TUBERCULOSIS AMONG CHILDREN IN SULAIMANI- CLINICAL PATTERN 2014 TO 2017

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ABSTRACT

BACKGROUND

Tuberculosis (TB) is one of the most important global health problems. The prevalence of TB is high in the developing world**.** Tuberculosis in children still remains as one of the main causes of morbidity and mortality throughout the world, Knowledge about childhood tuberculosis (TB) in Kurdistan is limited. This study aimed to determine the proportion of tuberculosis in children living in Sulaimani, north of Iraq and its outcomes. This retrospective study was carried out to find the clinical pattern of pulmonary and extrapulmonary tuberculosis in children in Sulaimani city-Iraq.

METHODS

Medical records of 38 patients aged 0-15 years with childhood TB who were diagnosed in Chest and Respiratory Disease Center. The medical records were reviewed regarding clinical, demographic, outcome data and investigations.

RESULTS

A total of 38 medical records of childhood TB patients were included in this study. 24 (63%) of them had extra pulmonary tuberculosis (EPTB) and 14 (37%) had pulmonary tuberculosis (PTB). female patients were more in both; PTB 57.1% and EPTB 54.1%, compared to the male proportions which were 42.9% in PTB and 45.8% in EPTB with no statistically significant difference ($p<0.859$) There was a significant difference between the incidence of PTB and the incidence of EPTB in deferent age groups. PTB was predominant in adolescent age, 78.6% of PTB patients were aged between 10-15 years. Vaccinated patient with BCG were less likely to get PTB (26.8%) compared to 70.8% of EPTB who were vaccinated with BCG. 42.9% of PTB had a history of contact with a TB patient, and 8.3% of EPTB had TB contact history (p value= 0.012). In relation to the sex and address of TB patients there was no statistically significant difference between EPTB and PTB patients, a statistically significant difference was observed among PTB and EPTB regarding the results of TB skin test, GeneXpert test, ESR and chest x ray. The results of TB skin tests were positive in 42% of PTB whereas none of EPTB patients had a positive TB skin test (p value <0.001). GeneXpert test and chest x ray were more sensitive in detecting PTB than EPTB. 64.3% of PTB cases had positive GeneXpert test results compared to 8.3% of EPTB cases that had positive result (p value<0.001). Similarly, 85.7% of PTB and 12.5% of EPTB had positive chest x ray results (p value <0.001). PTB obviously had a higher ESR test results, 7.1% of this group had ESR less than 50, and 50% of them had ESR result between 50 and 100 and 43.9% had ESR more than 100, in contrast EPTB group ESR results for same classification were 50%, 41.7% and 8.3% respectively ($p <0.006$; Table 2). Nevertheless, tissue biopsy test results in the two groups were not significantly different ($p<0.052$), but EPTB was more likely to have the positive result 95.8% versus 71.4% of PTB had positive results.

CONCLUSIONS

Majority of the patients had EPTB and pleural tuberculosis was the most common among patients with EPTB. Female patients were more common in both EPTB and PTB cases. Vaccinated child was less susceptible to pulmonary TB than EPTB, both PTB and EPTB were more common among crowded families.

KEY WORDS

Tuberculosis, Child, Epidemiology, Clinical Pattern

HOW TO CITE THIS ARTICLE: Salih KH. Tuberculosis among children in Sulaimani- clinical pattern 2014 to 2017. J. Evolution Med. Dent. Sci. 2019;8 (22):1800-1803, DOI: 10.14260/jemds/2019/395

BACKGROUND

In its 2017 report, the WHO estimates that, of the 10.4 million incident cases of TB in 2016, approximately one million occurred among children under age 15 Of the 10.4 million incident cases of TB reported in 2016, 6.9 percent were in children with an equal number of males and females. [1]

