Original Article

# A Retrospective Study of Seasonal Variation in the Number of Cases Diagnosed at a Tertiary Care Tuberculosis Hospital

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## ABSTRACT

**Objective.** To study the seasonality of tuberculosis (TB) in a tertiary care tuberculosis and respiratory hospital in Delhi.

**Methods.** Data from a tertiary care respiratory hospital in south Delhi over a six years period from April 2002 to March 2008 were analysed.

**Results.** ***Symptomatics*:** A total of 192,863 patients were registered newly in the hospital during this period. Maximum number of symptomatic patients reported to the out-patient department during April-June and the minimum during October-December. An increase of about 25% in symptomatics was observed ($p<0.05$) in the period from April to June in comparison to October to December. The amplitude of seasonal variation was estimated as 11% of the annual mean symptomatics. ***Tuberculosis cases*:** The maximum sputum-positive TB cases were diagnosed during the period from April to June and the number was least during October to December. There was an increase of about 34% in sputum-positive cases ($p<0.001$) during the period from April to June against October to December. The amplitude of seasonal variation was estimated as 14.4% of the annual mean smear-positives per quarter. The extra-pulmonary TB (EPTB) cases were the maximum during April-June. Chest symptomatics of all types of TB cases were the lowest in January.

**Conclusions.** A seasonal pattern of TB was observed for pulmonary TB and EPTB cases. This information would be useful for administration and managers to take extra care to arrange and provide extra facilities during the peak seasons.
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**Key words:** Seasonal variation, Tuberculosis.

## INTRODUCTION

There is a recent concern about the global climate change that is expected to have broad health impacts.[1-3] Such human health impacts are most likely to occur where extreme weather and a vulnerable population combine together. The health effects of extreme weather events include a spectrum of wide variety of impacts, like physical injury, poor nutritional status because of the effect of climate on food, increase in a variety of respiratory and diarrhoeal diseases, increased vector-borne diseases, an increase in allergic disorders and increased pollution levels. Seasonal variation of tuberculosis (TB) has been reported from different parts of the world,[4-10] although no definite and consistent pattern has been observed. One earlier report from India[8] has assessed trends using quarterly reports from districts with stable TB control programmes. According to this study in northern India, TB diagnosis peaked between April and June, and it reached a *nadir* between October and December. However, no seasonality was reported from South India.[8] We undertook the present study to examine the issue in a hospital setting.

## MATERIAL AND METHODS

The present study was undertaken in a tertiary care tuberculosis and respiratory diseases hospital situated in Delhi, which caters mainly to TB patients. The Institute runs a daily Out-patient Department (OPD) with facility for indoor treatment with a bed strength of 520. The patients seeking medical help not only come from Delhi but also from the adjoining states, like Haryana, Uttar Pradesh, Bihar, Rajasthan, etc. Patient data are maintained by a computerised system. Patients having any chest symptoms attending the OPD (symptomatics) were included in the data analysis. Three sputum smear examinations were done for acid-fast bacilli (AFB) as per the guidelines of the Revised National Tuberculosis Control Programme (RNTCP). Data from April 2002 to March 2008 (six years) were analysed in the present study. The OPD in the institute functions

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daily except on sundays and gazetted holidays. Seasonality record was calculated using this data. The months were grouped into quarters where the number of patients were not significantly different. The data were averaged over the quarters.

Further, to study the seasonality of TB, the symptomatics registered and TB cases diagnosed were averaged for six years. The significance of the difference between the highest and the lowest mean values was analysed for the type of study variables, *i.e.* sputum-positive, sputum-negative and extra-pulmonary TB (EPTB) cases.

## Statistical Analysis

Unpaired student's t-test for independent samples was used to test the significance of difference in mean values between the seasons, and a p value <0.05 was considered statistically significant.

## Seasonality Analysis

To study the seasonality of symptomatics and TB patients, the month-wise data were grouped into four quarters: Q1 (January-March), Q2 (April-June), Q3 (July-September), Q4 (October-December) in a year. The quarters in which the mean values of patients were highest or lowest were examined and tested for significance of difference. The amplitude of fluctuation in seasonality was estimated using the following equation[7]:

$$=(\text{Highest mean of the quarter} - \text{Lowest mean of the quarter})/2$$

and the ratio of the amplitude of fluctuation to annual mean per quarter was calculated according to gender and age (children/adults) for symptomatics and for TB cases according to age (children/adults) only.

