



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

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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



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<sup>th</sup>, 2016 to March, 19<sup>th</sup>, 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 ( $\pm 21.6$ ) and 48.10 ( $\pm 20.8$ ) 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

<i>Variable</i>		<i>Number</i>	<i>Percentage</i>
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
Age Group	Unknown	18	0.2
	<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
Education	>65	2779	29.3
	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
Type of disease	Ph.D. specialist and higher	13	0.1
	Pulmonary 6847	5076	53.7
Group therapy	Smear-positive	1771	18.7
	Smear-negative	2616	27.6
	Extra-pulmonary	8688	91.8
	Group therapy 1*	559	5.9
Group of disease record	Group therapy 2**	216	2.3
	Others	8789	92.9
	New	302	3.2
	Relapse	38	0.4
Degree of smear positivity in smear-positive TB at the time of diagnosis	Treatment after absence	334	3.5
	Others	2023	39.9
	+1 and less	1119	22
Patient referral center	+2	1934	38.1
	+3	3544	37.5
	Health network system (subordinate hospitalizing units)	2459	26
	Health network system (subordinate outpatient units)	2162	22.8
	Office – private clinic	356	3.8
	Direct referral of the patient to the tuberculosis center (self-introduce)		

	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 ( $\pm 201$ ) 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 ( $\pm 17.6$ ) 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	0.39
	Rural and nomads	1113	87.23	163	12.77	1276	
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	
HIV	Unknown	75	81.52	17	18.48	92	†<0.01
	Yes	98	75.97	31	24.03	129	
	No	2679	89.63	310	10.37	2989	
	Unknown	673	77.53	195	22.47	868	

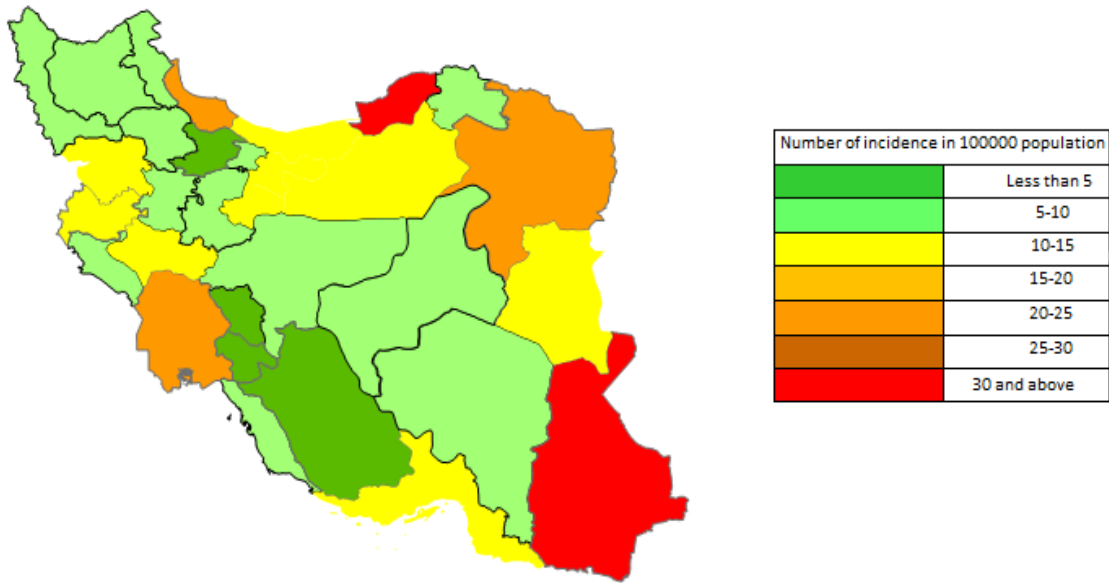
Using Chi-square test, a significant statistical difference was observed

**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 socio-economic 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  $\geq 87\%$  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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