In 2017, the WHO and colleagues estimated that there were 239,000 paediatric deaths due to TB (39,000 occurring in HIV-infected children), approximately 80 percent of these deaths occurred in children under age five. [2] Although tuberculosis is primarily the disease of affecting the lungs (Pulmonary Tuberculosis; PTB), it may have various manifestations and can affect many sites such as lymph nodes, central nervous system, bones, and gastrointestinal tract which is known as Extra-pulmonary tuberculosis (EPTB). [3,4] Tuberculosis (TB) in children is often diagnosed clinically. Because pulmonary TB in children typically presents with paucibacillary, non-cavitary pulmonary disease, bacteriologic confirmation is achievable in less than 50 percent of children and 75 percent of infants; in such cases, pulmonary TB is diagnosed by other clinical criteria, [5] For diagnosis of extrapulmonary TB, specimens for culture should be collected from any site where infection is suspected. Each specimen should be cultured regardless of acid-fast bacilli (AFB) smear results. [5]

'Financial or Other Competing Interest': None.
Submission 23-03-2019, Peer Review 18-05-2019,
Acceptance 23-05-2019, Published 03-06-2019.
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DOI: 10.14260/jemds/2019/395

A diagnosis of TB (Pulmonary or extrapulmonary) in a child is often based on the presence of the classic triad: 1. recent close contact with an infectious case, 2. a positive tuberculin skin test (TST) or interferon-gamma release assay (IGRA), and 3. suggestive findings on chest radiograph or physical examination. [6]

In this regard, the present retrospective study was aimed at finding the clinical pattern of pulmonary and extrapulmonary tuberculosis in children in Sulaimani city-Iraq.

METHODS

The present retrospective descriptive study was carried out at Chest and respiratory disease center in Sulaimani district at Kurdistan region of Iraq. The medical records of childhood TB patients aged 0 to 15 years for four years between 1st January 2014 and 31st December 2017 were reviewed. All patients with confirmed diagnosis of TB infection were included. A predesigned questionnaire was used to retrieve information of patients records which included; demographic data (Age, sex, residency, crowding index etc.), medical history (Vaccination, family history of TB, history of contact), investigation results (TB skin test, GeneXpert test, chest X-ray, ESR and tissue biopsy), prognosis outcome (Recovery, under treatment and death). The data coded and added to a Microsoft excel spread sheet, IBM-SPSS software version 22 was used for data analysis. Categorical variables were expressed via frequencies and percentages, and for comparison between categorical variables, to assess the significant association between observed proportions, the Chi square test and Fisher exact test were used (a p value < 0.05 was considered as a statistically significant cut-off of the tests).

RESULTS

A total of 38 medical records of childhood TB patients were included in this study 24 (63%) of them had extra pulmonary tuberculosis (EPTB) and 14 (37%) had Pulmonary tuberculosis (PTB). All enrolled patient**s** were Iraqi living in Sulaimani province. A higher proportion of female patients observed in both TB infections; PTB 57.1% and EPTB 54.1%, compared to the male proportions which were 42.9% in PTB and 45.8% in EPTB with no statistically significant difference (P<0.859) Table 1.

There was a significant difference between the incidence of PTB and the incidence of EPTB in different age groups. PTB was predominant in adolescent age, 11 (78.6%) of PTB patients aged between 10 -15 years, and 2 (14.3%) of them were less than 5 years old. While the EPTB was more prevalent in under-five children by 15 (62.5%) (p value<0.002) Table 1. Vaccinated patient with BCG were less likely to get PTB 4 (26.8%) compared to 17 (70.8%) of EPTB which were vaccinated with BCG. 6 (42.9%) of PTB had a history of contact with a TB patient, and 2 (8.3%) of EPTB had TB contact history (p value= 0.012).

In relation to the sex and address of TB patients there was no statistically significant difference between EPTB and PTB patients, Table 1.

