The pattern of pediatric tuberculosis and treatment outcomes from 2012 to 2016 in Erbil City, Iraq

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Abstract

Background and objective: *M. tuberculosis* is one of the main causes of morbidity and mortality in many countries and is considered a priority global health problem. Although it is a curable disease, every year about nine million people develop active disease, and two million die from it. This study aimed to find the pattern of tuberculosis among children in Erbil city and determine the treatment outcomes of pediatric tuberculosis.
Methods: From March 2012 to March 2016, 142 patients younger than 18 years with confirmed diagnosis of tuberculosis were registered and treated at the Chest and Respiratory Disease Centre in Erbil. The diagnosis of tuberculosis was performed based on routine tests at the center. AFB smear staining, GeneXpert assay, and culture methods when required for further confirmations using L-J media.
Results: The total number of the studied records of tuberculosis was 729 during five years (2012-2016). More than half (55.6%) of patients aged ≤ 18 years were males. It is evident that the number of cases is increasing with the progress of years, but the difference was not significant between the years (*P* = 0.534). The death rate was 9.1% among patients of the whole sample, but no significant association was detected between age and outcome and was highest (22.7%) among patients aged 7-12 years (*P* = 0.142).
Conclusion: Tuberculosis is still a very severe disease with high mortality rates in children. Early recognition of infection associated with correct early treatment, systematic entourage investigation, and chemoprophylaxis by isoniazide in all children under five years of age is essential for attempting to reduce these prognostic indices.
Keywords: *Mycobacterium;* Tuberculosis; Pediatric; Treatment; Outcome.

Introduction

Tuberculosis (TB) is globally one of the major causes of mortality among children, especially in developing counties.[1,2] Recent reports from the World Health Organisation (WHO) showed that from a total of 9 million patients with TB, approximately 10% have occurred in children. Additionally, it has been estimated that the annual deaths associated with pediatric TB were 210,000 cases.[3] The prevalence ratio of pediatric TB is more than 40% in high-burden countries with a high incidence rate of tuberculosis.[4] Therefore, over the last decade increased attentions have given to pediatric TB particularly in limited resource area.[5] The diagnosis of TB in infants and children continues to be a real challenge for detection, diagnostic accuracy, and therapeutic options.[1] The difficulty in sputum collection and low rate of microbiological confirmation are widely acknowledged.[6,7] Therefore, detection of the clinical criteria of pediatric TB is essential to directly diagnose tuberculosis and to make an earlier control of the disease.[5] WHO suggests that performing a routine examination for children living in close contact with an adult diagnosed with active TB is an important measure to improve the control of pediatric tuberculosis.[4,8] Failure of the national TB control program is one of the factors that led to the development of pediatric TB.[9]

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Another reason for increased latent pediatric TB is difficulties in diagnosis and delay of therapy of sputum smear-positive pulmonary TB in children.[4,10] Childhood TB can be considered as a reservoir for this bacterium that carries on transmission in the community consequently. One of the main functions of national TB control is to monitor pediatric TB management in order to assess the success or failure of treatment.[9] Childhood tuberculosis is neglected in endemic areas with resource constraints, as children are considered to develop mild forms of disease and to contribute little to the maintenance of the tuberculosis epidemic. However, children contribute a significant proportion of the disease burden and suffer severe tuberculosis-related morbidity and mortality, particularly in endemic areas.[11] Proper management of pediatric tuberculosis is essential for the control of tuberculosis as children also act as a source of infection within a community.[12] The aim of the national TB control program is to decrease the incidence ratio of pediatric TB to <1%.[13] The present study aimed to find the pattern of TB among children in Erbil city and to determine the treatment outcomes of pediatric TB.

