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Epidemiological Survey of Children with Tuberculosis in Iranian Population: a retrospective descriptive study of 9-Years

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Abstract: Background: Tuberculosis in children is significantly being considered as a main public health problem that contributes to the total global burden of disease. This survey sought to explore children with tuberculosis in Iranian population. Methods: A survey of nine years was conducted on 592 children with tuberculosis from 2005 to 2013 years. Data were extracted from the District Health Network (TB register software) on the basis of a sample- sheet that was evaluated by two experts. Mean and standard deviation were used to describe data of the study. Moreover, chi-square statistical test was run to assess differences between variables such as year, gender, season, place of residence and nationality in terms of TB disease. A significance level was considered less than 0.05. Results: The mean age of children was 5.96±9.94 year. The prevalence of the disease in girls (63.5%) was significantly higher than boys (36.5%)(p=0.001). Contrary to expectation, the season did not play a significant role in the prevalence of the disease (p=0.102). The vast majority of subjects 424 (74.67%) were positive smear. Pathologic findings cited that 30 (5.1 %) of cases were positive. Most of cases 354 (59.8%) were referred to the Primary Health Care system to begin the treatment of tuberculosis. In final, there was a significant difference between gender (p=0.001), place of residence (p=0.001) and nationality (p=0.001) about disease. Conclusion: Place and ethnicity reported as remarkable risk factors of Tuberculosis. Therefore, social and economic determinants of health factors must seriously be diagnosed and improved.

Keywords: Child, Ethnicity, Public Health, Tuberculosis

INTRODUCTION

Tuberculosis (TB) in children is remarkably being considered as a crucial public health problem that significantly contributes the total global burden of tuberculosis (1). It is stated that children represent 15-20% of the disease burden in the epidemic region that TB is poorly controlled (2).

TB remains a remarkable challenge in many low and middle-income countries across the world in spite of improvements in the prevention and control strategies (3). Children are usually at increased risk of developing crucial disease because of decreased ability of their immune system to cope with infection (4).

TB easily develops among children compared to adults. Adults and their family members are commonly the origin of infection (5). It is well-documented that 30 to 50% of household contacts of adults with TB cause infection. Children less than one year (young children) with untreated infection are at increased risk of TB up to 43% and approximately 24% for children aged one to five years (6).

The incidence rate of TB began to decrease in Iran around 40 years ago. In 1963, 142 cases per 100 000 suffered from TB, but recently a decline of 10-fold happen approximately, resulting in an incidence rate of 13.9 per 100 000. However, this decreasing trend was very slow in some areas, that indicated different patterns of the disease. In 1998 and 2005, Iran had an incidence and prevalence rate of 17.9 and 6.8 per 100 000, respectively. While, given a WHO report, 12 Iranians per 100 000 suffered from TB (7). According to the latest report of WHO, the total TB incidence in the Eastern Mediterranean reported 115 per 100, 000 (8).

The Golestan province is located in northeastern Iran, south of the Caspian Sea. This province has been suffering from infectious diseases, resulted from its ethnic diversity and geographic location. The prevalence of TB in Sistan and Baluchestan, Golestan and Khorasan provinces was reported as 44, 38 and 25 per 100 000, respectively, whereas the prevalence in the central part of Iran is lower. Golestan province is ranked second in terms of TB prevalence after Sistan and Baluchestan province (9). According to a study conducted in the Golestan province, the incidence and prevalence of TB were 20.88 and 38.15 per 100 000, accordingly (9). Children introduce as an important marker of ongoing transmission and failing of TB control in a country; therefore, diagnosing risk factors for infection and disease in children is vital in order to control and prevent the larger epidemic (10). Individuals usually fail to use health care for TB associated complications as infected cases with TB are not symptomatic in the early stages (11). Hence, strategies of active case finding are necessarily required to diagnose and treat TB patients that are not detected using the current passive approach (3).