Socio-Demographic Data	Pulmonary No. (%)	Extra-Pulmonary No. (%)	(p-Value)
Age			
Less than 5 years	2 (14.3)	15 (62.5)	*0.002
5 -10 years	1 (7.1)	4 (16.7)	
10 - 15 years	11 (78.6)	5 (20.8)	
Gender			
Male	6 (42.9)	11 (45.8)	#0.859
Female	8 (57.1)	13 (54.2)	
Address			
Inside city	7 (50)	11 (45.8)	#0.804
Outside city	7 (50)	13 (54.2)	
Crowd Index			
Index < 4	0 (0.0)	9 (37.5)	*0.009
Index >4	14 (100)	15 (62.5)	
BCG			
Vaccinated	4 (28.6)	17 (70.8)	*0.037
Un-vaccinated	2 (14.3)	2 (8.4)	
Un known	8 (57.1)	5 (20.8)	
FHTB			
Parent	0 (0.0)	1 (4.2)	*0.010
Sibling	5 (35.7)	1 (4.2)	
Grand parent	1 (7.1)	0 (0.0)	
No	8 (57.2)	22 (91.6)	
History Contact			
Yes	6 (42.9)	2 (8.3)	*0.012
No	8 (57.1)	22 (91.7)	

Table 1. Socio-Demographic Distribution of Pulmonary and Extra-Pulmonary TB

*p value calculated using Fisher's Exact Test.
p value calculated using Pearson Chi-Square.

Investigation Data	Pulmonary No. (%)	Extra-Pulmonary No. (%)	(p-Value)
TB Skin Test			
Positive	6 (42.9)	0 (0.0)	* 0.001
Negative	8 (57.1)	24 (100)	
GeneXpert Test			
Positive	9 (64.3)	2 (8.3)	* 0.001
Negative	5 (35.7)	22 (91.7)	
Chest X-ray			
Positive	12 (85.7)	3 (12.5)	* 0.001
Negative	2 (14.3)	21 (87.5)	
ESR			
< 50	1 (7.1)	12 (50)	* 0.006
50 - 100	7 (50)	10 (41.7)	
> 100	6 (42.9)	2 (8.3)	
Tissue Biopsy			
Positive	10 (71.4)	23 (95.8)	* 0.052
Negative	4 (28.6)	1 (4.2)	

Table 2. Pulmonary and Extra-Pulmonary TB Investigation Results

*p value calculated using Fisher's Exact Test
p value calculated using Pearson Chi-Square

Outcome	Pulmonary No. (%)	Extra-Pulmonary No. (%)	(p-Value)
Recover	9 (64.3)	15 (62.5)	* 0.585
Still treat	3 (21.4)	8 (33.3)	
Die	2 (14.3)	1 (4.2)	

Table 3. The Relationship Between Pulmonary and Extra-Pulmonary TB According to The Prognosis

Year	Pulmonary No. (%)	Extra-Pulmonary No. (%)	(p-Value)
2014	2 (14.3)	2 (8.3)	* 0.502
2015	7 (50.0)	7 (29.2)	
2016	3 (21.4)	10 (41.7)	
2017	2 (14.3)	5 (20.8)	

Table 4. The Relationship Between Pulmonary and Extra-Pulmonary TB According to The Year

*p value calculated using Fisher's Exact Test.
p value calculated using Pearson Chi-Square.

Table 2 shows the results of various investigations that were used to detect the TB infections, a statistically significant difference was observed among PTB and EPTB regarding the results of TB skintest, GeneXpert test, ESR and chest x-ray. The results of TB skin tests were positive in 6 (42%) of PTB whereas none of EPTB patients had a positive TB skin test (p value <0.001). GeneXpert test and chest x ray were more sensitive to detect PTB than EPTB. 9 (64.3%) of PTB cases had positive GeneXpert test results compared to 2 (8.3%) of EPTB cases that had positive result (p value<0.001).Similarly, 12 (85.7%) of PTB and 3 (12.5%) of EPTB had positive chest x-ray results (p value <0.001).

PTB obviously had a higher ESR test results, 1 (7.1%) of this group had ESR less than 50, and 7 (50%) of them had ESR result between 50 and 100 and 6 (43.9%) had ESR more than 100, in contrast EPTB group ESR results for same classification were 12 (50%), 10 (41.7%) and 2 (8.3%) respectively (P<0.006; Table 2). Nevertheless, tissue biopsy test results in the two groups were not significantly different (p< 0.052), but EPTB was more likely to have the positive result 23 (95.8%) versus 10 (71.4%) of PTB had positive results.