## Adjusting for the health seeking behaviour

To study the variation after adjustment of the health seeking behaviour, the following method was adopted. For all the six years expected number of TB cases diagnosed were calculated quarter-wise using the following formula.

$$\text{Expected number of TB cases per quarter assuming quarter-specific diagnosis rate} = \frac{\text{(TB cases diagnosed in a quarter)}}{\text{(Symptomatics in a quarter)}} \times \text{(Total symptomatics in a year)}$$

The expected number of TB cases for each quarter were compared.

# RESULTS

## Study Population

A total of 192,863 chest symptomatics were seen over a period of six years, and details about sputum status are presented in table 1. Out of these, 13,367 were sputum-positive TB cases and 7062 were sputum-negative cases, comprising a total of 20,429 pulmonary TB (PTB) cases. Besides this, 7732 EPTB cases were also diagnosed.

**Table 1. Number of patients analysed for seasonal trend in tuberculosis (TB)**

| Year | | Symptomatics | Sputum Positives | Sputum Negatives | Total Pulmonary TB Cases | Extra-pulmonary TB Cases |
|---|---|---|---|---|---|---|
| 2002-03 | Adults | 24790 | 2050 | 998 | 3048 | 855 |
| | Children | 3333 | 74 | 173 | 247 | 132 |
| | Total | 28123 | 2124 | 1171 | 3295 | 987 |
| 2003-04 | Adults | 26207 | 1934 | 1124 | 3058 | 1060 |
| | Children | 3414 | 50 | 152 | 202 | 238 |
| | Total | 29621 | 1984 | 1276 | 3260 | 1298 |
| 2004-05 | Adults | 28728 | 2152 | 1043 | 3195 | 1152 |
| | Children | 3498 | 70 | 153 | 223 | 255 |
| | Total | 32226 | 2222 | 1196 | 3418 | 1407 |
| 2005-06 | Adults | 31134 | 2190 | 1018 | 3208 | 1141 |
| | Children | 3937 | 59 | 172 | 231 | 244 |
| | Total | 35071 | 2249 | 1190 | 3439 | 1385 |
| 2006-07 | Adults | 30176 | 2175 | 888 | 3063 | 1150 |
| | Children | 3430 | 76 | 146 | 222 | 190 |
| | Total | 33606 | 2151 | 1034 | 3285 | 1340 |
| 2007-08 | Adults | 31106 | 2483 | 1067 | 3550 | 1132 |
| | Children | 3110 | 54 | 128 | 182 | 183 |
| | Total | 34216 | 2537 | 1195 | 3732 | 1315 |
| **Total** | **Adults** | **172141** | **12984** | **6138** | **19122** | **6490** |
| | **Children** | **20722** | **383** | **924** | **1307** | **1242** |
| | **Total** | **192863** | **13367** | **7062** | **20429** | **7732** |

## Seasonality Among Symptomatics

Month-wise trends for symptomatics for adults and children are shown in figure 1. The total number of symptomatics (adults and children) were highest during the quarter Q2 (April to June) (mean 8892.8±626.3) and the lowest (mean 7126.3±584.9) in the quarter Q4 (October to December) (p=0.0072). The overall amplitude of seasonal variation observed among the symptomatics was 11% of the annual mean symptomatics per quarter as shown in table 2. The data were further analysed according to gender and age (≤14 years) children and (age >14 years) adults (Table 2).