Recently, numerous investigations have brought remarkable attention to the global burden of TB in children such that the World Health Organization (WHO) presents their first evaluation of the global burden of childhood TB (12). TB diagnosis remains yet complex and also challenged by methods being inaccessible in developing regions (13).

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Therefore, the current survey was aimed to investigate the epidemiological status of children with TB contact in the Iranian city of Golestan.

METHODS

Study design and procedure

A retrospective descriptive study was conducted over a period of nine years on 592 children with TB contact between April 2005 and April 2013 years. The project protocol was granted by number of IR.GOUMS.REC.1396.25. In the Iranian Health System, a TB active registry system is routinely performing such that all new diagnosed cases report by different cities of the province, refer and record in the registry system located in the Golestan District Health Network. Given the (figure 1), data reporting process is accordingly as follows: from the Rural Health Centers (Health Houses) and Urban Health Centers (Health Posts) to the District Health Center, and finally to the District Health Network. The inclusion criteria were as follows; children aged 0-18 years diagnosed as TB during 2005 to 2013 years, cases referred to the health system of the Iranian country, and lived in the Golestan province. There was no exclusion criterion as all information of TB patients is carefully collecting in the health system.

Data Instrument

Considering the importance and high prevalence of tuberculosis in Iran and especially in Golestan province, data of the disease are recorded and reported regularly for health planning and policies in a software named TB registry software. In fact, archived data in the District Health Network registry system (TB register software) extracted and analyzed. According to the national tuberculosis control program, the provincial health system is obliged to provide medicines services to patients. Since all of them attended to government centers, there was practically no possibility of losing samples due to referring to other centers. As mentioned above, the current data represent all children with tuberculosis in the Golestan province (urban and rural areas).

In order to extract data, a sample- sheet was designed and developed based on the comments of two experts comprising a physician and an expert in disease control. This check list consisted of four general categorizations, including: a) general and demographic status (nationality, seasons, gender, age and etc), b) type of pulmonary and extra-pulmonary, c) method of diagnosis (acid fast bacilli sputum, sputum culture, and etc), and d) information about health system and outcomes (outcome of treatment, referral system, and etc).

Variables definition

According to the place of living, participants were categorized into urban and rural area. Cases of TB classified as follows; new diagnosed cases (a case diagnosed for the first time), standard treatment protocol (patients with positive smear test five months after failure in treatment or cases with negative smear test at the beginning of the treatment that changed in positive two months after treatment following failure), no laboratory (patients with an unknown smear history or extra-pulmonary). Iranian and non-Iranian cases considered for nationality. According to guidelines of Iranian Ministry of Health (14), results of smear test categorized into +1, +2, +3, a few (1-9), negative smear test and without laboratory tests. In terms of chest x-ray, results explained by the less, more and non suggestive cases (guidelines of Iranian Ministry of Health). Outcomes of the treatment classified as follows; completed treatment, dead, default, failure in treatment, healed, under treatment procedure, mistake diagnosis, migrated out and other (14). According to the Iranian treatment protocol of TB, patients diagnosed as negative smear or extra-pulmonary that not treated after drug consumption, moreover, in the positive sputum culture with non-mycobacterial growth, the treatment process is interrupted and considered as a mistake in diagnosis. Also, confirmed TB cases were as follows: Acid fast bacilli in sputum (s+, s++, s+++ and a few), Sputum culture for Mycobacterium tuberculosis complex (positive cases), Pathologic findings (positive) and Chest x-ray (more suggestive).

Data analysis

Descriptive statistics were utilized to present the mean and standard deviation of variables. In addition, chi-square statistical test was run to assess differences between variables such as year, gender, season, place of residence and nationality in terms of TB disease.

RESULTS

Majority of TB cases were found in 2012 year 98 (16.6%). Chi-square test showed a statistically significant difference between years of the study (p=0.001). The mean age of children was 9.94 ± 5.96 ranged 1> year to 17 years. Of those screened, 376 (63.5%) were female. In general, 159 cases aged < 5 years that 128 of them had family contact. The Chi-square test indicated a remarkable difference between gender (p=0.001), place of residence (p=0.001) and nationality (p=0.001) about TB disease. Although, contagion with TB was different statistically based on the years of the study, but this difference is not noteworthy. Trend of TB during nine years is revealed in (table 1). Chi-square and Fisher exact test indicated that except for seasons, other demographic variables had statistically significant differences.

