

Brief communication (Original)

Modeling tuberculosis incidence in Nepal

Sampurna Kakchapati^a, Sulawan Yotthanoo^a, Chamnein Choonpradup^b^aProgram in Research Methodology, ^bDepartment of Mathematics and Computer Science, Faculty of Science and Technology, Prince of Songkla University, Pattani Campus, Pattani 94000, Thailand.

Background: Tuberculosis (TB) constitutes a large burden of infectious disease in Nepal.**Objective:** Model incidence of TB between 2003 and 2008 in Nepal.**Methods:** A retrospective study was conducted in Nepal of tuberculosis incidence by gender and location over the six years period. Data were obtained for 198,719 tuberculosis cases from the Nepal Tuberculosis Center (NTC). A negative binomial model with two multiplicative components as predictors was used and provided a good fit.**Results:** The model extracted a decreasing trend during the first five years followed by a drop in 2008. The overall incidence of TB was 1.31 cases per 1,000 population with a male to female incidence rate ratio of 1.86. There were pronounced spatial variations with higher rates occurring in the Terai region, followed by the Hill, and Mountain regions.**Conclusion:** Tuberculosis incidence showed a steady decreasing trend, but the number of cases was still very high. Gender differences existed in TB incidence in Nepal. Higher rates were observed in the Terai Region and urban areas. These findings highlight the need for the tuberculosis control measures to remain on a sustained and long-term basis for the high TB burden rate of Nepal.**Keywords:** Modeling, negative binomial model, tuberculosis

Tuberculosis (TB) is a major public health problem in Nepal. Data from the National Tuberculosis Program of Nepal shows that there are more than 30,000 infectious cases and 5,000-7,000 deaths due to TB annually [1,2]. It is the most common cause of death in the most economically productive age group comprising adults aged 15 to 49 years [3]. As in other countries, the tuberculosis epidemic in Nepal can be traced in part to poor working and living conditions. Many of these conditions persist to this day, and along with the Multi Drug resistance (MDR-TB) and HIV/AIDS epidemic, have fueled the current high levels of tuberculosis disease in the country.

The National Tuberculosis Center (NTC) annual reports provide evidence that the magnitude of tuberculosis infection across the country is high and varies with location. The reported caseload is extremely high in the Terai and the Hill parts of the country and is high in many urban areas [1, 2].

Several studies have found a gender difference in tuberculosis incidence [4]. In Nepal, the female/male ratio was found to be below parity among TB suspects undergoing sputum examination and for all types of TB case detection [5].

Public health officials often need to compare the standardized disease incidence rate within the area and time frame, so that necessary actions can be taken. Statistical modeling provides the appropriate quantitative framework for investigating key issues related to tuberculosis incidence, transmission dynamics and predicting the effects of different interventions.

Investigating the regional and temporal pattern of disease can indicate areas with problems and possibly predict periods of likely disease epidemics. It can also help the concerned health authorities to plan an effective prevention program. The Poisson distribution and its extension to the negative binomial distribution to handle over-dispersion is a standard approach to modeling event count data.

The aim of the study is to model incidence of tuberculosis in Nepal between 2003 and 2008.

Correspondence to: Chamnein Choonpradup, Department of Mathematics and Computer Science, Faculty of Science and Technology, Prince of Songkla University, Pattani Campus, Pattani 94000, Thailand. E-mail: cchamnein@bunga.pn.psu.ac.th

Materials and methods

Study area and data source

Nepal is a landlocked country in South Asia. It has five development regions (eastern, central, western, mid western, and far western), 14 zones, 75 districts, and has a current population growth of 2.2% [6]. It is divided into three distinct geographical regions: Mountain (7% of the population), Hill (43%), and Terai (50%), in decreasing altitude.

Nepal is covered by the National Tuberculosis Control Program (NTC), which strictly follows the World Health Organization strategy defined as Directly Observed Treatment, Short Course, and regularly issues a progress report. The information used regarding cases was provided by NTC, Thimi, Bhaktapur. The reported cases for each year are available in computer files comprising characteristics of the disease, gender, address, and the severity of the illness. The independent variables are gender, location, and calendar year (2003-2008).

To simplify the effect of location of residence when calculating incidence rates, we grouped one or more contiguous districts in each zone and formed 64 “super-districts” containing populations of above 100,000.

