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**Original Article**

# The Pattern of Tuberculosis in Iran: A National Cross-Sectional Study

***Adel Doosti [1], Mahshid Nasehi [2,3], Ghobad Moradi [1], Daem Roshani [1], Saeed Sharafi [3], *Ebrahim Ghaderi [4]***

1. *Social Determinants of Health Research Center, Research Institute for Health Development, Kurdistan University of Medical Sciences, Sanandaj, Iran*
2. *Department of Epidemiology and Biostatistics, School of Public Health, Iran University of Medical Sciences, Tehran, Iran*
3. *Center for Communicable Diseases Control, Ministry of Health and Medical Education, Tehran, Iran*
4. *Health Policy Research Center, Institute of Health, Shiraz University of Medical Sciences, Shiraz, Iran*

***Corresponding Author:** Email: ebrahimghaderi@yahoo.com

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**Abstract**

**Background:** Despite of the remarkable achievement in control of tuberculosis, it is still a challenging health problem in Iran. Success in any health program depends on monitor the diseases epidemiology and finding the gaps. We aimed to describe the epidemiological profile of TB patients in Iran to find the gaps in the TB program and using the finding to set the program activities.

**Methods:** This cross-sectional study was performed based on the data of tuberculosis patients registered in Iran in 2016-2017. The information of all TB patients is registered in the TB registry software. The patients were followed during the treatment phase. The data were analyzed by SPSS 23 software using Chi-Square test.

**Results:** Overall 12% of cases were Afghans and 72.3% of patients had pulmonary tuberculosis. There was a significant difference in the success rate of treatment in smear-positive pulmonary patients by gender, HIV status, marital status, history of hospitalization and incarceration ($P$ <0.01). The highest prevalence of antibiotic resistance was related to isoniazid (9.9%). In close contact persons who requiring prophylaxis, 65.3% of adults and 73.6% of children received full period of prophylaxis,

**Conclusion:** Despite of the TB treatment success and low prevalence of MDR cases, TB incidence has not been decreased significantly in Iran. Delay in diagnosis, high TB burden in refugees and close contact investigation and prophylaxis are important issues in the TB control program in Iran to be considered in the control planning.

**Keywords:** Tuberculosis; Cross-sectional study; Public health; Epidemiology; Iran

## Introduction

Tuberculosis (TB) in the world and in developing countries, including Iran, is still a health problem and it has the ninth position of the global burden of diseases. TB, with about 10 million cases a year, is the cause of death of about 1.4 million people (1). In the world, more than 1.7 billion

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people are infected with mycobacterium tuberculosis, with 5 to 15% of these people will suffer from active TB during their lifetime (2).
The simultaneous onset of TB and HIV has made it more difficult to control the disease (3). Another serious and growing problem in many countries is the multi-drug resistance (MDR); its rate is 18% in the previous treated patients and 3.3% in the new cases (1). Another problem in the control of TB is the delay in the diagnosis of the active TB cases which cannot be diagnosed in the first visiting of the patients by physicians (4) and its can lead to spread the disease.
For control TB in the world, World Health Organization (WHO) has set the targets that should be achieved by the year 2025; 50% reduction in the incidence and 75% reduction in the number of death in comparison to 2015 and for 2035 these targets are suggested as 95% and 90%, respectively (5). In Iran, according to the report in department of TB and leprosy control at the ministry of health, the incidence of smear positive TB in 2015 was 6.3 per 100 thousand, the total number of TB types was 12.6 per 100 thousand, and frequency of TB death was 757 patients (6).
One of the most important parts of the successful implementation of any health program is to monitor the diseases epidemiology and data in surveillance reporting system to realize trends and finding gaps (7).
We aimed to describe the epidemiological profile of TB patients in the country to find the gaps in the TB program and using the finding to set the program activities.

