Eleven Year Epidemiological Study of Tuberculosis in Golestan Province, Northern of Iran

Mohammad Reza HONARVAR [1], **Abdurrahman CHARKAZI** [2], ***Kamal MIRKARIMI** [1], **Mahnaz SHEIKHI** [3], **Hamid Reza KAMALINIA** [3], **Elahe RAHIM ARBABI** [3]

1. Health Management and Social Development Research Center, Golestan University of Medical Sciences, Gorgan, Iran
2. Environmental Health Research Center, Golestan University of Medical Sciences, Gorgan, Iran
3. Golestan Province Health Center, Golestan University of Medical Sciences, Gorgan, Iran

Corresponding Author: Email: ak.mirkarimi@gmail.com

Abstract

Background: At present, researchers were aimed at exploring the epidemiology of tuberculosis (TB) in Golestan Province in North of Iran that usually ranks 2nd or 1st, alternatively.

Methods: An epidemiological study of 11 years was carried out over 8405 patients with TB from 2005 to 2014 years. Data were collected from Health System of the Ministry of Health in Iran using a patient- sheet. Descriptive statistics were applied to report the results.

Results: Of those screened, the vast majority of patients with newly diagnosed smear-positive 1799 (41.6%) and smear-positive with relapse 203 (56.5%) were referred from Health System (outpatient cases). Given the newly diagnosed TB, 3559 and 264 of smear-positive were treated and died, respectively; while, 1196 and 119 of smear-negative cases were accordingly treated completely and died.

Conclusion: The vast majority of TB cases are infected by pulmonary TB, educational preventive programs seem likely more useful to control the disease.

Keywords: Outpatients; Preventive health services; Recurrence; Tuberculosis

Introduction

Tuberculosis (TB) accounted for the second leading cause of death and also continues to be a remarkable global public health problem that caused 8.5-9.2 million cases and 1.2-1.5 million deaths across the world in 2010 (1).TB is caused phylogenetically by a group of closely related bacteria, concertedly entitled the Mycobacterium tuberculosis Complex (MTBC) (2). According to WHO and Millennium Development Goals (MDG), the prevalence of TB should be reduced to half of its value in 1990 by 2015 (3).

The case fatality rate in developing countries and global case fatality rate are accordingly 95% and 23% (4). In addition, over 90% of TB cases happen in developing countries, with a remarkable value in economically active age group of 15-54 yr(5). Countries with high TB incidence cited the risk of infection as 30%-50% greater than those indicated in developed countries (6). TB incidence is estimated 4.5, 5, 21, and 365 per 100000 in America, London, Spain, and Africa, respectively (7). However, TB incidence reported 23 per 100000 in Iran (8).

An epidemiological survey will able us to identify the geographic areas and special groups that are likely at higher risk of TB that, in final, provide

adequately us with necessary information to consider a plan for reducing morbidity and mortality of TB (7).

Thus, we sought to investigate the registered cases of TB between 2005 to 2016 years with a special interest in its epidemiology that may provide Health System with vital information to achieve their goals of TB control.

Materials and Methods

Study design and procedure
A retrospective survey of routinely collected data by Health System of the Ministry of Health in Iran was implemented. All newly diagnosed cases of TB routinely report by different cities of the province and register in the Iranian Health System in an online form. The hierarchy of TB reporting process is as follows: from the Rural Health Centers (Health Houses) and Urban Health Centers (Health Posts) to District Health Center, and finally to District Health Network.

Data Instrument
TB routinely registered data of study was used in the TB registry system of District Health Network. Data was extracted from TB online registry system.

Variables definition
Pulmonary TB categorized in subgroups of smear-positive (newly diagnosed and relapse), newly diagnosed of smear-negative, newly diagnosed of smear unknown, treatment after failure and treatment after default, as well as extra-pulmonary, MDR and other. According to Health System Network, all TB cases considered as five year age groups.

Data Instrument
All data of TB archived in the District Health Network registry system was assessed. At present, TB data are routinely registering and reporting to the higher level of Health System of Iran. Since all TB data finally reported to the Health System; therefore, accurate information exists to analysis.

Data analysis

To analyze, descriptive statistics were applied to present the mean and standard deviation of variables. Of course, a graph was used to show the Health System Structure in Iran.