The outcomes in both types of TB were nearly the same, more than 60% of patients were cured and between 4 to 15% died (p value = 585) Table 3.

No statistically significant difference has been noticed in the yearly occurrence of both types of the disease in 2014 to 2017 (Table 4).

DISCUSSION

This study conducted on 38 children with tuberculosis at Chest and respiratory disease center in Sulaimani district at Kurdistan region of Iraq from 1st Jan 2014 to 31st of December 2017, were 24 children had extra-pulmonary tuberculosis (EPTB) and 14 had pulmonary tuberculosis (PTB).

One of the main risk factor to development and progression of TB is age. [7] In the current study, TB among children at lower than 5 years old was highest compared to older groups. [8] EPTB were highest among children were at low ages (Less than 5 years old) compare to PTB children were most among children at higher ages (10-15 years) with significant relation between PTB and EPTB according to children age groups, same results observed in other studies [9-11] and other studies show that EPTB is higher in older adolescents compared to children. [12] Female children were more at risk to acquire TB than male children and female children were highest in both EPTB and PTB cases compare to male children with non-significant relationship. [9,13,14] However, other studies reported that male children more to EPTB but still it is not a significant relationship. [12,15] This differences among studies might relate to geo-demographic or type of sample size or collection method of the study. Majority of participate children were from rural areas, PTB was equal in both areas and EPTB were more from rural areas than urban with no significant relation. [16]

Vaccinated with BCG were higher among ESTB compare to PTB with a significant difference between the two groups. We found the same result in Kumar's [15] study but with non-significant relation and studies suggested that because of BCG cause complex cytokine profiles in both CD4+ and CD8+ T cells. [17] Children with BCG cause bias in biomarkers and skin TB test to detect between healthy and TB children. [18]

Majority of children participated in this study had negative contact and family history with TB for both categories. [13] This could be related to children in our society children at low ages only in continuous contact with the parents in state of in care centers. [19] Family history and previous contact were more among PTB compare to EPTB children with a non-significant relationship in our study and we found same results in other studies, were negative contact more among EPTB. [9,20] The Sreeramareddy's study found that history contact with TB significantly associated with PTB.

Majority of TB skin test were negatives for both groups, it might be related to those majority children in this region are vaccinated with BCG that make skin test limited benefit to diagnosis TB, some studies suggest that TB skin test is limited to declare difference between active and latent TB among children compared to adults and TB skin test among young children and infants not well studied. [10,21] EPTB skin tests were negative while 42.9% of PTB were positive cases with significant relation between skin test and two groups, same results observed in other studies and there are studies concluded smaller TB skin test in diameter among EPTB compare PTB children. [11] GeneXpert Mycobacterium tuberculosis/resistance to rifampin (MTB/RIF) assay results in our study show increase of test sensitivity among rapid tests for detection TB for both PTB and EPTB. [22,23]

An increase of WBC against active TB including ESR and PCR are bio-markers to detect TB. [15,24] However, in our study we found the opposite result and same as Devrim's study in Turkey [13] also ESR were lower among EPTB than PTB in both studies. Tissue biopsy was highly sensitive biomarker test to detect EPTB compare to other tests and it was higher than PTB. [15,25]

Chest x-ray test is primary radiologist test used to diagnosis patients suspect of TB after two or more weeks of a cough and chest pain, our results indicated that chest X-ray was highly positive in pulmonary, as one of the main tools for diagnosis of pulmonary TB is x-ray finding as may cause a change in lung parenchyma and appear on chest X-ray with time, and this is consistent with other studies. [26]

Outcome of most TB children participated in this study were recover and recover rate among EPTB children were more compare to PTB children with non-significant relationship, this opposite to Garcia study found that EPTB children more risk to TB complications and death rate were higher compare PTB children with significant relationship. [11]

CONCLUSIONS

Majority of the patients had EPTB and pleural tuberculosis was the most common among patients with EPTB. Female patients were more common in both EPTB and PTB cases. Vaccinated child was less susceptible to pulmonary TB than EPTB, both PTB and EPTB were more common among crowded families.

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