

Original Article**Evaluation of Crofton, Horne, Miller Scoring as Diagnostic Tool for Tuberculosis in Children**

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DOI: <http://dx.doi.org/10.3126/jonmc.v8i1.24478>**Abstract****Background**

Tuberculosis which is caused by Mycobacterium tuberculosis a chronic infectious disease, is considered the second most common infectious cause of mortality and morbidity in children around the world. This study was carried out to test the validity of Crofton, Horne and Miller scoring system for the diagnosis of children suffering from tuberculosis.

Materials and Methods

It was done in an inpatient ward of a pediatric tertiary referral centre, from Feb 2018 to Jan 2019 as a prospective case control study, including 92 children aged 2 years to 12 years admitted with clinical differential diagnosis of tuberculosis. Among them 46 children meeting the case definition were taken as cases and 46 were age, sex and disease presentation matched controls.

Results

Sensitivity of the score was low (50%) but the specificity was high (95%) with 92% positive predictive value and a negative predictive value of 65.67%. Contact with an adult suffering from tuberculosis, positive Mantoux test (>10mm induration) were found to be the most important indicators of TB in children. Males were found to be affected twice as much as the females.

Conclusion

From the findings of the study, it can be concluded that the Crofton, Horne, Miller score chart is a simple and cost-effective tool, which can be applied to improve the diagnosis of TB in children due to financial constraints faced by patients in resource limited countries like Nepal.

Keywords: Children, tuberculosis, Crofton horne miller scoring



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Introduction

Tuberculosis (TB) is a chronic infectious disease caused by organisms of the *Mycobacterium tuberculosis* (M tb) complex, which includes M tb, M bovis, M africanum, M chelonae, M fortuitum, M microti etc. *Mycobacterium* is the only genus of the family *Mycobacteriaceae* and order *Actinomycetales* [1]. M tb, M bovis and M africanum can cause TB in humans but only M tb is responsible for causing clinically and epidemiologically significant disease in adults and children [1, 2]. Diagnosing and estimating the burden of TB in children is challenging due to the difficulty in establishing a definitive diagnosis, concomitant presence of extra-pulmonary disease, consideration of childhood tuberculosis as lower public health priority and the lack of effective communication between pediatricians and the national tuberculosis programs [3].

Failure to confirm a diagnosis of TB in the majority of children has not only underscored the importance of the disease but also has been a major constraint in TB research in pediatrics [4]. Isolation of M tb and identification by Ziehl-Neelson (ZN) staining or by culture from specimens from body fluids or a tissue biopsy are the Gold Standard for the diagnosis [5]. In any child, who cannot effectively expectorate sputum or if the cough is absent or nonproductive, the best specimen for diagnosis of pulmonary TB is an early-morning aspiration of gastric contents which even under ideal circumstances, range from 28 to 40%, although rates can go up to 75% in infants [5]. A recent history of contact with an active case of tuberculosis, like a bacteriologically positive parent or other members of the family, has been strongly linked with manifestation of disease in a child [6]. To enable more accurate diagnosis of tuberculosis in children especially in low-income countries, various clinical, epidemiological and laboratory parameters have been used to devise effective, simple and reliable tests [6].

Various diagnostic approaches based on simple clinical and diagnostic tools prevail but most of these approaches have not been standardized, rendering comparison difficult, and only few of them have been properly validated [7]. Due to lack of proper health care services in many parts of Nepal, investigations useful for diagnosis such as X-rays, biopsy, histology, and culture of TB bacilli are not always available. To improve the

diagnosis of childhood TB, National TB Programme (NTP) of Nepal has included and advised the use of a score chart adapted from Crofton, Horne and Miller for the diagnosis of TB in children [8]. In this study, we propose to validate the Crofton, Horne and Miller Score for diagnosing TB in children.

Materials and Methods

This was a hospital based, prospective case control study conducted in Nobel medical college and teaching hospital, Biratnagar, Nepal over a period of one year from Feb 2018 to Jan 2019. Children 2 to 12 years of age who were admitted in the department of pediatrics with differential diagnosis of TB were included in the study.

Children less than 2 years and more than 12 years of age, children with known HIV status or children of known HIV positive mother, children who had taken ATT in the past, children with known immune-compromised status, children in whom a definitive diagnosis could not be made, children with congenital heart disease and gross congenital anomaly, children who needed intensive care treatment and children who showed no improvement during hospital stay or follow up visit with the treatment provided were excluded from the study.

Cases and controls were scored according to the CROFTON, HORNE, MILLER SCORING SYSTEM [8]. Score ≥ 7 was taken as positive and < 7 as negative. The score was not used to change the diagnosis or treatment being received. In a previous similar study carried out the sensitivity and specificity of the scoring system was found to be 84.9% and 78% respectively [9]. So using these data; for the population proportions, the sample size of this study for each case and control population is taken to be 460.