## Methods

This was a cross-sectional study. The data of all TB patients (pulmonary and extra-pulmonary), are recorded in the national TB registry from March 20$^{th}$, 2016 to March, 19$^{th}$, 2017 from all parts of the country diagnosed according to the WHO and national TB standard diagnostic guidelines. According to the national TB control program, all TB suspects from health home level at villages, health post in cities, hospitals and public or private clinics need to be evaluated by sputum specimens (three times) examination in the nationwide governmental TB laboratories.
The information of all TB patients is reported to the health center of the city and is registered in the TB registry software. After data is submitted to the province, the data recorded in the province are also checked by a TB coordinator physician and finally they are sent to the TB control and leprosy department at the Ministry of Health and Medical Education of the country. The patients are followed during the treatment phase and the outcomes will be evaluated and recorded in the data registry.
After obtaining the data of 2016 and cleaning and completing the missing values, the data was processed using spss19 software (Chicago, IL, USA). Arc GIS10.1 software was also used to prepare the GIS (Geographic information system) map. For data analysis, Kruskal-Wallis test was used to compare a variable median between some groups and, if significant, two-way Mann-Whitney U test was used to compare between the two groups and the *P*-values were corrected by Bonferroni correction. Chi-Square test was used to evaluate relation of two qualitative variables.

## Results

The number of registered TB cases was 9717 in a one-year period. Of these, 254 cases (2.5%) were excluded due to misdiagnosis (other types of mycobacterium and other diseases). The mean age of female and male patients were 51.14 (±21.6) and 48.10 (±20.8) years. In general, outpatient centers and admission units in the health system network with 63.4% cases of case finding had the most case finding, followed by clinics and private clinics, which referred 22.8% of cases (Table 1).

**Table 1:** Demographic and general information of patients with tuberculosis in Iran

| *Variable* | | | *Number* | *Percentage* |
|---|---|---|---|---|
| Sex | Male | | 5110 | 54 |
| | Female | | 4353 | 46 |
| Nationality | Iranian | | 8225 | 86.9 |
| | Afghan | | 1198 | 12.7 |
| | Others | | 40 | 0.4 |
| Residence | City | | 6638 | 70.1 |
| | Rural and countryside | | 2819 | 29.8 |
| | Abroad | | 6 | 0.1 |
| Marital Status | Married | | 5906 | 62.4 |
| | Single | | 2004 | 21.2 |
| | Divorced | | 282 | 3 |
| | Widow | | 1253 | 13.2 |
| | Unknown | | 18 | 0.2 |
| Age Group | <15 | | 240 | 2.5 |
| | 15-24 | | 999 | 10.5 |
| | 25-34 | | 1561 | 16.5 |
| | 35-44 | | 1398 | 14.8 |
| | 45-54 | | 1168 | 12.4 |
| | 55-64 | | 1318 | 13.9 |
| | >65 | | 2779 | 29.3 |
| Education | Illiterate | | 3965 | 41.9 |
| | Elementary | | 2152 | 22.7 |
| | Guidance school | | 1449 | 15.3 |
| | Secondary school and religious science | | 1307 | 13.8 |
| | Assistant until doctorate | | 577 | 6.1 |
| | Ph.D. specialist and higher | | 13 | 0.1 |
| Type of disease | Pulmonary 6847 | Smear-positive | 5076 | 53.7 |
| | | Smear-negative | 1771 | 18.7 |
| | Extra-pulmonary | | 2616 | 27.6 |
| Group therapy | Group therapy 1* | | 8688 | 91.8 |
| | Group therapy 2** | | 559 | 5.9 |
| | Others | | 216 | 2.3 |
| Group of disease record | New | | 8789 | 92.9 |
| | Relapse | | 302 | 3.2 |
| | Treatment after absence | | 38 | 0.4 |
| | Others | | 334 | 3.5 |
| Degree of smear positivity in smear-positive TB at the time of diagnosis | +1 and less | | 2023 | 39.9 |
| | +2 | | 1119 | 22 |
| | +3 | | 1934 | 38.1 |
| Patient referral center | Health network system (subordinate hospitalizing units) | | 3544 | 37.5 |
| | Health network system (subordinate outpatient units) | | 2459 | 26 |
| | Office – private clinic | | 2162 | 22.8 |
| | Direct referral of the patient to the tuberculosis center (self-introduce) | | 356 | 3.8 |