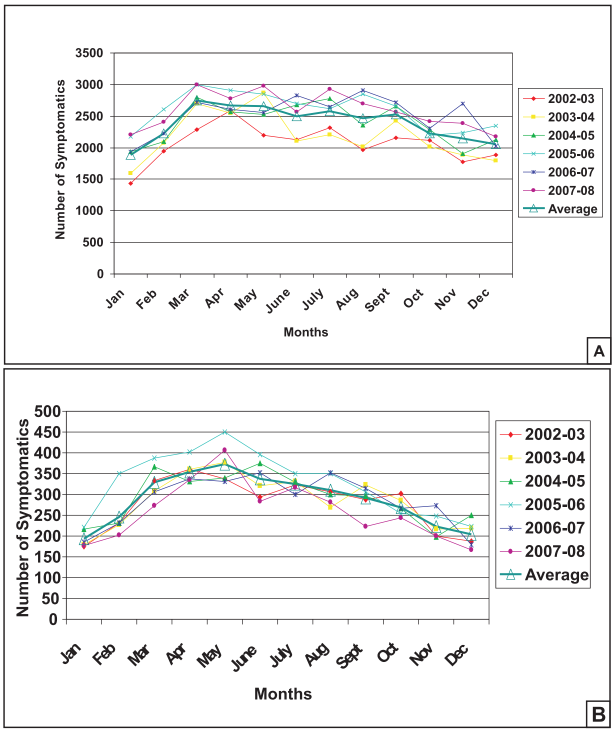


**Figure 1. Month-wise symptomatics; (A) adults, (B) children.**

### *Among adults*

The total number of symptomatics among adults during the quarter Q2 (April to June) were the highest (mean 7828.5±565.5) and the lowest during the quarter Q4 (October to December) (mean 6430.0±596.2) (p=0.002) (Table 2). The amplitude of seasonal variation among adults was estimated as 9.7% of the annual mean symptomatics. Gender-wise difference was not observed in the amplitude of fluctuation among the adult symptomatics (Table 2).

### *Among children*

The amplitude of fluctuation observed among the children (21%) was almost double the amplitude of fluctuation observed among the adults (9.7%). The number of symptomatics among children during the quarter Q2 (April to June) (mean 1064.3±92.9) were the highest and lowest during the quarter Q4 (October to December) (mean 695.8±43.4) (p<0.001). The amplitude of fluctuation observed was the same for male and female symptomatics in children (Table 2).

## Seasonality of Tuberculosis

*Seasonality of Pulmonary Tuberculosis*

The total PTB cases (combined for sputum positives and negatives) were highest during the quarter Q2 (April to June) (mean 989.7±69.5) and the lowest (mean 704.5±32.5) during quarter Q4 (October to December) (p<0.001). The overall, amplitude of seasonal variation observed among the PTB cases was 16.7% of mean number of PTB cases per quarter as shown in the table 3. However, monthly trends for PTB cases for adults and children are shown in figure 2.

Among adults, the mean PTB cases during the quarter Q2 (April to June) (917.0±66.4) were the highest and the lowest in the quarter Q4 (October to December) (mean 660.3±37.7) (p<0.0001) (Table 3). The amplitude of variation among adult PTB cases observed was 16.1% of mean number of PTB cases per quarter as shown in table 3.

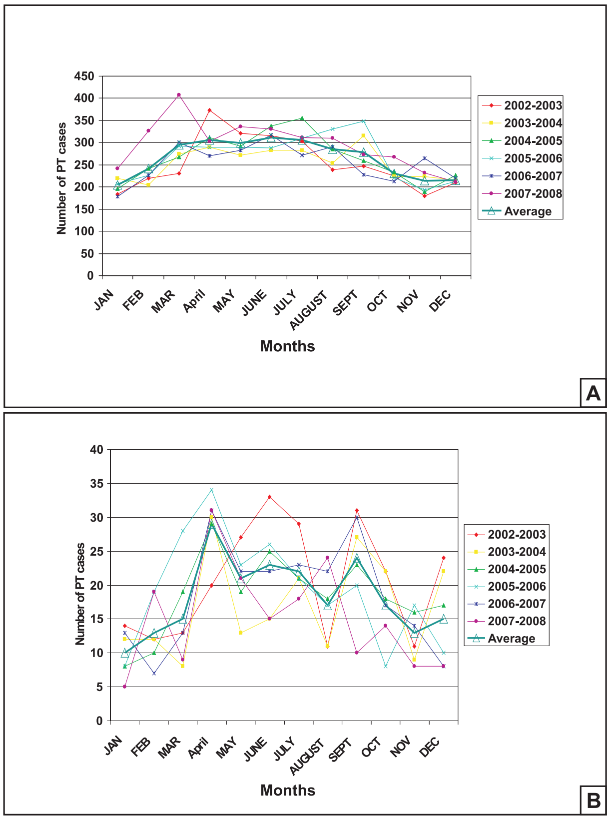


**Figure 2. Month-wise pulmonary tuberculosis cases; (A) adults, (B) children.**

**Table 2. Highest or lowest mean number of symptomatics in quarters with the amplitude of fluctuation around the annual mean values**

