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Original Article

Does tuberculosis have a seasonal pattern among migrant population entering Iran?

Mahmood Moosazadeh[1,3], Narges Khanjani[2], Abbas Bahrampour[3], Mahshid Nasehi[4,*]

Abstract

Background: There are few quantitative documents about the seasonal incidence of tuberculosis (TB) among immigrant populations. Concerning the significant role of recognizing seasonal changes of TB in improving the TB control program, this study determines the trend and seasonal temporal changes of TB among immigrants entering Iran.

Methods: In this longitudinal study, data from the Iranian TB register Program (from 2005 to 2011) was used. The aggregated number of monthly and seasonal TB cases was obtained by adding the daily counts. Data was analyzed by Chi-square, Independent T-test, ANOVA, and Poisson regression using Stata 11 and SPSS 20 software.

Results: Among 74,155 registered patients with TB, 14.3% (10,587) were non-Iranian who had immigrated to Iran from 29 different countries. The highest aggregated number of seasonal and monthly incidence of TB in immigrants was observed in spring (2824, P= 0.007) and in May (1037, P< 0.001). The number of non-Iranian patients with TB increased significantly over the years (β= 0.016, P= 0.001).

Conclusion: This study shows that immigrants constitute a significant portion of TB patients recorded in Iran and this trend is increasing. Also, the peak incidence of this disease is the second month of the spring.

Keywords: Tuberculosis (TB), Seasonality, Iran, Migrant

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***Correspondence to**:
Mahshid Nasehi
Email: mnasehi@yahoo.com

Introduction

Tuberculosis (TB) is a disease caused by Mycobacterium TB. It affects various organs and is spread from person to person through respiration (1,2). This disease can happen following a new infection with Mycobacterium TB or activation of latent TB infection; most cases in endemic countries are due to the transmission of new infection (3–5). TB is the second cause of death from infectious diseases worldwide. In 1993, World Health Organisation (WHO) announced that TB was a global emergency. At that time, 7–8 million people were estimated to have TB and 1.3 to 1.6 million people were estimated to die because of TB. Despite global attempts, no progress has been made in this regard and the number of patients and deaths was 8.5–9.2 million and 1.2–1.5 million respectively in 2010 (4–8). Historically, immigrants have had a great role in the spread of disease. The epidemiological importance of immigrants' disease transmission cycles is known. In countries with low incidence of TB, immigrants with TB have caused many problems for the TB control program and even years after the relocation of immigrants; this problem continues to increase (9,10). Moreover, new immigrants who come to these countries are at a higher risk of becoming infected to TB. Hence, screening all immigrants on arrival is necessary and investing in the global TB control program is valuable (9–13). A study in Kuwait showed that out of 2,328,582 screened immigrants, the incidence of pulmonary TB was 4608 cases or 198 in 100,000 and that the disease had a non-linear pattern (14).

Reviewing and identifying temporal changes and the seasonal pattern of TB, especially among migrant population is of great importance. As seasonal patterns are recognized, we can take action to estimate future health problems appropriately, develop, and improve effective public health programs, determine goals, and make more effective use of available resources (15).

Season may affect the mechanism of disease transmission and detection in different ways. On one hand, temperature, snow, and rain determine the time period when people spend indoors and facilitates the transmission of TB. On the other hand, the high workload in a particular season may inhibit patients' timely referral. Finally, season reflects when registration of disease is high thus, suitable programming can be provided (16–18).

It has been proven that the incidence of most respiratory infections has seasonal changes and this seasonal pattern has been confirmed in most studies that have examined the seasonal pattern of TB incidence (15,17–25). However, there is little documentation regarding the seasonal pattern of TB among emigrant populations. In this regard, only one study was carried out on the seasonality of TB incidence in immigrants in which the peak incidence of TB in immigrants was in spring (Late April) (26).

Despite the ongoing efforts made in Iran regarding TB control program, achieving the predicted objectives in TB control program is very difficult due to some uncontrollable problems such as having borders with Pakistan and Afghanistan which are among the world's 22nd most infected countries (3,7).