Statistical methods

Poisson models for disease counts are often over-dispersed due to clustering, in which case the negative binomial model is more appropriate. The negative binomial model is an extension of the Poisson model for incidence rates that allows for the over dispersion that commonly occurs for disease counts. If λ_{ijt} denotes the mean incidence rate for gender i , geographical location j and year t , an additive model with this distribution is expressed as

$$\ln(\lambda_{ijt}) = \ln(P_{ij}) + \mu + \alpha_i + \beta_j + \gamma_t. \quad (1)$$

In this model, P_{ij} is the corresponding population at risk in 1000s and the terms α_i , β_j and γ_t represent gender, location, and year effects that sum to zero, respectively, and μ is a constant encapsulating the overall incidence. The model fit is then assessed by the linearity in the plot of deviance residuals against normal quantiles, and also by examining plots of observed counts and appropriately scaled incidence rates against corresponding fitted values based on the model.

We investigated regional and temporal pattern of this disease using the additive model given by eq. 1 with the negative binomial distribution to account for over-dispersion, but found that this model still has excessive deviance. The incidence rate for tuberculosis depends strongly on gender, and in Nepal, this gender effect varies over districts. For this reason, we used the multiplicative equation 2 where the additive effect for gender in **Eq. 1** replaced by a sum of multiplicative factors combining gender and district as follows:

$$\ln(\lambda_{ijt}) = \ln(P_{ij}) + \alpha_{ij} + \sum_{k=1}^m \beta_j^{(k)} \gamma_t^{(k)}. \quad (2)$$

The sum contrasts [7] were used to obtain confidence intervals for comparing the adjusted incidence rates within each factor with the overall incidence rate. The confidence intervals for factor-specific incidence rates obtained from the model divide naturally into three groups according to their location entirely above the mean, around the mean, or entirely below the mean. We used this trichotomy to create schematic maps of super-districts according to their estimated tuberculosis annual incidence rates.

The R program was used for all statistical analysis, graphs, and maps [8, 9].

Results

Preliminary analysis

During the study period (2003-2008), 198,719 confirmed cases were notified. The number of cases varied from 0 to 1,801 per year, with 127,979 male cases and 70,740 female cases. The mean incidence rate of TB was 1.31 per 1,000 populations. The incidence rates by year are shown in **Table 1**.

Statistical analysis

Different models based on Poisson and negative binomial generalized linear models were considered, taking into account the need to provide a satisfactory fit to the data without an excessive number of parameters in the model.

This criterion proved difficult to meet with purely additive linear models. In the end we selected a nonlinear model with two multiplicative components ($m=2$ in **Equation. 2** similar to an extension of the Lee-Carter model used for mortality forecasting [10]. The negative binomial generalized linear model fitted the data quite well, as indicated by a plot of deviance residuals against normal quantiles.

Table 1. TB incidence rates by year.

Years	Number of TB cases	Population	Incidence/1000
2003	31,637	24,377,951	1.30
2004	32,903	24,516,400	1.34
2005	34,077	25,083,994	1.36
2006	33,206	25,266,229	1.31
2007	33,450	26,284,018	1.27
2008	33,446	26,805,469	1.25

The multiplicative components were estimated as eigenvectors of a covariance matrix [11], so it was possible to fit the negative binomial model straightforwardly. A linear trend decreased during the first five years followed by a drop in 2008.

Figure 1 shows plots of the adjusted annual TB incidence rates/1000 for males and females and their confidence intervals for each super-district. The vertical dotted line of represent the fourteen zones of Nepal and vertical line represent the five development regions. The horizontal line corresponds to the overall incidence rates for males and females combined (1.31 per 1,000 population). The dark line represents the males and the light line represents females. The dotted horizontal dark line corresponds to the mean incidence

rates for males (1.70 per 1000 population) and the dotted horizontal light line corresponds to the mean incidence rates for females (0.91 per 1000 population). In most super-districts, there is high incidence of TB in males.

Figure 2 shows a schematic map of the male and female adjusted incidence rates for super-districts, using the confidence intervals plotted in **Fig. 1** to classify these regions as above the mean (darkest shade), below the mean (lightest shade) or not evidently different from the mean (intermediate shade). Higher TB incidence rates occurred for males and females in most of the super-districts of the Terai region and some super-districts of the Hill region.