Methods

From March 2012 to March 2016, 142 patients of younger than 18 years with a confirmed diagnosis of TB were registered and treated at the Chest and Respiratory Disease Centre in Erbil. The patients were reviewed retrospectively and categorized by age into three groups: less than 7 years, 7 - 12 years, and 13 - 18 years. The diagnosis of TB was performed based on routine tests at the center, which included AFB smear staining, GeneXpert assay, and culture methods when required for further confirmations using L-J media. Criteria of TB diagnosis were: a history of closed contact with TB positive patients, clinical signs and symptoms of TB, positive chest x-ray (suggesting TB), bacterial evidence, smear or culture (PCR and

pathology examination if indicated), and TB skin test. Any child with three or more of the five mentioned criteria (except for positive bacterial evidence in which a positive test is enough for diagnosis) was defined as a TB case. Favorable treatment outcome (cured and completed treatment) and poor outcome (failure, default, and death) were measured after six months of the standard anti-TB regimen. Other definitions were as follows: Cured (C): A patient whose treatment started after 2-5 months her/his sputum (direct smear) changed from AFB-positive to AFB-negative. Treatment Completed (TC): A patient that completed 6 months of Cat 1 and clinically responded to treatment but with unknown bacteriologic status. The diagnosis of TB was performed based on the National Algorithm for presumptive pulmonary TB. Symptoms of TB include fever, chronic cough, weight loss, or failure to thrive. Any patient with an unexplained cough for 2-3 weeks or more, in which x-ray and routine diagnostic methods, including acid-fast bacilli and molecular PCR based method (GeneXpert), were used. In addition, fresh specimens were referred to culture when required. For managing the patients and treatment control, the TB specialist physician made decisions according to the international standard of TB care. Sex, age, the site of the disease (pulmonary or extrapulmonary), and treatment outcome were retrieved from patients' records. This project was approved by the Scientific and Research Ethics Committee at the College of Health Sciences, Hawler Medical University. For presumptive extrapulmonary TB such as TB meningitis and TB pleurisy, the diagnostic algorithm was different. Appropriate specimens were requested and examined by Xpert MTB/RIF (GenXpert) and/or TB culture. Depending on weather rifampin-resistant or sensitive, the treatment was started. According to the International Standards for TB Care, the final medical diagnosis and medications are typically performed by

TB specialist physicians. Patients with newly diagnosed pulmonary or extrapulmonary TB are typically provided with a treatment regimen containing six months of rifampicin, including two months of isoniazid, rifampicin, pyrazinamide, and ethambutol and four months of isoniazid and rifampicin (2HRZE/4HR) based on the WHO algorithm for treatment of TB patients. After this treatment period, if patients still give positive results, they are given the standardized 2nd line regimen (amikacin, cycloserine, ethionamide, and vitamin B6) or the Category 2 Regimen (streptomycin + HRZE) depending on whether they are MDR or sensitive in GeneXpert Diagnosis. As Category 2 treatment regimen is ineffective in MDR-TB, it is critical to detect MDR-TB promptly to provide an effective treatment regimen. A well-organized program for monitoring, supervision, and support is provided at the center by the International Organization for Migration for all TB patients. Any patient with a positive sputum smear or culture at the start of the treatment but with a negative smear or culture in the last month of treatment and at least one earlier time was considered a cured case. Any patient who completed treatment and not having a negative sputum smear or culture in the last month of treatment and one earlier time at the minimum was considered a treatment completed case. Any patient with a positive sputum smear or culture at five months or later during the treatment was considered a fail case.

Statistical analysis

Data were analyzed using the statistical package for the social sciences (SPSS, version 22). The Chi-square test of association was used to compare proportions. Fisher's exact test was used when the expected count of more than 20% of the cells of the table was less than 5. A P value of ≤0.05 was considered statistically significant.