Concerning the importance of being aware of TB temporal

Full list of authors' affiliations is available at the end of the article.

changes among migrants in improving the TB control program, the present study examines the effect of season on the incidence of disease among migrants entering Iran in order to suggest strategic guidelines.

Methods

In this longitudinal study, data from the Iranian TB Register Program was used. For ethical concerns, the first name and last name were excluded. Also, the use of these data was approved by the office of TB in Iran. The sample included all TB cases diagnosed among migrants entering Iran from 2005 to 2011.

The time variables in this study were month and season. The aggregated number of TB cases per month was obtained by adding the daily cases. Thus, according to the study period (2005–11), 84 time points (months) were obtained. Spring included the months of April to June, summer included July to September, autumn was October to December and winter was January to March.

The main definitions were as follows: In the present study, an "immigrant" was a person who did not have an Iranian nationality and came to Iran in order to seek work and settlement. A "new case" was a patient who had never received treatment for TB or who had taken anti-TB drugs for less than 4 weeks. A "retreatment case" was a patient who had taken anti-TB drugs for at least 4 weeks (8).

In order to investigate the nature of data in terms of equality of variances and normality, Leven test and Kolmogorov-Smirnov test were used, respectively. ANOVA test was used to evaluate the effect of season and month on incidence. Also, Chi-square was used for categorical variables and independent T-test was applied to compare age mean by gender and Poisson regression tests were utilized to determine the trend of TB incidence among immigrants. The significance level equal to or less than 0.050 was considered significant. The SPSS 20 (SPSS Inc., Chicago, IL, USA) and Stata 11 (Stata Corporation, College Station, Texas) software was used to analyze the data.

Results

Out of 74,155 patients with TB (recorded between 2005 and 2011), 14.3% (10,587 persons) were non-Iranian and had immigrated to Iran from other countries. From them, 97.1% (10278 persons) were Afghanian, 0.6% were Iraqi (n= 61), and 0.4% were Pakistani (n= 38). The remaining patients were from Azerbaijan, Africa, Jordan, Uzbekistan, Algeria, United Arab Emirates (UAE), Bahrain, Bangladesh, Tajikistan, Thailand, Turkmenistan, Turkey, China, Russia, Zimbabwe, Senegal, the Philippines, Kazakhstan, Kuwait, Georgia, Oman, Russia, Tanzania, Kenya, Lebanon, and India.

Regarding gender, 5531 (52.2%) of patients were female. Women were significantly more than men ($P< 0.001$). The average age of patients with TB among migrants entering Iran was 39.4 ± 20.2. The average age and standard deviation (SD) of men and women was 38.1 ± 20.5 and 40.5 ± 19.8, respectively and this difference was statistically significant ($P< 0.001$). Moreover, 7940 (75%) of the patients had pulmonary TB and 25% had extra-pulmonary TB. 5970 (75.2%) of patients with pulmonary TB were smear positive. According to the results of sputum tests prior to treatment, 220 (3.7%) were 1–9 bacilli, 2199 (36.8%) were 1 positive, 1340 (22.4%) were 2 positive, and 2211 (37%) were 3 positive.

Regarding treatment, 8.3% of patients were in the retreatment group, 3.7% were in the relapse group, and 3.5% were in the default of treatment group. The number of patients varied from 1311 (12.4%) people in 2007 to 1654 (15.6%) people in 2011. Poisson regression analysis showed that every year the number of non-Iranian TB cases increased significantly ($P= 0.001$).

During 84 months of the study (from 2005 to 2011), minimum and maximum number of TB in migrant population was 83 and 169, respectively. The highest monthly average incidence of TB was in spring (134.5 ± 21.3). The average was 123.9 ± 18.0 in winter, 124.6 ± 16.1 in summer, and 116.1 ± 11.2 in fall and these differences were significant ($P= 0.007$). Based on Post-hoc test, the difference between spring and autumn ($P= 0.001$) and autumn and winter ($P= 0.018$) was significant. Figure 1 also shows that the highest number of aggregated TB patients (2824 people) were in the spring.