| | Highest (Mean±SD) (A) | Lowest (Mean±SD) (B) | Significance (p-value) | Annual Mean (AM) (per quarter) | Amplitude of Fluctuation to Annual Mean [(A-B)/2*AM] and (95% CI) |
|---|---|---|---|---|---|
| **Number of Years** | **6** | **6** | | | |
| **Symptomatics** | | | | | |
| Adults | | | | | |
| Male | (April-June) 5151.7±349.4 | (October-December) 4245.0±378.4 | P=0.0125 | 4704.8 | 0.096 (0.088, 0.105) |
| Female | (April-June) 2676.8±218.2 | (October-December) 2185.0±226.6 | P=0.0125 | 2467.8 | 0.099 ( 0.088, 0.111) |
| Total | (April-June) 7828.5±565.5 | (October-December) 6430.0±596.2 | P=0.002 | 7172.6 | 0.097 (0.091, 0.104) |
| Children | | | | | |
| Male | (April-June) 590.5±53.6 | (October-December) 386.3±18.0 | P=0.0009 | 483.2 | 0.211 (0.175, 0.248) |
| Female | (April-June) 473.8±51.7 | (October-December) 309.5±28.2 | P=0.000 | 380.3 | 0.216 ( 0.175, 0.257) |
| Total | April-June 1064.3±92.9 | (October-December) 695.8±46.2 | P<0.0001 | 863.5 | 0.213 (0.186; 0.241) |
| **All combined symptomatics** | **April-June 8892.8±626.3** | **October-December 7126.3±651.2** | **P=0.0072** | **8036** | **0.110 (0.103 , 0.117)** |

*SD=Standard deviation*

Among children, the mean number of PTB cases during the quarter Q2 (April to June) (72.7±9.1) were the highest and lowest during the quarter Q1 (January to March) (38.7±8.7) (p<0.001). The amplitude of fluctuation observed among the PTB cases in children (31.2%) was almost double the amplitude of fluctuation observed among the adults (16.1%) as shown in table 3.

### *Seasonality of Smear-negative Tuberculosis*

Combined for adults and children, the overall amplitude of seasonal variation among smear negatives was estimated as 21.1% of the annual mean number of smear negatives per quarter. The mean number of smear-negative PTB cases during the quarter Q2 (April to June) (361.7±34.1) were the highest and lowest during the quarter Q4 (October-December) (237.3±35.4) (p=0.0001).

The mean number of smear-negative TB patients among adults during the quarter Q2 (April to June) were highest (mean 307.7±33.6) and the lowest (207.5±29.4) in Q4 (October to December) (p=0.0003). The amplitude of seasonal variation among smear-negative adults was estimated as 19.6% of the annual mean number of smear negatives per quarter as shown in table 3.

Among children, the mean smear-negative TB cases during the quarter Q2 (April to June) were highest (54.0±7.8) and lowest (24.5±10.1) during quarter Q1 (January to March) (p=0.0002). The amplitude of seasonal variation among the children was estimated as 38.3% of the annual mean smear-negative TB cases, which is almost double of the adults (19.6%) as presented in table 3.

Data for sputum-negative and sputum-positive TB for adults and children are presented in figures 3 and 4.

### *Seasonality of Smear-positive Tuberculosis*

The data were analysed according to age (≤14 years) children and (>14 years) adults. The mean number of smear-positive TB patients (adults and children combined) during the quarter Q2 (April to June) (628.0±55.3) were the highest and lowest (467.2±42.4) in quarter Q4 (October to December) (p=0.0002). The amplitude of seasonal variation among total smear positives was estimated as 14.4% of the annual mean smear-positive TB cases. Among the smear positives, though the amplitude of seasonal variation was higher among children (15.6%) as compared to adults (14.5%) as shown in table 3. It was not found to be statistically significant.

### *Seasonality of Extra-pulmonary Tuberculosis*

The total EPTB cases were highest during the quarter Q2 (April to June) 384.5±57.6 and lowest (251.3±17.4) during quarter Q4 (October to December) (p=0.0056).