Table (1): Demographic characteristics of children with TB.

Variables		Frequency	Percent	P-value (chi-square)
Years	2005	56	9.5	0.001✷
	2006	45	7.6	
	2007	68	11.5	
	2008	56	9.5	
	2009	81	13.7	
	2010	51	8.6	
	2011	73	12.3	
	2012	98	16.6	
	2013	64	10.8	
	Total	592	100	

Variables		Frequency	Percent	P-value (chi-square)
Seasons	Spring	161	27.2	0.102
	Summer	146	24.7	
	Autumn	124	20.9	
	Winter	161	27.2	
	Total	592	100	
Gender	Male	216	36.5	0.001✷
	Female	376	63.5	
	Total	592	100	
Place of residence	Rural	382	64.5	0.001✷
	Urban	210	35.5	
	Total	592	100	
Nationality	Iranian	571	96.5	0.001✷
	Non-Iranians	21	3.5	
	Total	592	100	
Age		Mean	Standard deviation	
		9.94	5.96	

Results show that 424 (74.67%) were positive smear. Moreover, given the extra-pulmonary TB, lymph nodes 53 (9%) and larynx 1 (0.2%) were respectively the most common and the rarest organs afflicted by the TB. According to Chi-square test, cases of pulmonary and extra-pulmonary was remarkably different (p=0.001). Moreover, in terms of extra-pulmonary tuberculosis, fisher exact test presented that type of tuberculosis was statistically different (p=0.001) (Table 2).

Table (2): Type of pulmonary and extra-pulmonary TB among children.

Type of tuberculosis		Frequency	Percent	P-value (within group)	P-value (between group)
Pulmonary		**424**	**74.67**	0.001*	0.001*
Extra-pulmonary	Bone	11	1.9		
	Central nervous system	10	1.7		
	Ears	2	0.3		
	Genital	3	0.5		
	Gastro-intestinal tract	7	1.2		
	Larynx	1	0.2		
	Lymph nodes	53	9		
	Meningitis	9	1.5		
	Miliary	7	1.2		
	Peritoneum	8	1.4		
	Pleura	30	5.1		
	Skin	9	1.5		
	Total	150	25.33		

Chi square/ Fisher exact test*

According to (table 3), most of cases 59 (10%) were smear +++. Chest x-ray also stated that 199 (33.6%) were more suggestive. Furthermore, pathologic findings cited that 30 (5.1 %) of cases were positive. According to the methods of diagnosis, chi-square/fisher exact test showed significant statistical difference regarding acid fast bacilli in sputum, pathologic and chest x-ray (p=0.001) as well as sputum culture for mycobacterium tuberculosis complex (p=0.036).

Table (3): Children with TB based on methods of diagnosis.

Results of tests		Frequency	Percent	P-value
Acid Fast Bacilli in sputum	S+	51	8.6	0.001*
	S++	44	7.4	
	S+++	59	10	
	A few (1-9)	11	1.9	
	Negative	93	15.7	
	No laboratory test	334	56.4	
	Total	592	100	
Sputum culture for Mycobacterium tuberculosis complex	Negative	20	3.4	0.036*
	Positive	30	5.1	
	Total	50	8.5	
Pathologic	Positive	30	5.1	0.001**
	Suspicious	1	0.2	
	Total	31	5.3	
Chest x-ray	Less suggestive	89	15	0.001*
	More suggestive	199	33.6	
	Non-suggestive	23	3.9	
	Total	311	52.5	