The highest average incidence of TB in migrants entering Iran was in May (148.1 ± 14.0), followed by March (140.7 ± 15.4), June (139.6 ± 20.6), July (133.9 ± 7.8), February (128.7 ± 12.9), September (120.6 ± 21.6), August (119.3 ± 13.7), October (117.9 ± 16.8), January (117.3 ± 19.0), December (116 ± 8.4), April (115.7 ± 15.1), and October (114.6 ± 7.9) respectively; these differences were significant ($P< 0.001$). According to Post-hoc test (Table 1), the differences observed between May and April, August, September, October, November, December, January, and February were significant. Also, the average incidence of TB was significant between April and June, July and March, and between June and August, September, October, November, December, and January.

It should be noted that the highest monthly incidence of TB (1037 people) among the migrant population entering Iran was in May (Figure 2). Also, according to Figure 3, the highest aggregated number of pulmonary TB with sputum smear results of 1–9 bacilli and 1 positive was in winter, while for 2 positive and 3 positive, it was in spring.

Discussion

This study shows the seasonal pattern of TB incidence among migrant populations entering Iran. More than one seventh of patients recorded in Iranian TB registry Program are non-Iranian and this trend is increasing. The peak of incidence is in spring and May. After May, the incidence of disease declines with the lowest reported number in November. Moreover,

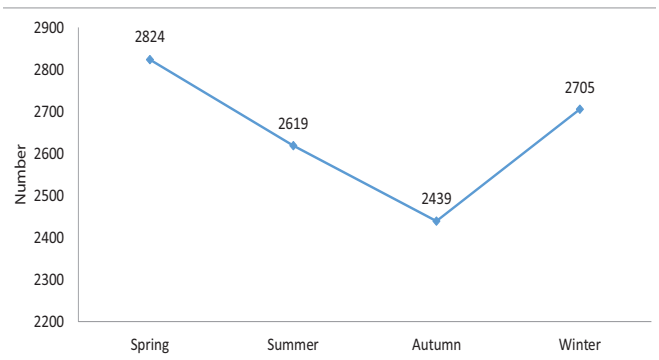

Figure 1. Aggregated seasonality tuberculosis number in immigrant population in Iran

Table 1. The result of Post Hoc test to investigate the differences observed between the monthly average of TB recorded in immigrants

	April	May	June	July	August	September	October	November	December	January	February	March
April		0.001	0.004	0.028	NS	NS	NS	NS	NS	NS	NS	0.003
May			NS	NS	0.001	0.001	0.001	0.001	0.001	0.001	0.019	NS
June				NS	0.014	0.021	0.009	0.003	0.005	0.007	NS	NS
July					NS	NS	NS	0.020	0.030	0.044	NS	NS
August						NS	NS	NS	NS	NS	NS	0.010
September							NS	NS	NS	NS	NS	0.015
October								NS	NS	NS	NS	0.006
November									NS	NS	NS	0.002
December										NS	NS	0.003
January											NS	0.005
February												NS
March												

NS: Non-significant

another peak can be found in the last month of winter (March). One of the most prominent points in this study is that, spring is the peak of pulmonary TB cases with laboratory results of culture or sputum smear 2 positive and 3 positive, while winter has the peak with 1 positive and 1–9 bacilli.

In this study, the incidence of TB was higher among female non-immigrants and this was similar to what is seen in Iranian patients (27). Also among all TB cases, smear positive pulmonary TB was higher in non-Iranian patients than in Iranians. Sputum smear in the majority of non-Iranian patients was 2 positive and 3 positive which probably reflects more delay in diagnosing this group due to various reasons including the lack of access to diagnostic facilities, poor information, unstable residence, etc. (3,28). The average age of TB registered cases is lower in migrants than Iranians which can be due to the fact that most migrants are middle-aged people who come to Iran as workforce.