Results

Overall, 8405 patients with TB were assessed from 2005 to 2014 years. The mean age of cases was 46.47 yr aged <1 to 99 yr old. In the cases of newly diagnosed pulmonary TB cases with positive smear culture, relapse cases of pulmonary TB with positive smear culture and newly diagnosed pulmonary TB cases with negative smear culture, the most TB cases were found in the age group of >65 yr. Moreover, newly diagnosed cases with extra-pulmonary TB were frequently observed in the age group of 25-34 yr (Table 1).

Given the newly diagnosed TB, 3559 and 264 of smear-positive were treated and died, respectively; while, 1196 and 119 of smear-negative were accordingly treated completely and died. Overall, 803 and 1113 of newly diagnosed patients with TB were male and female; while, in terms of retreated TB cases, in a conversely form, 546 and 446 were male and female, correspondingly (Table 2). From history of hospitalization point of view, 873 (24.3%) of pulmonary smear-positive and 327 (28.4%) of pulmonary smear-negative had a history of hospitalization. According to contact history, most TB cases 886 (16.8%) had a history contact of < 2 yr (Table 3). Most cases with co-infection of HIV+ and TB were aged >15 yr in the two groups of newly diagnosed smear-positive 13 (0.3%) and newly diagnosed of smear-negative 11 (0.8%) (Table4). The vast majority of patients with newly diagnosed with smear positive 1799 (41.6%) and smear-positive with relapse 203 (56.5%) were referred from Health System (outpatient from). Mostly, self-referred cases, Social Security organization, private department and military section had the lowest role in referring TB cases such that no MDR cases were referred from these aforementioned organizations or sections.

Table 1: Status of pulmonary and extra-pulmonary TB cases based on age groups and gender in Golestan Province, Iran

Pulmonary TB															Extra-pulmonary			Total		
Smear positive sputum						Smear negative sputum			Smear unknown sputum											
Newly diagnosed cases			Relapse cases																	
Male	Female	Total	Male	Female	Total	Male	Female	Total	Male	Female	Total				Male	Female	Total	Male	Female	Total
2181	2139	4320	196	163	359	684	688	1372	265	253	518				761	1075	1836	4087	4318	8405

Newly diagnosed pulmonary TB cases with positive smear culture

Age group	0-4	5-9	10-14	15-24	25-34	35-44	45-54	55-64	>65	Total
Male	4	2	5	214	425	283	310	316	622	2181
Female	4	6	36	401	261	163	231	374	663	2139
Total	8	8	41	615	686	446	541	690	1285	4320

Relapse cases of pulmonary TB with positive smear culture

	0-4	5-9	10-14	15-24	25-34	35-44	45-54	55-64	>65	Total
Male	0	0	0	10	29	31	31	26	69	196
Female	0	0	1	15	12	13	17	49	56	163
Total	0	0	1	25	41	44	48	75	125	359

Newly diagnosed pulmonary TB cases with negative smear culture

	0-4	5-9	10-14	15-24	25-34	35-44	45-54	55-64	>65	Total
Male	3	7	8	45	104	83	92	124	218	684
Female	5	9	16	81	74	61	91	164	188	688
Total	8	16	24	126	178	144	183	288	405	1372

Newly diagnosed pulmonary TB cases with unknown smear culture

	0-4	5-9	10-14	15-24	25-34	35-44	45-54	55-64	>65	Total
Male	94	24	2	17	28	18	17	18	45	265
Female	72	15	8	41	28	6	12	28	42	253
Total	166	39	10	58	56	24	29	46	87	518

Newly diagnosed cases with extra-pulmonary TB

	0-4	5-9	10-14	15-24	25-34	35-44	45-54	55-64	>65	Total
Male	15	10	14	110	161	116	104	90	141	761
Female	11	12	32	183	328	196	121	99	92	1075
Total	26	22	46	293	489	312	225	189	233	1836

Table 2: Total status of newly diagnosed and Retreatment for TB cases in Golestan Province, Iran