*Chi-square

**Fisher exact test.

4. Outcomes of treatment, causes of death, referral status and hospital admittance in children with tuberculosis.

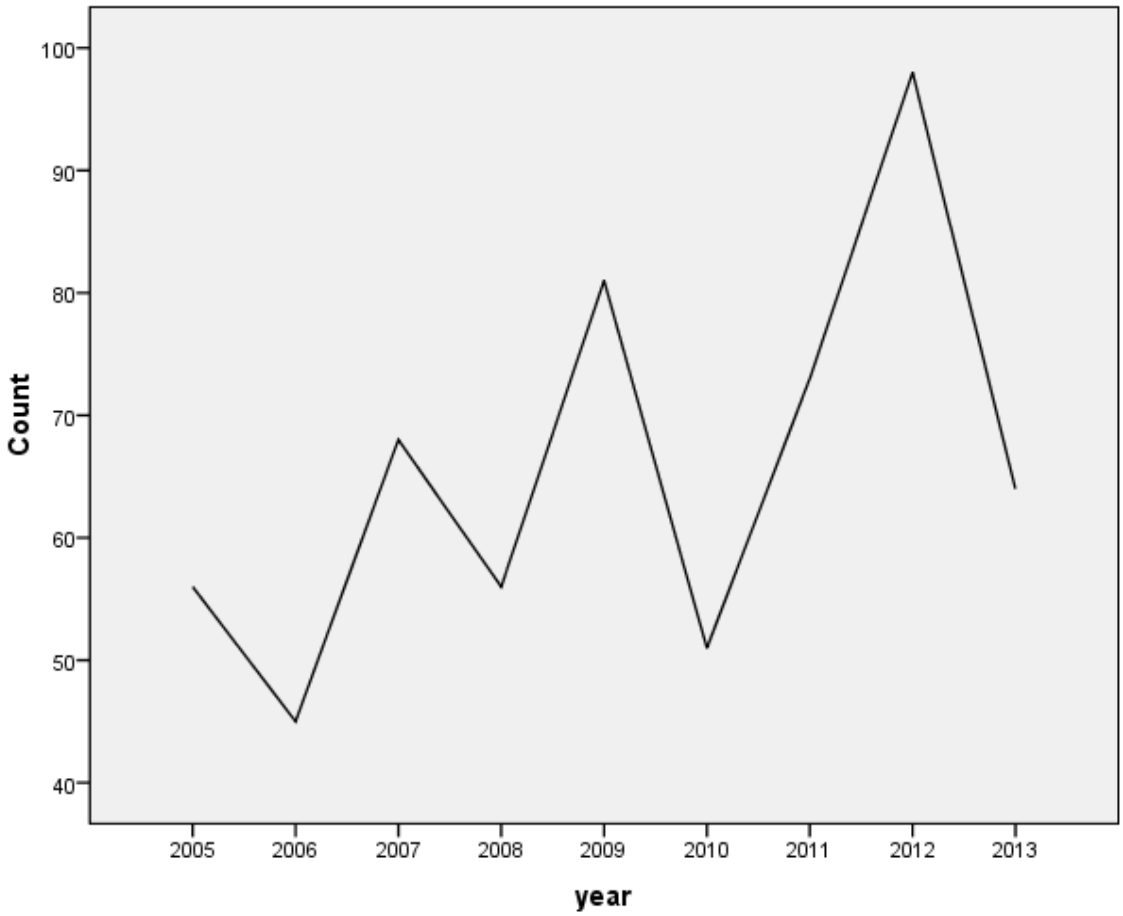
Variables		Frequency	Percent	P-value
Outcomes of treatment	Completed treatment	368	62.2	0.001*
	Dead	12	2	
	Default	3	0.5	
	Failure in treatment	7	1.2	
	Healed	144	24.3	
	Under treatment	34	5.7	
	Mistake diagnosis	14	2.4	
	Immigrated out	9	1.5	
	Others	1	0.2	
	Total	592	100	
Cause of death	TB	2	0.3	0.048
	Other	6	1	
	Unknown	3	0.5	
	Total	11	1.8	
Referral status	Auto-referring TB center	1	0.2	0.001*
	Primary health care system	354	59.8	
	Private office	125	21.1	
	Social Security organization	1	0.2	
	Other	111	18.8	
	Total	592	100	
Hospital admittance Status	Yes	389	65.7	0.001*
	No	99	16.7	
	Unknown	104	17.6	
	Total	595	100	

*Fisher exact test.