In a study conducted on migrants entering Kuwait, the peak incidence of TB was in the spring and late April (26). In another study about the seasonal pattern of TB in the native Iranian population, it was shown that TB had a seasonal pattern and its peak was on the 14th of June (29). In studies conducted on native populations of other countries, the peak incidence of this disease was summer in Britain (17) and Hong Kong (18); spring and summer in Taiwan (23) and Ireland (24); spring and late fall with the peak being in March in the United States (25); summer in Japan (24); late winter and spring in Spain (in a study carried out by Luqureo *et al.*) (20); summer and autumn in a study by Rios *et al.* (16); spring and summer in South Africa (in a study by Fares *et al.*) (24); and late winter and early spring in a study by Schaaf *et al.* (21). In north of India (17), the peak incidence of TB was in spring and summer (highest in April and June, and lowest in October and December), while no seasonal pattern was observed in the south of India (10). The seasonal scope of TB was broad in the above-mentioned studies with spring being the peak; results of this study are also in line with the results of the above studies.

An important point in this study was that, the beginning of the peak in TB incidence was in the last month of winter (March) and its decrease was in the first month of the spring (April). This might be due to the fact that health and treatment centers in Iran do not work for about fifteen days of April (during Iranian New Year holiday) and that people are very busy in these fifteen days. Owing to the chronic nature of this disease, patients tolerate the conditions in these days and postpone their visits. Therefore, it causes aggregated diagnosis and registration after the holiday season. Another

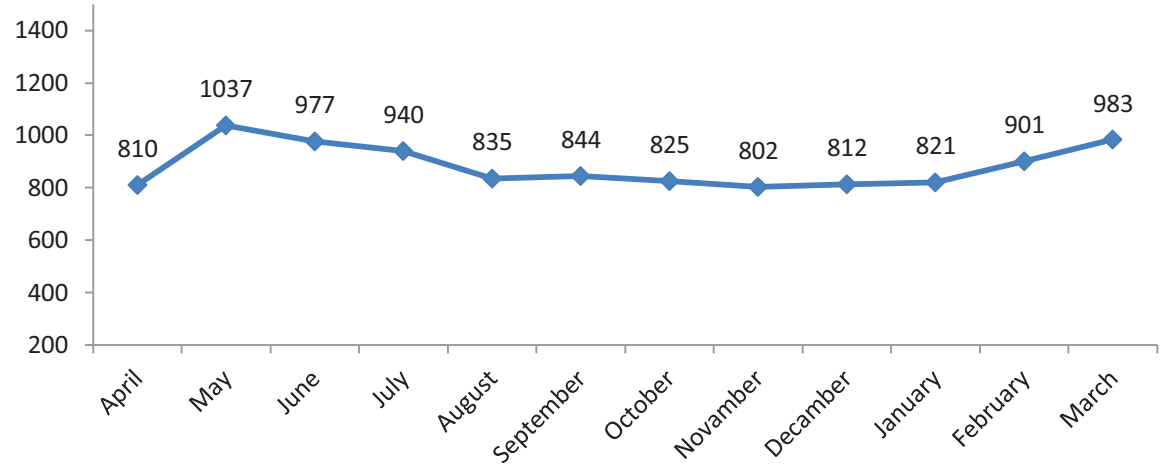

Figure 2. Aggregated monthly tuberculosis number in immigrant population in Iran

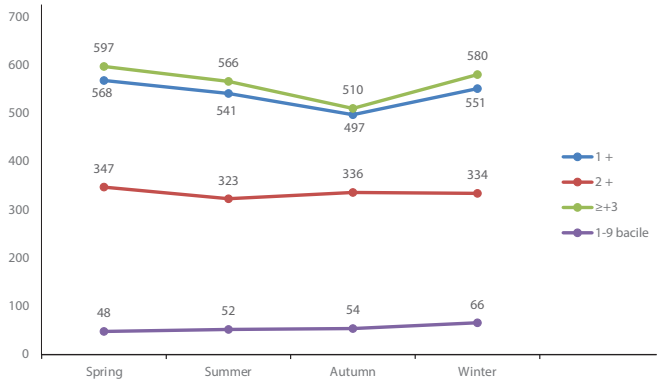

Figure 3. Aggregated seasonality the number of positive sputum or culture in immigrant population in Iran

point here is that physicians, in winter, may confuse this disease with other common seasonal diseases and may in most cases, regard symptoms like a cough as viral diseases; thus, TB is not diagnosed quickly in winter and it is postponed until the next spring.