| | | | |
|---|---|---|---|
| | imprisonment history | 312 | 3.3 |
| | Social security | 119 | 1.3 |
| | Health – treatment units of military forces | 89 | 0.9 |
| | Others | 306 | 3.2 |
| | Unknown | 116 | 1.2 |
| HIV Virus infected | Unknown | 2499 | 26.4 |
| | No | 6608 | 69.8 |
| | Yes | 356 | 3.8 |
| Prisoner | No | 9085 | 96 |
| | Yes | 378 | 4 |
| Diabetes | Yes | 891 | 9.4 |
| | No | 6776 | 71.6 |
| | Unknown | 1796 | 19 |
| Chronic kidney failure | Yes | 159 | 1.7 |
| | No | 7346 | 77.6 |
| | Unknown | 1958 | 20.7 |
| Injection addiction | Yes | 280 | 3 |
| | No | 7151 | 75.5 |
| | Unknown | 2032 | 21.5 |
| Long-term treatment with corticosteroids | Yes | 105 | 1.1 |
| | No | 7394 | 78.1 |
| | Unknown | 1964 | 20.8 |
| Malignancy, leukemia and Hodgkin's disease | Yes | 23 | 0.24 |
| | No | 7438 | 78.6 |
| | Unknown | 2002 | 21.2 |
| Silicosis disease | Yes | 13 | 0.1 |
| | No | 7471 | 79 |
| | Unknown | 1979 | 20.9 |

* Attack phase of 2 months of HRZE and preserving phase of 4 months HR
** Attack phase of 2 months of HRZES and then one month HRZE and in preserving phase 5 months of HR

The mean interval between the onset of symptoms and the diagnosis was 114 days (±201) and a median of 59 days. The highest delay was observed in extra-pulmonary cases with 158.2 days and a median of 68 days, and then in the cases of pulmonary smear-negative cases, an average of 112 days with a median of 58 days and finally smear-positive pulmonary cases was observed with a mean of 91.5 days and a median of 56 days. The mean interval between diagnosis and initiation of treatment was 3.9 days (±17.6) totally, and the median was one day, which in this case, the highest delayed onset of treatment belonged to patients with extra-pulmonary. The difference between the onset of symptoms and the diagnosis of the disease, as well as the interval between diagnosis and treatment onset, were statistically significant in comparison with patients with smear-positive and smear-negative ($P$<0.001). However, there was no statistically significant difference between patients with smear-positive and smear-negative pulmonary cases whether in terms of the gap between symptom onset to diagnosis ($P$=0.16) or that between diagnosis to treatment onset ($P$=0.07).

Treatment success rate was 87.5% in total and 85.6% in smear positive pulmonary cases. There was a statistically significant difference in the success rate of treatment in smear-positive pulmonary patients by gender, HIV status, marital sta-

tus, history of hospitalization and incarceration ($P$ <0.01), but no statistically significant difference was found in patients' residence ($P$=0.39) (Table 2). According to the results of all the regional laboratory and national reference and with the rapid and normal method, the highest antibiotic resistance was related to isoniazid (9.9%), followed by rifampin (6.2%) and drug resistance to streptomycin 2.5% and Ethambutol 4.2% (Table 3).

**Table 2:** Comparison of the success rate of smear-positive patients whose treatment outcome is specified (3986 cases) based on the characteristics of patients

| *Variable name* | | *The success of the treatment* | | *Failure& Death* | | *Total* | *P-value* |
|---|---|---|---|---|---|---|---|
| | | No. | % | No. | % | | |
| Sex | Male | 1939 | 85.30 | 334 | 14.7 | 2273 | †<0.01 |
| | Female | 1511 | 88.20 | 202 | 11.8 | 1713 | |
| Marital status | Married | 2093 | 87.87 | 289 | 12.13 | 2382 | †<0.01 |
| | Single | 735 | 91 | 72 | 9 | 807 | |
| | Divorced or widow | 631 | 79.17 | 166 | 20.83 | 797 | |
| Residence | City | 2337 | 82.23 | 373 | 13.77 | 2710 | |
| | Rural and nomads | 1113 | 87.23 | 163 | 12.77 | 1276 | 0.39 |
| Imprisonment status | Imprisonment history | 194 | 92.38 | 16 | 7.62 | 210 | †<0.01 |
| | Non- imprisonment history | 3256 | 86.23 | 125 | 13.77 | 3776 | |
| The history of admission due to tuberculosis | Yes | 1074 | 80.87 | 254 | 19.13 | 1328 | †<0.01 |
| | No | 2301 | 89.67 | 265 | 10.33 | 2566 | |
| | Unknown | 75 | 81.52 | 17 | 18.48 | 92 | |
| HIV | Yes | 98 | 75.97 | 31 | 24.03 | 129 | †<0.01 |
| | No | 2679 | 89.63 | 310 | 10.37 | 2989 | |
| | Unknown | 673 | 77.53 | 195 | 22.47 | 868 | |