**Table 3. Quarters during which the mean number of tuberculosis (TB) patients were highest or lowest in various stage of TB and the amplitude of fluctuation around the annual mean values**

| Type of Disease | Highest (Mean±SD) Per Quarter (A) | Lowest (Mean±SD) Per Quarter (B) | Significance (p-value) | Annual Mean (AM) Per Quarter | Amplitude of Fluctuation to Annual Mean [(A-B)/2*AM] and (95% CI) |
|---|---|---|---|---|---|
| Number of Years | 6 | 6 | | | |
| **Pulmonary Tuberculosis (Combined for Sputum-positives and sputum-negatives)** | | | | | |
| Adults | April-June 917.0±66.4 | October-December 660.3±37.7 | p<0.0001 | 796.7 | 0.161(0.136, 0.187) |
| Children | April-June 72.7±9.1 | January-March 38.7±8.7 | p<0.0001 | 54.5 | 0.312 (0.189, 0.435) |
| Both Combined* | April-June 989.7±69.5 | October-December 704.5±32.5 | p<0.0001 | 851.2 | 0.167 (0.142, 0.193) |
| **Sputum Negatives** | | | | | |
| Adults | April-June 307.7±33.6 | October-December 207.5±29.4 | p=0.0003 | 255.8 | 0.196 (0.147, 0.245) |
| Children | April-June 54.0±7.8 | January-March 24.5±10.1 | p=0.0002 | 38.5 | 0.38.3 (0.230, 0.537) |
| Both Combined* | April-June 361.7±34.1 | October-December 237.3±35.4 | p=0.0001 | 294.3 | 0.211 (0.165, 0.258) |
| **Sputum Positives** | | | | | |
| Adults | April-June 609.3±51.8 | October-December 452.8±45.1 | p=0.0002 | 541 | 0.145 (0.115, 0.174) |
| Children | April-June 18.7±5.0 | January-March 13.7±5.3 | p=0.124 | 16.0 | 0.156 (-0.022, 0.334) |
| Both Combined* | April-June 628±55.3 | October-December 467.2±42.4 | p=0.0002 | 557 | 0.144 (0.115, 0.174) |
| **Extra-pulmonary Tuberculosis** | | | | | |
| Adults | April-June 317.5±33.8 | October-December 211.0±19.1 | p=0.0032 | 270.4 | 0.197 (0.180, 0.245) |
| Children | April-June 67.0±25.9 | January-March 40.3±9.4 | p=0.0276 | 51.7 | 0.258 (0.140, 0.378) |
| Both Combined | April-June 384.5±57.6 | October-December 251.3±17.4 | p=0.0056 | 322.1 | 0.207 (0.163, 0.251) |

*=Since the periods of lowest mean per quarter is different for children and adults, the total may not match.
*CI=Confidence interval; SD=Standard deviation*

