3.28, 95% CI [1.83-5.88], *P*<0.0001)
23	Altitude above sea level (0-2500)	NA	Altitude above sea level correlated with TB incidence (*r*=−0.74, 95% CI: −0.87-−0.53, *P*<0.0001)
26	Altitude	Nomads, population density, literacy rate, household size, life expectancy rate, nutritional status	The log notification rates negatively associated with altitude (*r*=−0.71, 95% CI: −0.51-0.83, *P*<0.001)
22	Altitude	Air quality, education, health service, population density, economic level, unemployment	Altitude factor (−0.595) had a significant effect on TB prevalence

NA: No information about variable adjustment, TB: Tuberculosis, CI: Confidence interval, RR: Relative risk, OR: Odds ratio

This is potentially due to differences in the temperature measurement (monthly/annually). As well, seasonality, social context, and medical and health conditions of the residents in Qinghai province could influence TB transmission.[25] Specifically, overcrowding, the amount of co-infection with HIV, malnutrition, and type 2 diabetes have been implicated.[31]

Our findings support the notion that lower altitudes are advantageous for TB transmission, since TB notifications declined with increasing altitude.[32] This might be explained by lower levels of crowding and population density at higher altitude, with residents not staying indoors for long periods.[13,25,33,34] In addition, UV-B exposure is higher at higher altitudes, leading to higher levels of Vitamin D which might enhance immune response and decrease consequent reactivation of TB.[30,35]

Limitations of this review include those related to residual confounding, measurement of the exposure variable, and lack of an established mechanism underlying the apparent effect of temperature and altitude on TB. Some studies did not adjust for known drivers of TB during analysis and included latent (unmeasured) variables in the analysis. Climate factors associated with TB are likely to operate as secondary factors, unlike proximal factors such as HIV. Therefore, well-designed studies on the direct and indirect effects of temperatures and/or altitude factors on TB transmission are needed. In addition, the review did not control for year of the study published (1981–2016), sample size (not all studies reported), socioeconomic characteristics, and the health profile of each country.

Other possible limitations relate to inconsistencies in the classifications of temperature (hot and cold) and altitude (highland and sea level) which could lead to misclassification bias. In addition, analyses are restricted to TB notifications which may not reflect the timing of actual incidence, thus leading to mismatch when notifications are linked to time-dependent climate data.

Finally, most studies (seven studies) in the review used retrospective registry-based community-level data sources and findings may not be the same for individual-level data, that is, findings could be vulnerable to the ecological fallacy. Despite limited data, heterogeneity of measurements, design, and quantitative effect estimates among the studies were included in this review; this systematic literature review demonstrates that temperature/altitude is associated with TB disease notifications. This should encourage policymakers and program managers to consider seasonality and altitude differences in the design and implementation of TB prevention and control strategies.

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Conflicts of interest

There are no conflicts of interest.

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Supplement 3

Table 3: Quality assessment of the impact of climate and altitude variability on tuberculosis transmission using Newcastle-Ottawa Scale for cross-sectional studies

Studies references	Selection (maximum 6 star)	Comparability (maximum 2 star)	Outcome (maximum 3 star)
24	****	**	**
21	***		*
25	***		*
29	**	**	**
27	****	**	**
28	**	**	***
23	**	**	***
26	**	**	*
22	****	*	*

*Scale score