Results

The total number of the studied records of tuberculosis was 729 for five years (2012-2016). More than half (55.6%) of patients aged ≤ 18 years were males compared with 42.8% of patients aged > 18 years (P = 0.006), as presented in Table 1 and Figure 1. The table shows that 62.4% of cases were extrapulmonary, but no significant difference was detected between the two age categories (P = 0.515). The death rate was 9.1% among patients of the whole sample, but no significant association was detected between age and outcome (P = 0.595). It is evident that the number of cases is increasing with the progress of years, but the difference was not significant between the years (P = 0.534).
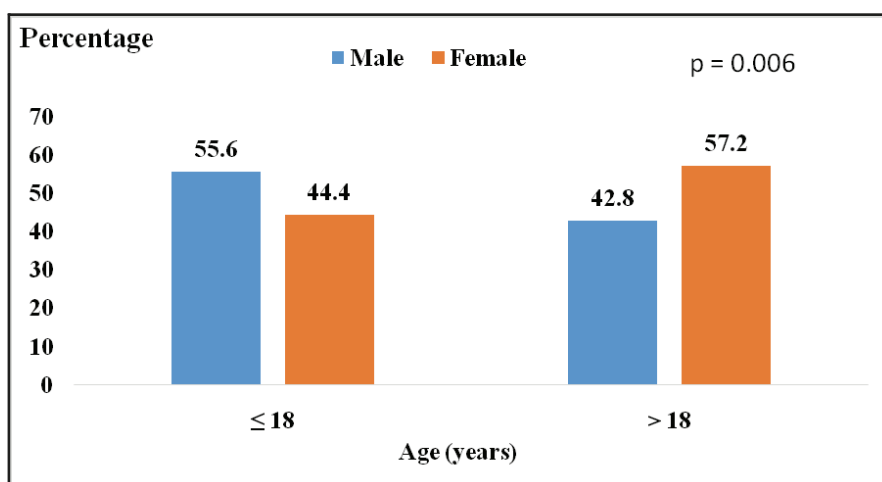

Figure 1: Gender distribution by age.

Table 1: Patients' characteristics by age categories.

	≤ 18 years		> 18 years		Total		
	No.	**(%)**	**No.**	**(%)**	**No.**	**(%)**	***P* value**
Gender							
Male	79	(55.6)	251	(42.8)	330	(45.3)	0.006
Female	63	(44.4)	336	(57.2)	399	(54.7)	
Site							
Pulmonary	50	(35.2)	224	(38.2)	274	(37.6)	0.515
Extra-pulmonary	92	(64.8)	363	(61.8)	455	(62.4)	
Outcome							
Cured	23	(16.2)	115	(19.6)	138	(18.9)	
Treatment completed	107	(75.4)	418	(71.2)	525	(72.0)	0.595
Died	12	(8.5)	54	(9.2)	66	(9.1)	
Year							
2012	17	(12.0)	104	(17.7)	121	(16.6)	
2013	29	(20.4)	106	(18.1)	135	(18.5)	
2014	26	(18.3)	113	(19.3)	139	(19.1)	0.534
2015	34	(23.9)	127	(21.6)	161	(22.1)	
2016	36	(25.4)	137	(23.3)	173	(23.7)	
Total	142	(100.0)	587	(100.0)	729	(100.0)	

Table 2: Gender, site of TB, and outcome by age categories of young patients.

	Age (years)						
	< 7		7-12		13-18		*P* value
	No.	**(%)**	**No.**	**(%)**	**No.**	**(%)**	
Gender							
Male	21	(56.8)	11	(50.0)	47	(56.6)	
Female	16	(43.2)	11	(50.0)	36	(43.4)	0.846
Site							
Pulmonary	12	(32.4)	7	(31.8)	31	(37.3)	
Extra-pulmonary	25	(67.6)	15	(68.2)	52	(62.7)	0.818
Outcome							
Cured	5	(13.5)	3	(13.6)	15	(18.1)	
Treatment completed	31	(83.8)	14	(63.6)	62	(74.7)	
Died	1	(2.7)	5	(22.7)	6	(7.2)	0.142*
Total	37	(100.0)	22	(100.0)	83	(100.0)	

*By Fisher's exact test.

Discussion

The total number of the studied records of tuberculosis was 729 during five years (2012-2016). From which 142 were aged less than 18 years. The results presented in this study show alarmingly high rates of pediatric TB infection. The highest rate was seen in 2016, which was 25% (36 cases) from the total cases, followed by 24% (34 cases) in 2015. Reasons for the increased incidence of pediatric TB in Erbil might be due to low socioeconomic levels during recent years as a consequence of political conditions. Furthermore, migration of people from neighboring countries due to the wars may also affect the economic conditions in the Kurdistan region; Since TB is a disease of poverty that thrives where social and economic determinants of ill-health prevail. On the other hand, the diagnosis of tuberculosis in younger children remains challenging, and most of them end up with antituberculosis treatment without confirmation. This leads to a delay in the diagnosis and treatment of other serious complications.[14] Male cases were 55% (79 patients) among those children, 45% were female cases. Different ratios were reported from other studies. In a study carried out by Alavi et al., 2015, the incidence rate of pediatric TB was 4.9% among all TB disease burden.[15] The mean age was 10.7±4.3 years old, and 75.7% of them were females. Of the 216 child contact with active TB in adults among those 37 children, 59% were under five years old, 54% were female.[16] A retrospective review that was conducted on 203 patients aged less than 19 years admitted to a referral TB hospital in Iran from 2006 to 2011the medium age of the patients at the time of diagnosis was 15 years, of which 60% were ranging from 1 year to 18 years, and57 % were female. 83% of them had pure pulmonary TB.[17] In the present study, from the total number of pediatric patients, the predominant age group was 13-18 years, with 83 cases (58%). While the number of cases in the age group of less than 7 and 7-12 was 37