Total number of TB cases			Type of TB	Treated	Completed treatment	Dead due to				Failure in treatment	Default in treatment	Immigrated		Other	Fault in diagnosis	Unevaluated
						TB	other	Unknown	total			In	Out			
Male	Female	Total								Newly diagnosed TB						
2193	2150	4343	SP	3559	127	77	151	36	264	294	38	24	3	2	23	9
712	722	1434	SN	0	1196	11	83	25	119	24	28	4	0	0	62	1
273	257	530	SU	3	448	7	29	11	47	9	8	2	0	0	12	1
803	1113	1916	EP	0	1660	23	62	20	105	1	24	16	1	2	80	27
Male	Female	Total								Retreatment						
199	165	364	R	296	12	17	15	2	34	8	2	2	0	1	5	4
9	1	10	TD	8	0	0	0	0	0	0	2	0	0	0	0	0
194	119	313	FT	252	11	4	2	3	9	17	9	2	0	2	9	2
20	9	29	MDR	13	3	0	2	0	2	0	1	1	0	0	1	8
124	142	266	Other	7	209	4	10	2	16	1	7	2	1	2	17	4
546	446	982	Total	576	235	25	29	7	61	26	21	7	1	5	32	18

SP: Smear Positive
SN: Smear Negative
SU: Smear Unknown
EP: Extra-pulmonary
R: Relapse
TD: Treatment after Default
FT: Failure in Treatment

Table 3: History of hospitalization and contact in patients with TB in Golestan Province, Iran

Type of TB	History of hospitalization					
	No		Yes		Unknown	
	N	%	N	%	N	%
Pulmonary smear positive	2699	75	873	24.3	27	0.8
Pulmonary smear negative	816	70.8	327	28.4	10	0.9
Newly diagnosed of pulmonary smear unknown	367	79.8	92	20	1	0.2
Newly diagnosed of extra-pulmonary TB	980	61.9	579	36.6	23	1.5
Relapse	233	79.3	51	17.3	10	3.4
Treatment after failure	221	87.4	32	12.6	0	0
Treatment after default	7	87.5	0	0	1	12.5
Other	153	70.5	62	28.6	2	0.9
MDR	7	28	18	72	0	0
Total	5483	71.5	2034	26.5	74	1
	History of contact					
	N			%		
No/ unknown	3515			66.7		
Yes < 2 yr	886			16.8		
2-5 yr	290			5.5		
> 5 yr	576			10.9		
Total	5267			99.9		

Table 4: Co-infection of HIV and TB in patients with TB in Golestan Province, Iran

Type of TB	N	HIV+				HIV-				Unknown HIV			
	`	≤15	>15	total	%	≤15	>15	total	%	≤15	>15	Total	%
Newly diagnosed of smear positive	4320	0	13	13	0.3	7	537	544	12.6	79	3684	3763	87.1
Newly diagnosed of smear negative	1372	0	11	11	0.8	4	78	82	6	49	1230	1279	93.2
Newly diagnosed of smear unknown	518	0	3	3	0.6	4	6	10	1.9	217	288	505	97.5
Newly diagnosed of extra-pulmonary	1836	0	3	3	0.2	6	147	153	8.3	110	1570	1680	91.5
Relapse	359	0	1	1	0.3	0	41	41	11.4	2	315	317	140.7
Treatment after default	10	0	0	0	0	0	2	2	20	0	8	8	80
Treatment after failure	304	0	2	2	0.7	0	40	40	13.2	1	261	262	86.2
MDR	28	0	0	0	0	1	11	11	39.3	0	17	17	60.7
Other	249	0	0	0	0	0	12	12	4.8	7	230	237	95.2
Total	8996	0	33	33	0.4	22	873	895	9.9	465	7603	8068	89.7

Discussion

At present survey, the mean age of patients was 46.47 yr. In Iran, mean age of 41 and 44.3 yr were reported for TB cases, respectively (9, 10). Age group of >65 yr stated the highest frequency in pulmonary TB cases that may also purpose the effect of decreased immunity in the lungs in the elderly.

In dealing with type of TB, around 50% of cases were positive smear TB associated with a survey (9) reported 52% of sputum smear-positive. At present, newly detected TB was higher among women than men; while, men reported higher frequency in retreatment than women. In a meta-analysis (10) over 56 TB prevalence studies on 2.2 million patients in 28 countries, TB prevalence is higher among men than women. These differences may be likely caused by the fact that

most of women, in Golestan Province, are lived in rural areas and also are housewife that forced them to spend most of their time at houses with poorly provided health that likely expose them to TB. Moreover, according to health care facilities focusing mostly on women and children, men are usually inaccessible in the Health System of Iran compared to the two aforementioned groups that may interfere with following health care by men. In a survey run in north of Iran, 55.1% and 44.9% of subjects were lived respectively in village and city(11). Given the documents, men are low well-providedby health services than women (12, 13). Male patients with TB usually postpone health care longer than female patients(14).