And as 460 cases and control for pediatric TB was not feasible to obtain within a 1yr period, for thesis purpose, 10% of 460 that is 46 cases and 46 matched controls were taken. So using these data; for the population proportions, sample size was determined to be 92. Data were entered and analyzed using SPSS 20.0 software. Percentage, proportions and contingency tables were used for description of the data and Chi-square test for analysis of the proportions and measurement of significance. A p value < 0.05 was considered as significant.



Results

Out of 92 cases included in the study, 63% (58 cases) were males and 37% (34 cases) female with male: female ratio of 1.7:1. Highest number of cases were in the age group of 8-12 years i.e 52.2% (n=46).

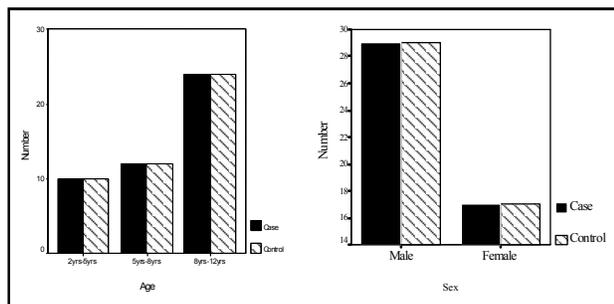


Figure 1: Bar graph showing age and sex distribution of cases and control groups under study.

Table 1: Evaluation of the Scoring system

Score	Number/Percentage	Case	Control	Total	X ²	Df	p value
<7	Number	23	44	67	24.22	1	0.000
	Percentage	50%	95.7%	72.8%			
≥7	Number	23	2	25			
	Percentage	50%	4.3%	27.2%			
Total	Number	46	46	92			
	Percentage	100%	100%	100%			

X²= Chi-square value; df= degree of freedom; p value = probability value

As shown in table 2, among the cases 23(50%) had a positive score (true positive) and 23(50%) a negative score (false negative). Among the controls, 44(95.7%) had a negative score (true negative) and just 2(4.3%) had a positive score (false positive). Statistical significance of the scoring system calculated by chi-square was 0.000 which is <0.05, hence highly significant

Table 2: Sensitivity and Specificity of the Scoring system

Score	Case	Control	Sensitivity %	Specificity %	PPV %	NPV %	+LR	-LR
<7	23	44	50	95	92	65.6	11.5	0.52
≥7	23	2				7		
Total	46	46						

PPV=Positive Predictive value; NPV=Negative Predictive Value; +LR=Positive likelihood ratio; - LR=Negative Likelihood Ratio

Sensitivity of the scoring system was low (50%) but the specificity was quite high (95%) with high PPV (92%) and NPV (65.67%). High positive likelihood ratio of the score 11.5 implies that the ≥7 score indicating TB infection is high but the low negative likelihood ratio of 0.522 indicates <7 score does not rule out the infection. As such the scoring system cannot be utilized as a screening tool as chances of missing out cases are high but it can be a useful diagnostic tool due to its high specificity

Table 3: Evaluation of the Mantoux test.

Mantoux	Number/Percentage	Case	Control	Total	X ²	Df	p value
0mm	Number	11	44	55	51.08	3	0.000
	Percentage	23.9%	95.7%	59.8%			
1-5mm	Number	2	0	2			
	Percentage	4.3%	0.0%	2.2%			
5-10mm	Number	5	2	7			
	Percentage	10.9%	4.3%	7.6%			
>10mm	Number	28	0	28			
	Percentage	60.9%	0.0%	30.4%			
Total	Number	46	46	92			
	Percentage	100.0%	100.0%	100.0%			

Positive Mantoux, >10mm induration was seen in 60.9% of the cases against 0% of the controls. No induration was seen in 95.7% of the controls against 23.9% cases. Intermediate results (1-5mm and 5-10mm induration) was not significantly different among the two groups.

Table 4: Sensitivity and Specificity of the Mantoux test.

Mantoux	Case	Control	Total	Sensitivity %	Specificity %	PPV %	NPV %	+LR	-LR
0mm	11	44	55						
1-5mm	2	0	2	60.86	100	100	71.87	∞	0.39
5-10mm	5	2	7						
>10mm	28	0	28						
Total	46	46	92						

∞ = infinity, PPV=Positive Predictive value; NPV=Negative Predictive Value; +LR=Positive likelihood ratio; -LR=Negative Likelihood Ratio

Results of the Mantoux test imply that the test is highly specific for the infection (100%) with a high PPV (100%) but is less sensitive (60.86%). Results are almost similar to that of the scoring but with even higher sensitivity and specificity. This may have been due to the fact that a positive Mantoux is given three points in the scoring (almost half of the required 7). The association is significant (p value = 0.000 ; <0.05).