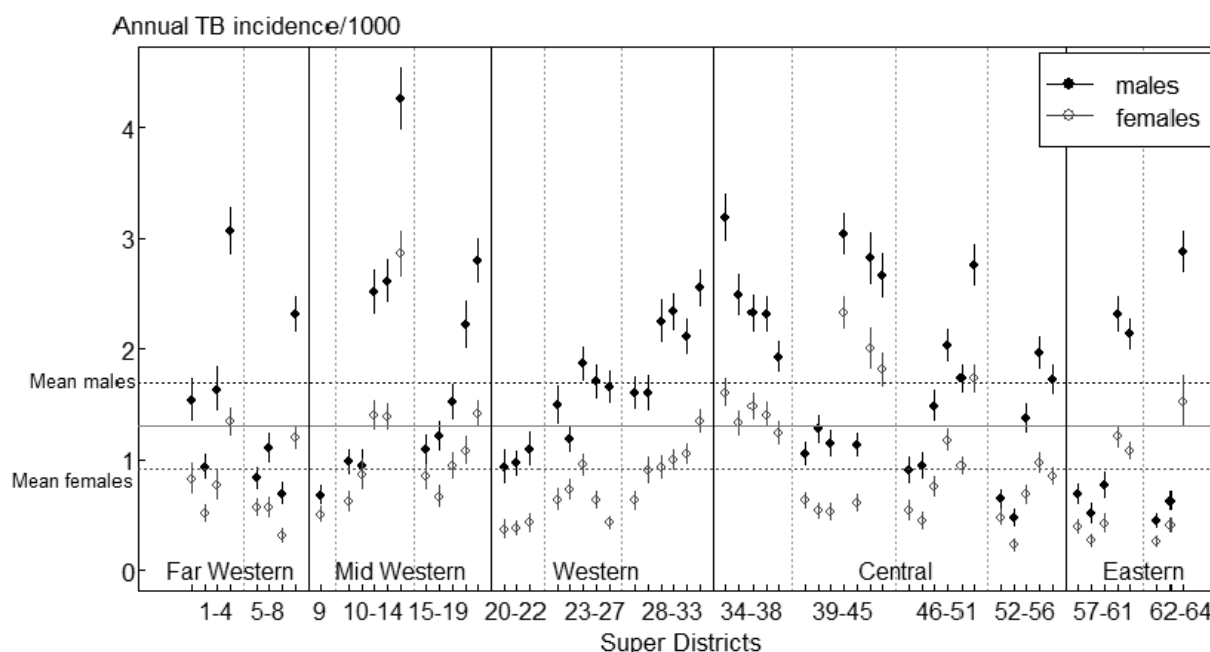


Fig. 1 Annual TB incidence/1000 for males and females in 64 super-districts (1-64) of Nepal.