Most of TB cases are infected by pulmonary TB associated with study conducted in Saudi Arabia (1) and a survey carried out in Iran that indicated that the ratio of smear-positive TB to smear-negative and extra-pulmonary TB was 1.46 (15). In a study conducted in the Golestan Province, 52% of cases were new smear-positive cases (16). Moreover, another study implemented in the Golestan Province reported 62.7% of cases were smear-positive (17). In Iran, smear-positive TB was 8.76% compared to extra-pulmonary TB 5.76%(18). While, in some studies, patients were usually contaminated with extra-pulmonary TB (19, 20). To compare extra-pulmonary TB based on gender, similar results were observed between the present study and study conducted by Rafiee et al in North of Iran with a predominance in females (16).

As we screened, 33 persons had a co-infection of Human Immunodeficiency Virus (HIV) and TB. Additionally, all co-infection cases aged higher than 15 yr that obviously indicated the inconsiderable role of mother-to-child transmission. Moreover, all infection caused by contaminated syringes and unsafe sexual relationships as have widely been cited by numerous studies in Iran (21-23). Advanced HIV infection is related to the greatest relative risk of re-activation that means that a risk of 10 times than individuals without HIV, approximately (24, 25). Overall, HIV infection effectively treated by antiretroviral therapy, afflicted only by 20% of the TB risk which is in line with untreated HIV infection (26). Thus, treatment of latent TB infection is required and necessary for all HIV patients with TB.

The maximum percent of hospitalization observed in MDR (72%) and pulmonary smear-negative (28.4%). A few days of hospitalization for pulmonary smear-negative and positive might be likely caused by the starting treatment immediately and considerable recovery consequently; while MDR cases need longer hospitalization due to the importance of bacterial resistance.

According to referring status, the highest and lowest number of TB cases were referred to Health System (outpatient unit) 1799 (41.6%) and military section 7 (0.2%). In North Khorasan Province of Iran, the same results reporting 155 (38.7%) in Health System (outpatient unit) and 2 (0.4%) in Health unit of military section and prison (27). These refer might be explained by the fact that majority of cases lived in rural area that routinely and easily have access to health services.

Conclusion

Since TB known as a communicable disease, providing individuals with useful information in terms of prevention, diagnosis, and treatment appeared to be likely useful.

Ethical 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.

Acknowledgements

Conflict of interests

The authors declare that there is no conflict of interests.

References

1. Memish ZA, Bamgboye EA, Abuljadayel N et al (2014). Incidence of and risk factors associated with pulmonary and extra-pulmonary tuberculosis in Saudi Arabia (2010–2011). *PLoS One*, 9(5): e95654.

2. Dabernat H, Thèves C, Bouakaze C et al (2014). Tuberculosis Epidemiology and Selection in an Autochthonous Siberian Population from the 16 th-19 th Century. *PLoS One*, 9(2):e89877.

3. WHO, Strategic and Technical Advisory Group for Tuberculosis (STAG-TB): report of the tenth meeting. Geneva: World Health Organization, 2010 http://www.who.int/tb/advisory_bodies/stag_tb_report_2010.pdf (Accessed 1 December 2010)

4. Waheed M (2014). Tuberculosis in Children Attending Outpatient Clinic and Compliance to Treatment. *Pak J Med Res*, 53(4):79-83.

5. Beiranvand R, Ghalavandi S, delpisheh A et al (2014). Epidemiological investigation of Tuberculosis in Ilam province between 2005-2011. *Journal of Ilam University of Medical Sciences*, 21(7):1-8.

6. Nakaoka H, Lawson L, Squire B et al (2006). Risk for tuberculosis among children. *Emerg Infect Dis*, 12(9):1383-8.

7. Beiranvand R, Karimi A, Delpisheh A et al (2016). Correlation Assessment of Climate and Geographic Distribution of Tuberculosis Using Geographical Information System (GIS). *Iran J Public Health*, 45(1):86-93.

8. Jabbari Sh (2007). Statistic department of Markazi health center. *Sci J Arak Uni Med Sci*, 4-14.

9. Kunkel A, zur Wiesch PA, Nathavitharana RR et al (2016). Smear positivity in paediatric and adult tuberculosis: systematic review and meta-analysis. *BMC Infect Dis*,16:282.