Using Chi-square test, a significant statistical difference was observed

**Table 3:** Resistance to drugs of tuberculosis treatment by conventional methods of national laboratory during treatment

| *Drug* | *Total no. of examined cases* | *Total no. (%) of sensitive cases* | *Total no. (%) of resistant cases* |
|---|---|---|---|
| Isoniazid | 942 | 848 (90) | 94 (10) |
| Rifampin | 994 | 932 (93.8) | 62 (6.2) |
| Ethambutol | 826 | 805 (97.5) | 21 (2.5) |
| Streptomycin | 144 | 138 (95.8) | 6 (4.2) |

The average number of close contacts in smear-positive patients was 4.1 adults and 0.54 children. Overall, 2892 children had close contact in which 2522 examined, 1846 received full prophylaxis and 23 children had active TB (18 patients were smear positive) and in 21427 close contact adults, 20245 were examined, 78 received full prophylaxis and 87 person diagnosed as active TB (62 patients were smear positive).

The incidence of positive-smear TB was 5.7/100000 and the total number of types of TB was 11.4/100000. Golestan province with the incidence rate of 35.9, and Sistan and Baluchestan with 34.2 per 100000 had the highest rate and Chaharmahal and Bakhtiari province with 3.06 and Fars province with 3.2/100000 had the lowest incidence (Fig. 1).

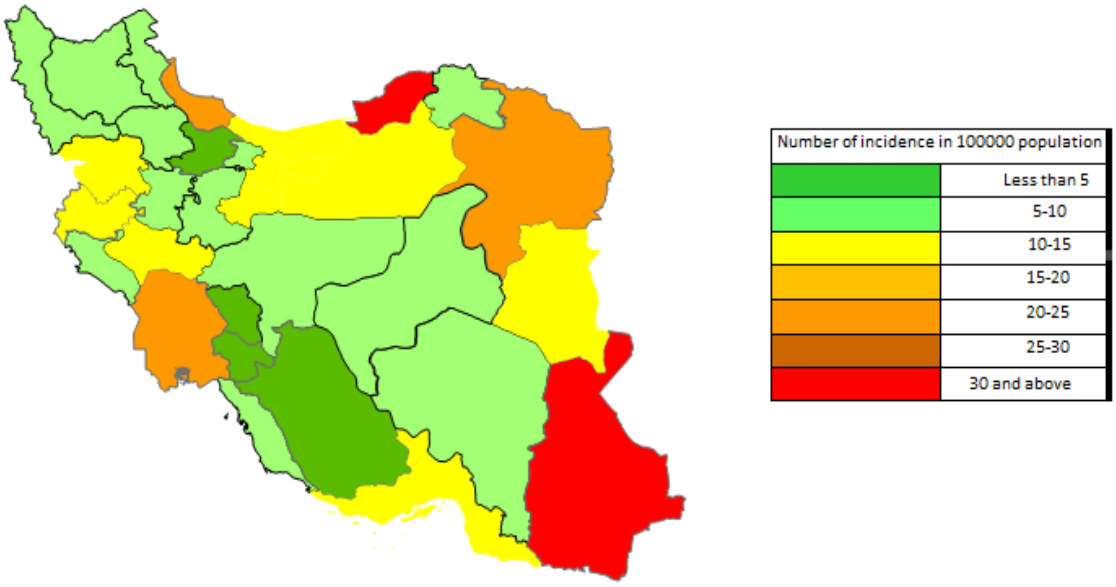


**Fig. 1:** GIS map of the incidence of new cases of tuberculosis in 100 thousand populations in 2016

## Discussion

According to our data, the percentage of female TB patients is 46% and male was 56%, which is consistent with the study in Saudi Arabia and study in Zambia and eight other African societies, and many other studies (8, 9). Sex differences can be explained by the increased social activity of men and the presence in centers and public places with high population densities, and in some studies, difference in the ratio is women even three times as much as men (10). 68.2% of patients aged 14-65 years old, which is the age of economic activity, indicate the high socioeconomic importance of the disease.