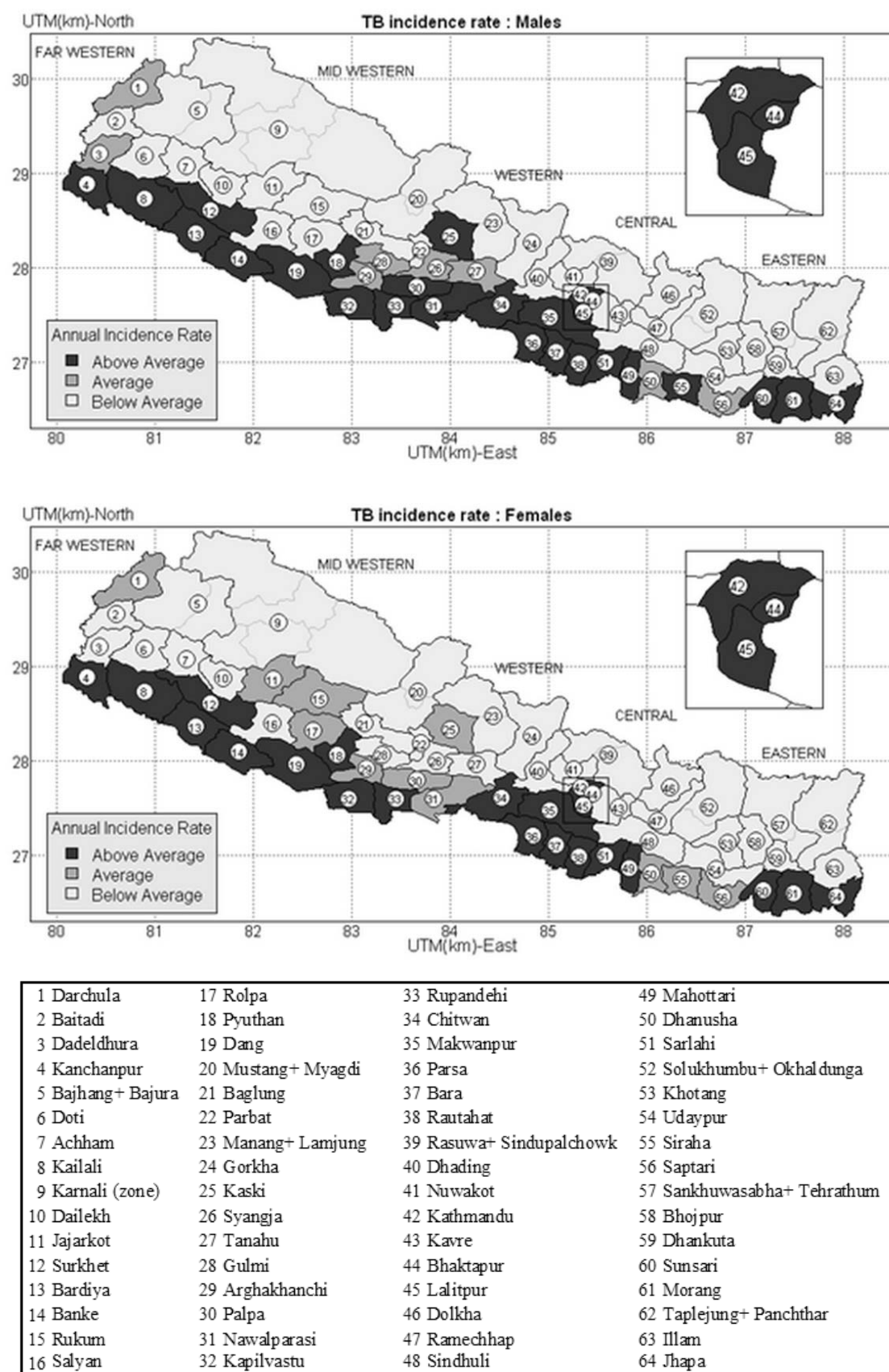


Fig. 2 Schematic map of annual tuberculosis incidence rates for males and females in 64 super-districts of Nepal.

Discussion

In Nepal, tuberculosis is a serious public health problem where more than 30,000 cases occur every year; half of them are infectious with the disease spreading in these communities.

The findings showed that gender differences existed in the incidence of TB; the male to female incidence ratio was 1.86. This is reasonably consistent with TB incidence and gender patterns found in recent studies in Nepal [5].

Epidemiological findings demonstrate that in most settings, tuberculosis incidence rates are higher for males, at all ages except in childhood, when they are higher for females. Studies have reported that sex differentials in prevalence rates begin to appear between 10 and 16 years of age, and remain higher for males than females thereafter [12].

The decreases in trends of TB incidence over the six-year periods were consistent with the WHO report and NTC annual report on tuberculosis. The decrease in TB incidence may be attributed to successful TB control program in the country with the expansion of DOTS, case finding and treatment success in the recent years in Nepal [1,2].

There were pronounced spatial variations in TB incidence for males and females with higher rates occurring in the Terai region, followed by the Hill and Mountain regions. Thus, it can be concluded that tuberculosis is more prevalent in the Terai region. Studies from the UK and Spain have shown seasonal variations in tuberculosis rates and higher notification rates over summer and in hotter regions [13, 14]. This increase has been attributed to impaired host defense mechanisms [15]. However, the notification rate in the Terai region can be attributed to not only medical factors, but also social and environmental factors. The Terai region is characterized by high temperatures, low socio-economic status, malnutrition, high levels of poverty, and social deprivation, all contributing to TB infection. However, the lower incidence rates of tuberculosis in mountain areas are consistent with studies from Kenya and Mexico, which reported that the tuberculosis incidence decreases strongly with increasing altitude [16, 17].

TB incidences were also found to be higher in urban areas. The high number of cases in cities may be due to increasing poverty, migration, and homelessness in cities that seems to be linked with the reemergence of TB. Associations among tuberculosis, urbanization, and poverty have been noted

in studies from countries as diverse as India [18] and the Philippines [19]. It is clear that growing numbers of poor, malnourished people living in unhygienic, overcrowded conditions can facilitate the transmission of TB in Nepal.