With regard to the outcomes of the treatment, in overall, 368 (62.2%) completed the treatment process. While, 12 (2%) lost in the treatment process because of default 3 (0.5%) and immigration out 9 (1.5%). The vast majorities of cases 354 (59.8%) were referred to the Primary Health Care (PHC) system to begin the treatment of TB. In total, 555 (93.8%) of children with TB were the new cases. Plus, 6, 5 and 1 cases were respectively failure in treatment, relapse and MDR. Medical factors 1 (0.2%)

and migration 1 (0.2%) were the reasons of the default cases. In the hospital admittance status point of view, majority of cases 389 (65.7%) had not a history of admittance. In final, the average of period of hospital admittance was 6.5 ± 1.88 ranged 0 to 90 days. Chi-square/fisher exact test indicated a remarkable statistical difference about outcomes of treatment and referral status (p=0.001) and cause of death, as well (p=0.048) (table 1).

As indicated in (Graph 1), the TB cases were gradually increasing with the lowest and highest frequency in 2005 and 2012 years, respectively.



DISCUSSION

At present survey, females were more afflicted by TB compared to male children that is associated with Salak et al survey (15) conducted on children aged 0-14 years. In a study implemented in Cambodia among children, prevalence rate of positive smear pulmonary TB was higher in females aged 10 to 14 years than males (16) that might be likely caused by the effect of maturation process and hormonal factors. However, aforementioned status is different in developed countries reporting the higher incidence among men than women (15). Additionally, in Iranian country as a traditional country, girls usually work and play at home, therefore, they may be at higher risk of contagion than boys.

In a review article carried out by Metanat et al (17), 14 % of TB cases were not Iranian; while, in the current survey, only 3.5 % was non-Iranian. In another exploration (18), 17.5 % of TB cases were non-Iranian. It might be caused by the fact that, at present, children were not able to move rapidly similar to adults that usually assessed by other studies; therefore, they have less chance to consequently be contaminated.

Given the findings, more than half of children (64.5%) were lived in the rural area. In a population tested by Farazi et al (18), 46.9% lived in the rural area that is not in accordance with the present survey. In overall, most studies (19-21) stated that TB is more common in the urban areas than the rural areas. This may be resulted by the fact that rural areas accounted a remarkable population ratio in Golestan province compared to other areas of country because of fertile land for agriculture. According to the provincial statistics more than half (51%) of the population of Golestan are villagers.

At present, TB was more common in the season of spring and winter. In Taghizadeh et al (22) study aimed at exploring the seasonality pattern of TB, disease more occurred in the spring that is in relevance with our study results. Douglas et al indicated winter as the most important season (23) of TB incidence. In cold seasons, people tend to sit near a heater or heating source and gather in a closed place without proper ventilation that probably puts them at greater risk.

In the current investigations, pulmonary TB was 74.67 %. Extra- pulmonary TB was 25.33 % in the explored children reporting lymph nodes as the most common extra-pulmonary TB. In a five-year study carried out in Iranian city of Zahedan (24), 23.2% of TB cases had extra-pulmonary TB (lymph nodes as the highest extra-pulmonary TB) that is similar to the current survey. Study undertaken on children aged less than 18 years,

reported prevalence of extra-pulmonary TB as 23% and lymph nodes and pericarditis as the most and lowest affected organs with TB (25, 26). Farazi et al (18), in a study of ten-year comparing the pulmonary with extra-pulmonary TB found that extra-pulmonary TB prevalence was 24.2 % that is partly in relevance with our survey. They also presented lymph nodes TB as the prevalent extra-pulmonary TB. According to type of organs affected in extra-pulmonary TB, Sofian et al (27) study reported lymph nodes and larynx as the most common and rarest organs as the same as our survey.