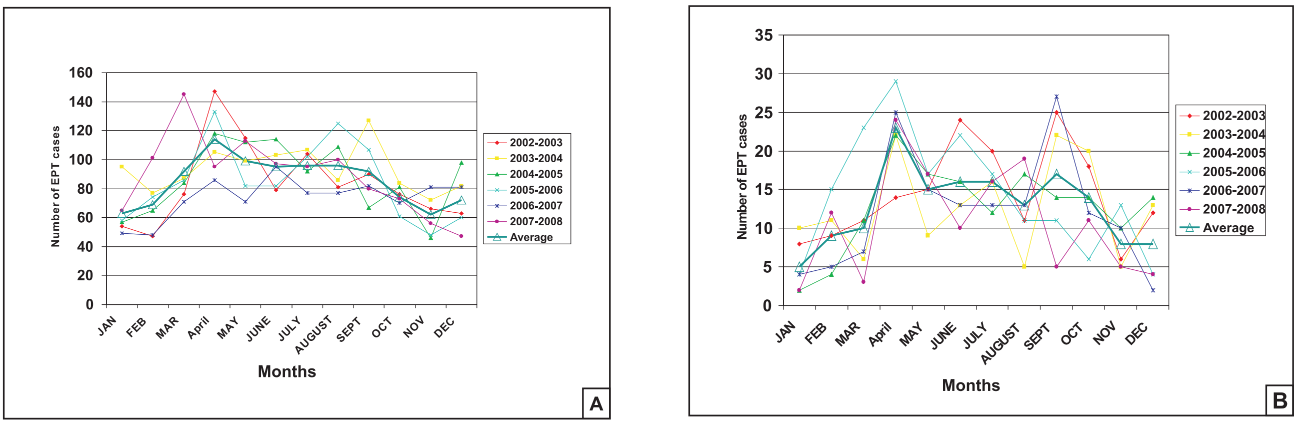


**Figure 3. Month-wise sputum-negative tuberculosis cases; (A) adults, (B) children.**

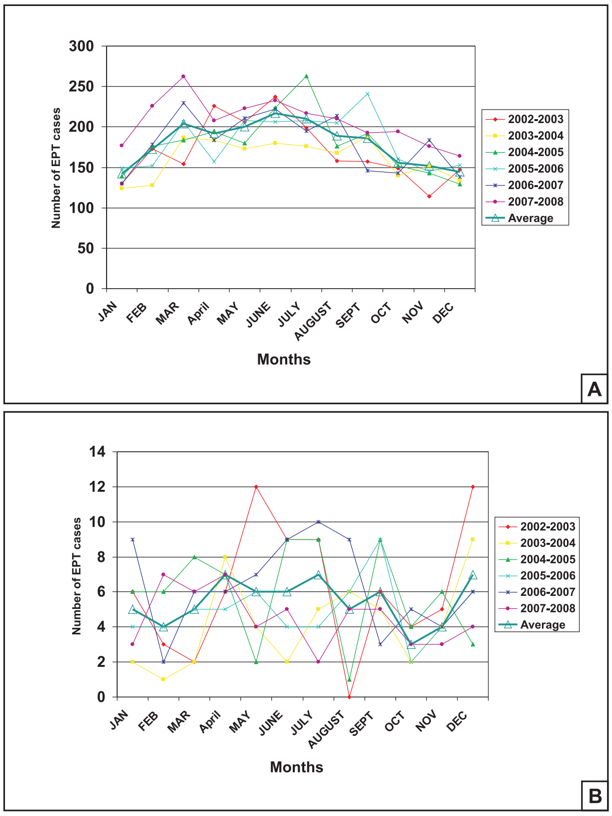


**Figure 4. Month-wise sputum-positive tuberculosis cases; (A) adults, (B) children.**

The amplitude of seasonal variation observed among the EPTB cases is 20.7% of the mean number of EPTB cases per quarter as shown in table 3.

The data were further analysed according to children and adults. Among the adults, the mean EPTB cases during the quarter Q2 (April to June) (317.5±33.8) were the highest and the lowest in the quarter Q4 (October to December) (211.0±19.1) (p=0.0032). The amplitude of variation among adults EPTB cases observed was 19.7% of the mean number of EPTB cases per quarter (Table 3).

The mean number of EPTB cases among children during the quarter Q2 (April to June) (67.0±25.9) were the highest and lowest during the quarter Q1 (January to March) (40.3±9.4) (p=0.0276) (Table 3). The amplitude of fluctuation observed among the EPTB cases in children (25.8%) was higher than the amplitude of fluctuation observed among the EPTB in adults (19.7%) as shown in table 3. Month-wise trends of EPTB cases for the six years are presented in figure 5.

## Adjusting for the health-seeking behaviour

### *Among adults*

After adjusting for the health-seeking behaviour, the four expected annual number of TB cases [Q1 (3009±448.7), Q2 (3357.6±268.2), Q3 (3298.9±313.5), Q4 (2946.6±179.20] were not significantly different

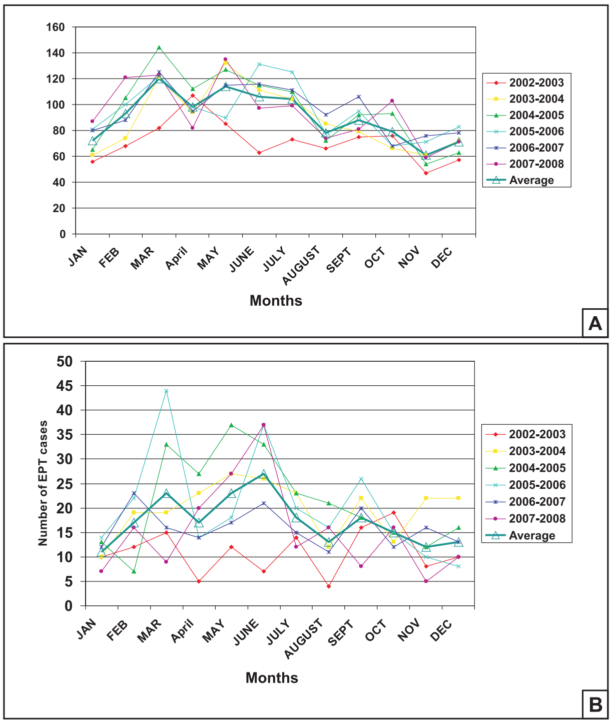


**Figure 5. Month-wise extra-pulmonary tuberculosis cases; (A) adults, (B) children.**

(p=0.131). However, Q2 (3357.6±268.2) and Q4 (2946.6±179.2) were significantly different (p=0.0123) (Table 4).