and 22 cases, respectively. Non-similar data showed by Alavi et al., 2015, in which more than 84% of TB infected children were 10 years or older, whereas young children (< 5 years old) accounted for 5.6%.[15] In another study in 2014, less than 5% of all cases of TB in Canada occurred in children aged 14 years and younger. Rates of TB in children under 1, 1–4, and 5–14 years of age were 2.9, 2.0, and 0.8 cases per 100 000, respectively.[18] In a study carried out by Gosai et al. In 2014 the age distribution showed that 62% of EPTB cases fall into the age group of 6 months - 5 years and 38% of cases in the age of 5-12 years.[19] Tuberculosis commonly affects young children (<5 years) in countries with high rates of child mortality. The global public health focus to control tuberculosis has traditionally aimed to reduce transmission through early case-finding and effective treatment of the most infectious cases.[20] Regarding the site of infections, EPTB has a higher ratio compared to PTB, as the data showed that about 65% (92 cases) were suffering from EPTB compared to 35% of PTB cases. In contrast to our study, retrospective data from China, taken from 2008 to 2017, 33.4% had extrapulmonary TB, and 66.6% had pulmonary TB. Opposite to our results, it was observed a predominance of the pulmonary form, with 52 cases out of the total 67 cases.[21] It has been shown that childhood extrapulmonary tuberculosis is common in the pediatrics population, mainly in children <5 years. Extrapulmonary tuberculosis is commonly seen in low socioeconomic classes, with moderate to severe malnutrition.[19] In the treatment outcome data, death rates seem high, as results showed that 8.5% died during the treatment process. Similar to our study, Loh et al., 2018 observed in their 9 year retrospective study of pediatric TB in Singapore 75 patients were diagnosed as having active TB 65% with PTB and 35% with EPTB. Patients with EPTB were more likely than those with PTB to be younger than five years old, and the death

rate was 8%.[22] The hospital mortality rate among TBP children in the city of Lubumbashi (Africa) reached a rate of 23.3%. The mortality rate among children under five years of age was significantly higher than those over five years of age.[14] Mortality due to tuberculosis in children is underestimated because, for many children who die from tuberculosis, the cause of death is listed as pneumonia, HIV/AIDS, meningitis, or malnutrition.[23] In the presence of less than 100 CFU/ml there is a possibility to be detected by culture method.[20] In addition to the household, that plays an important role in the transmission of the infection to the young children, in areas with a low incidence of tuberculosis community is responsible for the transmission of the disease such as at the nursery, school, playground area, malls etc.[24] In order to prevent the infection in infants and children and prevent them from becoming infectious adults it is necessary to diagnose the disease early followed by effective antituberculosis treatment of the patients in household.[18] There is no gold standard method for diagnosis of suspected pediatric tuberculosis, as it is a real challenge to be confirmed bacteriologically due to paucibacillary nature in this age group and a small number of bacteria during culturing. It has been observed that the sensitivity of sputum culture isless than 50% in suspected positive cases.[21] In limited resources area, AFB is the most commonly available method for the diagnosis of pediatric TB, but the specificity is very low about 10-15% of cases.[25]

Conclusion

In this study, more TB pediatric patients were found among 13-18 years, especially males. Early diagnosis of children at risk of developing TB infection is crucial for disease control. TB is still a very dangerous disease with high death rates in children. Early treatment, systematic investigation, and chemoprophylaxis by isoniazid in all children, specifically under five years of

age, are essential for reducing these prognostic indices.

Competing interests

The author declares no competing interests.

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