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Seasonality and trend analysis of tuberculosis in Lahore, Pakistan from 2006 to 2013

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Abstract Tuberculosis (TB) is a respiratory infectious disease which shows seasonality. Seasonal variation in TB notifications has been reported in different regions, suggesting that various geographic and demographic factors are involved in seasonality. The study was designed to find out the temporal and seasonal pattern of TB incidence in Lahore, Pakistan from 2006 to 2013 in newly diagnosed pulmonary TB cases. SPSS version 21 software was used for correlation to determine the temporal relationship and time series analysis for seasonal variation. Temperature was found to be significantly associated with TB incidence at the 0.01 level with $p = 0.006$ and $r = 0.477$. Autocorrelation function and partial autocorrelation function showed a significant peak at lag 4 suggesting a seasonal component of the TB series. Seasonal adjusted factor showed peak seasonal variation in the second quarter (April—June). The expert modeler predicted the Holt—Winter's additive model as the best fit model for the time series, which exhibits a linear trend with constant (additive) seasonal variations, and the stationary R^2 value was found to be 0.693. The forecast shows a declining trend with seasonality. A significant temporal relation with a seasonal pattern and declining trend with variable amplitudes of fluctuation was observed in the incidence of TB.

1. Introduction

Tuberculosis (TB) is one of the biggest health challenges which the world is facing and is the second major cause of mortality, particularly in poor and low economic countries [1,2]. TB is a respiratory

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infectious disease caused by *Mycobacterium tuberculosis* and spreads through air droplets by sneezing and coughing of the infected person [3]. Globally, 8.6 million people developed TB throughout the world in 2012; 1.1 million (13%) were coinfected with human immunodeficiency virus (HIV). Throughout the world, 6.1 million cases of TB were registered to the national TB program, and of these, 5.7 million were newly diagnosed cases [4]. Pakistan is ranked fifth among the 22 high TB burden countries. In 2012, nearly 2.6 million new cases of TB were notified of which 1.1 million (42%) were sputum smear-positive. The incidence and prevalence rates of Pakistan in 2012 inclusive of HIV were 231/100,000 population and 376/100,000 population, respectively, with a mortality rate of 0.66/100,000 population [5].

It is a well-known fact that TB demonstrates seasonality. Seasonality of TB has been reported in many studies, such as in Kuwait, where the peak of case notification is in summer [6], in India with summer as the peak season [7], and in China where summer is the peak season [8]. In Iran, a high number of TB cases were observed in spring and summer [9]. The review of various studies has shown a rise in TB case notification at the end of the winter and the start of summer [10]. The exact mechanism underlying this seasonality is not known, but it has been suggested that various environmental, social, and host-related risk factors such as temperature, humidity, rainfall, sunlight, indoor activity, crowding, pollution, immunosuppression, and diagnostic delays are involved in TB seasonality, specially, in winter [11]. Various demographic and epidemiological factors have been characterized that explain the trend and seasonality of TB [12,13]. Identification of seasonality and the trend pattern of TB is very important for two reasons. Firstly, to find out the major risk factors involved in the spread of the disease and secondly, to plan the strategies to control the prevention of the disease. TB case notification has been reported with different peaks in different seasons, such as in South Africa where it peaks from winter to early spring [15], in the UK and Hong Kong where summer is the peak season [14,15], and in Spain and Japan, where the maximum number of cases were reported in summer and autumn [16,17].

To our knowledge, no study has described the seasonality of TB in Pakistan. Therefore, the present study is aimed to find the possible seasonal variation in newly diagnosed pulmonary TB cases notified to the directly observed short treatment program (DOTS) of the national TB program in Lahore, Pakistan from 2006 to 2013.

2. Methods

A retrospective study was performed on the data obtained from DOTS, the regional center of Punjab in Lahore, Pakistan, to determine the seasonality and temporal relationship of TB. Here, seasonality is defined as the characteristic of the time series in which data exhibit regular and predictable changes which recur at every defined interval of time (quarter of the year in this case). From the Lahore region, DOTS covers the population of nearly 7 million. The data of newly diagnosed sputum smear-positive pulmonary TB cases from 2006 to 2013 were obtained. To notify a TB case, three sputum smears were performed for acid-fast bacilli through the Ziehl—Neelson stain method as per the guidelines of the World Health Organization. The cases with two positive reports were considered as true TB cases and registered as TB smear-positive cases to DOTS. The study was confined to smear-positive pulmonary TB cases for two reasons. Firstly, the diagnosis of other forms of TB is uncertain with poorly developed culture facilities in countries like Pakistan. Secondly, the proportion of other forms of TB was very small as compared to sputum smear-positive pulmonary TB. The data obtained from DOTS was on a quarterly basis. All of the data were grouped by sex into seven age groups. For the temporal relationship of TB, correlation and regression analysis was performed between the quarterly number of notified TB cases and quarterly mean temperature. The temperature data were obtained from the meteorology department of Lahore. All of the data were entered in Microsoft Excel (2010 version).

Expert modeler of SPSS version 20 software (SPSS Inc., Chicago, IL, USA) was used to fit the best suitable model for the time series data. The stationarity of the data was checked by autocorrelation function and partial autocorrelation function. The peak of seasonal variation was determined by seasonal adjusted factor. The Ljung—Box (modified Box—Pierce) test was used to determine if the model was correctly specified. Forecasting of the incidence of quarterly TB cases was also performed using the best fit model.

3. Results

The reporting time period of 2006—2013 constituted 32 epidemiological quarters during which a total of 55,636 newly diagnosed sputum smear-positive cases were registered to DOTS. The average number of cases notified/quarter was 1738