### *Among children*

The four expected number of TB cases among children were calculated for each quarter [Q1 (171.0±28.1), Q2 (236.4±33.3), Q3 (233.7±25.9), Q4 (217.8±48.1)]. The expected mean number of TB cases during the quarter Q2 (April-June) (mean 236.4±33.3) were the highest and the lowest in the quarter Q1 (January-March) (mean 171.0±28.1) (p=0.0043) (Table 4).

**Table 4. Highest or lowest expected number of all tuberculosis cases diagnosed out of total symptomatics of the year assuming quarter-specific diagnosis rates**

| Children/ Adults | Highest (Mean±SD) (A) | Lowest (Mean±SD) (B) | Significance p-value |
|---|---|---|---|
| Number of Years | 6 | 6 | |
| Children | April-June 236.4±33.3 | January-March 171.0±28.1 | P=0.0043 |
| Adults | April-June 3357.6±268.2 | October-December 2946.6±179.2 | P=0.0123 |
| Both combined | April-June 3575.7±279.5 | October-December 3177.1±152.5 | P=0.0154 |

## Combined for adults and children

The expected mean number of TB cases per quarter among all the patients (Adult + children) were [Q1 (3284.4±449.5), Q2 (3575.7±279.5), Q3 (3530.4±298.5), Q4 (3177.1±152.5)], these were not significantly different (p=0.113). However, the expected mean number of TB cases during the quarter Q2 (April-June) (3575.7±279.5) were higher than the quarter Q4 (October-December) (3177.1±152.5) (p=0.0154) with an amplitude of variation of 5.9% of the annual mean per quarter as shown in table 4.

## DISCUSSION

In an assessment of seasonal trends, Thorpe *et al*[8] reported that diagnosis of TB peaked between April and June, and reached *nadir* between October and December. Seasonal variation in TB incidence has also been reported from Europe and South Africa particularly in children.[8,14,15]

The present study demonstrated the seasonality of symptomatic patients for TB and TB cases in a tertiary care tuberculosis and respiratory diseases hospital in south Delhi. The chest symptomatics and TB cases were more in the period from April to June and less in the period from October to December. The study corroborates with the observations by Thorpe *et al*[8] showing the seasonal variation which were peaked between April and June and dropped during October and December. Areas in the north India had the highest seasonal variation and low or no seasonality was noted in central and southern regions of India in that study. Similar observations of seasonal variation has also been reported by others from different countries.[5,7,14,16-18] The causes of seasonality of TB are still unclear. There could be many speculations about the high number of TB cases during summer; one of the reasons could be that the process of transmission of TB infection is intensified by increased time spent in overcrowded, poorly ventilated housing conditions and by an increased frequency of coughing from other respiratory infections. It could also be due to a rise in temperature during summer. It is speculated that because of harvesting period of wheat crop in north India during this period from March to May, lots of dust particles come out when the wheat's seed is taken out and very fine particles are dispersed in the atmosphere producing air pollution. Other possible explanations of such variability given by different authors include low levels of vitamin D which are known to affect macrophage function and cell-mediated immunity that might result in impaired cellular immunity leading to reactivation of dormant mycobacterial infection.[14,19] However, the exact cause of such variability is currently unexplained.

In the present study, the seasonality was observed for symptomatics, PTB and EPTB cases. Being a retrospective study, there are certain limitations of the study: information on occupation, travel, support of family etc, was not available and this could not be taken into account. The study is an observational study and cause and effect could not be established. Only those patients who were suspected for human immunodeficiency virus (HIV) are tested and also the data for these patients were not available in the present record, therefore the HIV status of the patients studied is not known.

The variation according to gender has been calculated among the symptomatics but it could not be obtained among the TB cases, as the data could not be obtained from the records. The gender status of TB cases was not available for all TB cases as the TB cases were referred back to respective directly observed treatment short-course centres for further treatment. It is also to be noted that it is a hospital-based study and more sick people are likely to attend the hospital as compared to a population-based study, therefore it is difficult to predict the variation in the actual population. Another limitation is the duration of onset of symptoms and time-lag for attending the doctor in the hospital which could not be analysed.

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