10. Horton KC, MacPherson P, Houben RM, et al (2016). Sex Differences in Tuberculosis Burden and Notifications in Low-and Middle-Income Countries: A Systematic Review and Meta-analysis. *PLoS Med*, 13(9):e1002119.

11. Mohammadzadeh KA, Ghayoomi A, Maghsoudloo D (2016). Evaluation of factors associated with failure of tuberculosis treatment under DOTS in northern Islamic Republic of Iran. *East Mediterr Health J*, 22(2):87-94.

12. Lim SS, Vos T, Flaxman AD et al (2012). A comparative risk assessment of burden of disease and injury attributable to 67 risk factors and risk factor clusters in 21 regions, 1990–2010: a systematic analysis for the Global Burden of Disease Study 2010. *Lancet*, 380(9859):2224-60.

13. Wang H, Dwyer-Lindgren L, Lofgren KT et al (2012). Age-specific and sex-specific mortality in 187 countries, 1970–2010: a systematic analysis for the Global Burden of Disease Study 2010. *Lancet*, 380(9859):2071-94.

14. Van den Hof S, Najlis CA, Bloss E, Straetemans M. A systematic review on the role of gender in tuberculosis control. Report prepared for Tuberculosis Control Programme (TB CAP) September. 2010.

15. Khazaei HA, Rezaei N, Bagheri GR et al (2005). Epidemiology of tuberculosis in the Southeastern Iran. *Eur J Epidemiol*, 20(10):879-83.

16. Rafiee S, Besharat S, Jabbari A, Golalipour F, Nasermoaadeli A (2009). Epidemiology of tuberculosis in northeast of Iran: a population-based study. *Iran J Med Sci*, 34(3):193-7.

17. Salek S, Salek S, Emami H et al (2008). Epidemiologic status of tuberculosis in Golestan province. *Tanaffos*, 7(3): 63-68.

18. Taghizadeh Asl R, Mohammad K, Majdzadeh R (2005). Seasonality pattern of Tuberculosis in Iran. *Journal of School of Public Health and Institute of Public Health Research*, 3(2):1-9.(in Persian)

19. Al-Otaibi F, El Hazmi MM (2010). Extra-pulmonary tuberculosis in Saudi Arabia. *Indian J Pathol Microbiol*, 53(2):227-231.

20. Abouzeid MS, Zumla AI, Felemban S et al (2012). Tuberculosis trends in Saudis and non-Saudis in the Kingdom of Saudi Arabia– a 10 year retrospective study (2000–2009). *PLoS One,* 7(6):e39478.

21. 21.Salehi L, Salehi F, Shakibazadeh E (2009). Education-based needs assessment: a step toward effective prevention of AIDS. *J Qazvin Univ Med Sci*,13(1):73-8.

22. Lotfi PRS, Ravari A, Akbarinasab J (2011). Knowledge, attitude and practice of non-medical students to the ways of transmission

and prevention of AIDS in Rafsanjan city. *Iranian Journal of Nursing Research*, 6(22): 31-39.

23. Ilami O, Sarkari B, Khosravani A, Tori MA, Hosseini Z (2012). HIV seroprevalence among high-risk groups in Kohgiloyeh and Boyerahmad Province, Southwest of Iran, a behavioral surveillance survey. *AIDS Behav*, 16(1):86-90.

24. Corbett EL, Churchyard GJ, Clayton TC et al (2000). HIV infection and silicosis: the impact of two potent risk factors on the incidence of mycobacterial disease in South African miners. *AIDS*, 14(17):2759-68.

25. Jones JL, Hanson DL, Dworkin MS, DeCock KM (2000). HIV-associated tuberculosis in the era of highly active antiretroviral therapy. *Int J Tuberc Lung Dis*, 4(11):1026-31.

26. Horsburgh CR Jr (2004). Priorities for the treatment of latent tuberculosis infection in the United States. *N Engl J Med*, 350(20):2060-7.

27. Shoraka H HS, Alizade H, Alavinia SM (2011). Epidemiology of tuberculosis and its related factors in North Khorasan Province during 2005 to 2010. *Journal of North Khorasan University of Medical Sciences*, 3(3):43-50.