The highest non-Iranians TB patients belonged to Afghanistan with 12.6% of all TB patients due to being neighbors with Afghanistan and the high TB incidence over the past several years and it is consistent with the study of Hassanzadeh et al (11). Among the provinces of the country, Golestan province with the incidence of 35.9/100000 population is ranked first, while in previous years, the province of Sistan and Baluchestan was ranked first. Due to the religious similarities between these two provinces and the large migrations from Sistan and Baluchestan province to Golestan due to some reasons, these two provinces are similar in the TB incidence.

In all completed treatment or deceased cases (68148 cases), treatment success was 87.5% and treatment failure was 2.34% which improved the treatment status compared to studies in some parts of the country (12). According to the End-TB Strategy, achieving to the targets need to ≥87% treatment success rate, which Iran has achieved to this target, however it is necessary to maintain this achievement. There was a significant relation between the treatment success rate and gender, HIV status, marital status, history of hospitalization and imprisonment history but there was no significant relation with place of residence which was significantly different from Shahab Rezaian et al. in Hamedan province which can be due to the low number of HIV positive cases studied in Rezaian et al. and the high number of unspecified cases in this study (12).

In comparing with other study, the number of new patients has decreased from 10525 to 9463 cases, which shows a decrease of 10.1% in new cases in 5 years (2% per year) in Iran (11). While achieving the goal of the End TB Strategy, we need to reduce 4-5% of new cases each year (7). In our study, 75.3% of patients were tested for

HIV, but it is far from the WHO's stated goal of examining all patients which is relatively favorable. Expanding the use of Rapid Test kits and raising the public health literacy can be a reason for the relative improvement in the percentage of tested cases. The prevalence of 5.1% of HIV among tested TB patients shows a higher prevalence, which can be seen as a sign of an increase in the prevalence of HIV in the population because of increasing incidence or much survival of HIV patients. But in general, the status of HIV infected patients does not seem to be high compared with other countries, where its incidence among TB patients is 52% (13).

According to the type of referral system, 63.4% of patients were referred by the hospitalization and outpatient units of the health network system. Due to the wide and comprehensive health system in the country and the implementation of the family medical physician in some provinces, it is less than expected and compared to the other study in 2010, it has dropped from 72% to 62% (11). In South India, 39% TB patients were identified by the public sector and 61% by private sectors, which are different from the findings of the present study (10). Perhaps this is due to an increase in insurance cover in our country and willing to be visited by private sectors or delay in diagnosis and led to hospitalization of the patients. The interesting point is the referral of 3.8% of patients with self-introduce to TB centers, which may indicates increased level of public health literacy and public awareness of TB.

BMI is one of the important related variables to TB, and low weights increase the chance of death by 2.14 times (14). In the present study, 43.7% of patients had a BMI less than 18 which in comparison with study in Taiwan with BMI below 18.5 was 25.2%, which has a large difference (14). Malnutrition is a known risk factor for TB and it seems that the high TB incident provinces have high prevalence of malnutrition.

In adults, 94.4% and in children 86.3% of close contacts with smear-positive TB patients have been investigated, and in cases requiring prophylaxis, only 65.3% of adults and 73.6% of children received full period of prophylaxis, indicating a follow-up problem or un-recorded prophylaxis and this issue needs to be studied well.

Delay in TB diagnosis is one of the problems, especially in the smear-positive patients. This delay may lead to spread of the infection. In our study the delay in diagnosis was about two months which is high and differs from the Hui-Ping et al study (15). There was no statistically significant difference in the delay in diagnosis between the private and public sectors, which is consistent with the other study (10). The delay in TB diagnosis should be consider as a serious issue and need to be studied for its reasons.

The percentage of deaths was 7.5% (711 people), of which only 1% (95 people) died directly due to TB, and 517 death cases was attributed to other reasons and 99 cases was unclear cause of death which is in direction of the main goals.

## Conclusion

Despite of the TB treatment success and low prevalence of MDR cases, TB incidence has not been decreased significantly in Iran. Delay in diagnosis, high TB burden in refugees and close contact investigation and prophylaxis are important issues in the TB control program in Iran to be considered in planning.

## Journalism Ethics considerations

Ethical issues (Including plagiarism, informed consent, misconduct, data fabrication and/or falsification, double publication and/or submission, redundancy, etc.) have been completely observed by the authors.

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## Conflict of interest

None to declare

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