According to Acid Fast Bacillus in sputum, 10 % of cases were smear +++. In a study conducted by Shoraka et al (28), the aforementioned status was 44.7% that is different with the present study; while, in terms of 1-9 bacillus item, there is the same results, 1.58% compared to 1.9% in our study. The vast majority of cases (334) had no laboratory test. It seems usual because of children TB diagnosis method that done by using of family history of contact, gastric juice test and chest X-ray.

The same findings found in the Sofian et al (27) exploration such that they reported treatment completed, default, failure in treatment, and immigrated out as 86.2%, 0.5%, 1.9% and 1.6% compared to our survey as 62.2%, 0.5%, 1.2% and 1.5%. In addition, 56.4%, 8.5% and 5.3% of cases diagnosed respectively by the Acid Fast Bacilli (AFB), culture and pathology tests that is approximately similar to Sofian et al study declared 54%, 3.2% and 30.5 %, except for pathology. At present, negative cases with sputum culture for mycobacterium tuberculosis complex were 20 numbers that indicates notable numbers. It might cause by the fact that TB cases usually not easily diagnosed in children due to different methods including family history of contact, gastric juice test and chest X-ray that a set of them is used for diagnosis in the country health system.

Most of the patients 354 (59.8%) attended to the Primary Health Care system (PHC) for treatment. Although, a significant number of patients attended to other institutions or organizations, but their condition will report to the PHC, in final. As a result, a valid data was provided to researchers. Following the implementation of Directly Observed Treatment Short-Course (DOTS) strategy, the success rate of treatment reached to 90%–95%, or even greater, approximately. Nowadays, it is accepted that the most important reason of failure in TB treatment is irregular drug-taking by patients (29). DOTS strategy showed that treatment failure is much lower than in the non-DOTS group (30, 31). DOTS strategy has been conducting in the health referral system of the country that may lead to beneficial outcomes in patients.

TB cases have gradually increased from 2005 to 2012 years with some intermittent declines. Given studies conducted in Iranian society (32, 33), there is no clear pattern of increase or decrease in TB cases in Iran. To justify, Iran has wide borders with the countries of Afghanistan and Pakistan, which are highly prevalent regions of TB. Two aforementioned countries have a common border with the Sistan - Balouchestan Province of Iran that its inhabitants have been immigrating in Golestan Province to a great extent. Moreover, health activities such as health care and screening can likely affect the fluctuations of TB, as well.

Since, data were collected in the past several years, some missing of data was inevitable. However, due to the high incidence of tuberculosis in Golestan province and its potential risk, data were usually collected with great attention of authorities. In final, authors were not provided by population statistics in detail to calculate other status such as incident among at risk age groups, therefore the research team recommends that this issue carefully reviews to clarify the importance of disease in the province.

In Iranian Health System, all new cases of TB record in a data bank monitored by the District Health Network (governmental) that indicates the fact that there is no other TB infection in the private parts. In the final, the study protocol investigated children with contact for a period of nine years that had not previously been conducted in Iran. Therefore, our findings can be likely useful for making decisions in the field of prevention, control and treatment of tuberculosis, when be available for the decision makers of health sector providers.

CONCLUSION

At present, place and ethnicity reported as remarkable risk factors of TB. These variables have usually been associated in the Golestan province due to poor socioeconomic status of immigrants. In addition, nationality was an effective factor for TB, because most of them were immigrated in from Afghanistan with poor socioeconomic status. Therefore, diagnosing and improving of social and economic determinants of health factors might likely be beneficial.

Ethics approval and consent to participate

The present study was a retrospective descriptive that conducted over the existed data and a period of nine years between April 2005 and April 2013 years. The project protocol was approved by the ethical number of IR.GOUMS.REC.1396.25

Consent for publication

I hereby confirm the accuracy of the information in the paper and express my consent for the publication of the article.

Availability of data and materials

This study was done based on the existed data in the Health System of the Golestan Province.

Author's contribution

All activities were done by Dr Kamal Mirkarimi

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