Table 5: Evaluation of contact history

Contact History	Number/ Percentage	Case	Control	Total	χ^2	df	p value
No	Number	23	42	65	18.92	1	0.000
	Percentage	50.0%	91.3%	70.7%			
Definite	Number	23	4	27			
	Percentage	50.0%	8.7%	29.3%			
Total	Number	46	46	92			
	Percentage	100.0%	100.0%	100.0%			

χ^2 = Chi-square value; df= degree of freedom; p value = probability value

The results again are similar to that of the scoring with 50% of the cases having positive history of contact with a household adult with TB, against only 8.7% of the controls. Contact history had significant association with TB infection (p value=0.000).

Table 6: Sensitivity and Specificity of contact history

Contact History	Case	Control	Total	Sensitivity %	Specificity %	PPV %	NPV %	+ LR	- LR
No	23	42	65	50	91.3	85.18	64.61	50	0.54
Definite	23	4	27						
Total	46	46	92						

PPV=Positive Predictive value; NPV=Negative Predictive Value; +LR=Positive likelihood Ratio; -LR=Negative Likelihood Ratio

Contact history, defined as a positive contact with a household adult with sputum positive PTB within the past two years, was also highly specific (91.3%) but less sensitive (50%), similar to the overall scoring.

Discussion

Tuberculosis (TB) is amongst one of the leading causes of death among children worldwide; however, since most of them are sputum smear negative. Diagnosis of TB in children is a challenging task to a clinician because of a relative lack of sputum production and also unavailability of other diagnostic methods, especially in developing countries like Nepal [3]. Moreover recent technological advancements in diagnosis of TB have not been validated in children as compared to in adults [7]. A major challenge of childhood TB is establishing an accurate diagnosis. Less than 15% of cases are sputum acid-fast bacilli smear positive, and mycobacterium culture yields are 30%–40% [10,11].

In this thesis study we have attempted to evaluate the CROFTON, HORNE, MILLER scoring

system and its significance in diagnosis of TB in children. Evaluation of the demographic profile of the study population revealed that, 2-5 years old age group (21.7%), 5-8 years old (26.1%) and most number of cases were in the age group of 8-12 years (52.2%). Males (63%) were almost double the number of females (37%), which was similar to the sex ratio of NTP annual report 067/0687 (M:F=69%:31%), and that shown by the study done in Dhulikhel Hospital (M:F= 68.3%:31.7%) [12].

Among the 46 cases 23 (50%) had a positive score (true positive) and 23 (50%) a negative score (false negative). Among the 46 controls, 44(95.7%) had a negative score (true negative) and just 2(4.3%) had a positive score (false positive). Sensitivity of the scoring system was low (50%) but the specificity was quite high (95%) with high positive predictive value of 92% and negative predictive value of 65.67%. The positive likelihood ratio (+LR) was 11.5 and the negative likelihood ratio (-LR) was only 0.5227. Statistical significance of the scoring system calculated by chi-square was 0.000 which is <0.05, hence highly significant. A similar study by Sarkar S, Paul DK, Chakrabarti S, Mandal NK, Ghosal NG at North Bengal Medical College and Hospital, Darjeeling District, North Bengal, among 53 confirmed TB cases and 50 randomly selected confirmed non-TB controls found 15.1% false negative and 22% false positive results and the sensitivity and specificity of the scoring system to be 84.9% and 78% respectively, with a positive predictive value of 80.36% which is similar to our study [9]. Evaluation of the Mantoux test showed that, 28(60.9%) of the cases had positive Mantoux measuring >10mm and none of the controls had positive Mantoux. Sensitivity of the test was found to be 60.86% and the specificity was 100%. Study conducted by Narayan S, Mahadevan S and Serane VT in Jawaharlal Institute of Postgraduate Medical Education and Research (JIPMER), Pondicherry found that 54% of the cases diagnosed to have TB were TST positive which was almost similar to the present study [13].

Evaluation of the contact history revealed similar results to the overall scoring itself with 23(50%) of the cases giving positive history of contact with a household adult diagnosed with sputum positive PTB within the past two years. The association of positive contact with TB in the study population was found to be significant (p value=0.000).



Sensitivity was 50% (similar to the scoring) and the specificity was 91.3%, almost similar to the scoring system. Similarly in a study done in South Africa, Hatherill M et al found that contact with an adult with TB was reported for 952 children (65.9%) [14].

Conclusion

The present study concludes that in children with indicative clinical features, Crofton, Horne, Miller score can be a definitive guideline for the diagnosis of tuberculosis especially in places where diagnostic facilities are limited. However it should be remembered that the score should not be used as a screening tool due to its low sensitivity and high false negative value. It can rather be used as an adjunctive method for the diagnosis along with the clinical features, history of contact and other simple available tests like chest x-ray, Mantoux test, ESR and ADA level of lymphocytic exudative serous fluids. But multicentric studies with larger sample size including cases with definitive diagnosis of TB and comparing the scoring system with the definitive diagnostic tests are required, before the scoring system can be considered as a diagnostic tool for the diagnosis of TB in children.

Limitations

Our study was limited due to small number of patients and lack of gold standard for diagnosis for comparison.

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Conflict of interest

We declare no conflict of interests.

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