Our study had some limitations. We analyzed a short period (from 2003 to 2008). Additional analyses are needed to evaluate the trends of tuberculosis using data for a longer study period, or more detailed incidence data (monthly, quarterly). Second, we could not incorporate age, which is considered as one of the risk factors for tuberculosis, due to unavailability of age-specific incidence data.

Conclusion

This study presents insights into the incidence of TB by gender, year and location. These findings require further investigation, but highlight the importance of selectively monitoring geographic locations and the planning of future intervention strategies.

Acknowledgements

This study was partially funded by the Graduate School, Prince of Songkla University, Thailand. We would like to express our gratitude to the National Tuberculosis Center (NTC), Thimi, Bhaktapur, for permission to use their data. We are indebted to Prof. Don McNeil for supervising our research.

The authors have no conflict of interests to declare.

References

1. SAARC Tuberculosis and HIV/AIDS Centre (STC). Tuberculosis Control in the SAARC Region-An update 2007. STC. Thimi, Bhaktapur 2007; p. 36-40.
2. Department of Health Services, Government of Nepal. Annual Report. Kathmandu; 2008.
3. Harries A, Maher D, Uplekar M. National Tuberculosis Programme of Nepal: A Clinical Manual, National Tuberculosis Centre. Thimi, Bhaktapur; 1998.
4. Uplekar MW, Rangan S, Weiss MG, Ogden J, Borgdorff MW, Hudelson P. Attention to gender issues in tuberculosis control. *Int J Tuberc Lung Dis*. 2001; 5: 220-4.
5. Shrestha L, Jha KK. Gender disparity among TB suspects and new TB patients-a record-based retrospective study in SAARC member states. *SAARC J. Tuberc, Lung Dis HIV/AIDS* 2007; 4:8-18.
6. Wikipedia. The free encyclopedia (on line). 2009 [cited 2009 Mar 19] Available from: http://en.wikipedia.org/wiki/List_of_countries_by_population.

7. Tongkumchum P, McNeil D. Confidence intervals using contrasts for regression model. *Songklanakarin J Sci Technol.* 2009; 31:151-6.
8. Venables WN, Smith DM, the R Development Core Team. An introduction to R: notes on R: a programming environment for data analysis and graphics. Version. 2.6.2. 2008.
9. Murrell P. R Graphics. 1st ed. London:Chapman & Hall/CRC; 2006.
10. Lee RD, Carter LR. Modeling and forecasting U.S. Mortality. *J Am Stat Assoc.* 1992; 87:659-71.
11. Maindonald JH. Least squares computations based on the cholesky decomposition of correlation matrix. *JSCS.* 1997; 5:247-58.
12. World Health Organization. Gender and tuberculosis global tuberculosis control. WHO Report 2003 (on line). 2003 [cited 2009 Jan 13]. Available from: www.who.int/entity/gender/documents/en/TB.factsheet.pdf.
13. Douglas AS, Strachan DP, Maxwell JD. Seasonality of tuberculosis: the reverse of other respiratory diseases in the UK. *Thorax.* 1996; 51:944-6.
14. Rios M, Garcia JM, Sanchez JA, Perez D. [A statistical analysis of the seasonality in pulmonary tuberculosis.](#) *Eur J Epidemiol.* 2000; 16:483-8.
15. Davies PDO. Seasonality of tuberculosis. *Thorax.* 1997; 52:398.
16. Mansoor JR, Kibuga DK, Borgdorff MW. Altitude: a determinant for tuberculosis in Kenya? *Int J Tuberc Lung Dis.* 1999; 3:156-61.
17. Vargas MH, Furuya ME, Perez-Guzman C. Effect of altitude on the frequency of pulmonary tuberculosis. *Int J Tuberc Lung Dis.* 2004; 8:1321-4.
18. Rangan S, Gupte H, Bandiwadekar A, Girishambe. Tackling tuberculosis in urban areas: experiences from Mumbai City. *Health Administrator.* 2003; 15:72-9.
19. Tupasi TE, Radhakrishna S, Quelapio MID, Villa MLA, Pascual MLG, Rivera AB, et al. Tuberculosis in the urban poor settlements in the Philippines. *Int J Tuberc Lung Dis.* 2000; 4:4-11.