Although the exact interpretation mechanism of the seasonal pattern of TB patients is not completely understood, several studies have regarded social and environmental factors such as temperature, humidity, sunlight, crowded areas, close person-to-person contacts as seasonality resources of TB. The hypothesis proposed here is that since winter is a cold season, people mainly live in closed environments and thus, transmission of disease happens in winter; after a period of incubation in winter, symptoms are diagnosed and registered in spring (24). Rios *et al.* (16) stated that the higher incidence of TB in winter and spring was due to frequent respiratory diseases, flu and incidence of immunodeficiency as well as more transmission in winter due to living in closed areas. Yamamoto *et al.* mentioned that low immune function due to decreased vitamin D in winter causes the higher incidence of TB but, since the incubation period of this disease was between 1 and 4 months, higher reported cases of this disease is seen in the summer (22). In Hong Kong, Leung *et al.* showed that reduced sunlight and decreased vitamin D significantly increases the cases of TB with positive smear and sputum culture in the summer (18).

Limitations

The main limitation of this study was the fact that we did not know the total number of migrants entering Iran. Thus, comparing the incidence of TB among migrants and native Iranians was not possible. The pattern of refugees' immigration per month in Iran was not known either, and therefore, one may argue that the number of immigrants goes up in the spring and then down in the winter. Changes might also exist in the immigrant health information or the time of entry to the country and could have affected these results. Moreover, examining the role of climatic conditions such as temperature, precipitation, humidity, and dust in the incidence of disease was not possible due to the characteristics of the migrants i.e. not being tied to a certain place and time.

Conclusion

This study reveals that a large number of TB patients in Iran are non-Iranian. The seasonal scope of this disease is broad and its incidence is relatively high from February to July (the first month of summer). However, there are two distinct peaks in this group: the second month of spring and the last month of winter.

Concerning the mentioned problems, one of the main points in improving the quality of TB control program is to screen migrants more carefully and completely which requires international efforts. Initial effective screening is also recommended to decrease delays in diagnosis and to prevent spread of disease to others. Moreover, teaching people how to observe their personal health, especially in winter in which respiratory diseases and influenza as well as coughs and sneezes are more common, is of great importance. Being exposed to the sunlight from the second month of fall to late winter is also suggested. In the case of presence of TB basic symptoms especially coughs, physicians are asked to consider TB in all seasons especially in winter.

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Ethical issues

The study protocol was approved by the the office of TB in Iran.

Competing interests

The authors declare that they have no competing interests.

Authors' contributions

MM, Nkh, and MN contributed to writing introduction, discussion, and conclusion. Also MM and AB participated in data cleaning, data analysis, and writing methodology and findings.

Authors' affiliations

[1]Mazandaran University of Medical Sciences, Sari, Iran. [2]Neurology Research Center, Shafa Hospital, Kerman University of Medical Sciences, Kerman, Iran. [3]Department of Biostatistics and Epidemiology, Faculty of Health, Kerman University of Medical Sciences, Kerman, Iran. [4]Department of Epidemiology, School of Public Health, Iran University of Medical Sciences, Tehran, Iran.

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Key Messages

Implications for policy makers

- Understanding the seasonal pattern of TB in immigrants provides the opportunity for appropriate policy making to promote the current status of the tuberculosis (TB) control program.
- One of the problems of TB control programs in Iran is the uncontrolled arrival of immigrants from countries with high prevalence of TB.
- The frequency of TB diagnosis among immigrants is higher in some seasons and months of the year.
- The possibility of timely case finding is not possible among immigrants due to their illegal arrival and this situation facilitates the spread of disease to native populations.
- Compliance and proper use of anti-TB drugs is low in immigrants.
- Surveillance of proper drug use in immigrant populations is difficult.

Implications for public

Tuberculosis (TB) is one of the most contagious chronic diseases that the international community has not been able to overcome it yet. This disease is higher in some groups, such as immigrants from countries with high prevalence of TB. According to the result of this study, most cases of TB recorded among immigrants entering Iran was in spring and May. Given the incubation period of TB, it would be likely that transmission of TB in this group occurs mainly in winter, and is due to deficiency of vitamin D, sunlight, and crowded living conditions. However, the disease diagnosis and registration happens a few months later.