

# Radiographic and other diagnostic tools used in tuberculous malnourished children in Kassala hospitals, Eastern Sudan

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SUMMARY

**Objective:** To evaluate the use of the WHO clinical criteria and the accelerated BCG test in diagnosing tuberculosis in malnourished children below five years of age admitted as diagnosed cases of tuberculosis to Kassala hospitals in the eastern part of Sudan.

**Materials and Methods:** A cross sectional hospital based study done in Kassala Teaching Hospital and Kuwaiti Paediatric Hospital during the period from January 2010 to December 2011. Data was collected through a questionnaire detailing full socio-demographic, nutritional and medical history. Examination, anthropometric measurements and investigations of the children included in the study.

**Results:** This study has included 84 children of almost equal gender distribution. The mean (SD) age was 28.8 months. Almost all were of low socio-economic class. 51(60.7%) were BCG vaccinated. Chest signs were seen in 66 of these patients (87.6%). The mantoux test was positive in 18 (21.7%) patients. The BCG test was accelerated in 51 (60.7%) of the 66 tested children. Chest radiographic changes were present in 88% of the study group. Pulmonary TB was diagnosed in 72.6% of this group. The WHO score was positive of  $\geq 7$  in 65 (78.6%) of the study group and was statistically significantly related to the chest radiography ( $p$  value $>0.027$ ) but association with the accelerated BCG test was not significant. ( $p>0.22$ ). The IUATLD clinical score chart was positive of  $\geq 5$  in 75 patients (89.3%).

**Conclusion and Recommendation:** Conclusions are that pulmonary TB is prevalent in the study group. The use of accelerated BCG as a diagnostic test is feasible, sensitive and did not show any side effects. The use of the WHO and IUATLD clinical scores both were sensitive measures of diagnosis, but they use nonspecific criteria. The recommendation from this study is it has been advised to use of accelerated BCG testing in Mantoux negative patients in the diagnosis of tuberculosis in malnourished children.

**Key words:** tuberculosis, malnutrition, WHO TSC score, IUATLD clinical score, accelerated BCG

**Abbreviations:** TB: Tuberculosis; WHO: World health organization; TSC: Tuberculosis Score Chart; IUTLD: International Union against Tuberculosis and Lung Disease; BCG: Bacille-Calmette-Guerin Vaccination; MOH: Ministry of Health; PPD: Purified Protein Derivative; TST: Tuberculosis Skin Test

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## INTRODUCTION

Tuberculosis is one of the most important public health problems in Sudan and the in the federal MOH reported TB as the fourth leading cause of health service utilization, the fourth most frequent cause of hospital deaths (16%) of all hospital deaths and the most frequent reason for hospital admission (11.6% of all hospital admissions) [1].

Tuberculosis in Sudan constitute 9% of new cases in North Africa and the Middle East region making the country the third affected one in that region [2]. In June 2000 the coverage of directly observed treatment was 75% with a cure rate of more than 87% [3].

Tuberculosis in Sudan is the average Annual Risk of Infection (ARI) which is the proportion of population that is likely to be infected over a period of one year. This is estimated in Sudan to be 1.8% putting Sudan among countries of high prevalence for TB in the East Mediterranean region. The incidence of all forms of TB is therefore about 180 per 100,000 with a detection rate of only 43.6% in the beginning of this century. Prevalence of infection between 35% and 40% with death rate of about 60 per 100,000 cases [1, 3-5]

Malnutrition increases the susceptibility and or severity of tuberculosis and exerts many detrimental effects on many aspects of host immune response against mycobacterial infection [6,7]. In children it is estimated that 1.3 million children are infected annually and the annual deaths due to TB in children reaches 450,000 worldwide [8]. TB may be responsible of about 10% of hospital admission of children in the developing countries and about 10% of hospital deaths [9].

The size of the Mantoux test was associated with the degree of malnutrition and malnutrition was associated with atypical presentation of pulmonary TB in one study [10]. BCG vaccination should not be considered in the interpretation of a positive PPD test [11]. In a Turkish study on adults and adolescents with TB the authors evaluate the results of simultaneous application of PPD and BCG tests in order to assess their efficacy. The conclusion was that BCG is more sensitive and specific than PPD in diagnosis of TB in the study group [12]. Diagnosis of TB in children is mainly epidemiologic and clinical with use of chest radiographs and skin testing bacteriological diagnosis is of lower yield in childhood tuberculosis even in developed

countries and for most children with pulmonary Tb culture confirmation is not needed [13,14]. Use of 5 tuberculin units of PPD is the standard method to detect TB infection but host factors may affect and diminish the area of induration. The test should be read within 48 to 72 hours [13-16]. Radiology should be used in a positive TST child case and it may show evidence of lymphadenopathy or lung parenchymal changes pleural lesions and cavitation are not common in tuberculosis children [15]. DNA amplification tests with polymerase chain reaction are sensitive and specific but they do not replace the routine ZN staining for AFB or culture. PCR gave positive yield results in some studies ranging from 25% to 100% [17-19]. Despite a lot of studies serology has found little place in routine diagnosis of TB example is ELISA test [20].

Diagnostic BCG test in tuberculosis children the reaction to BCG is accelerated with papules, pustule and scar appearing in few days instead of 2 to 3 months with particular importance in malnourished children [11,12]. A study in Turkey showed positive accelerated BCG in healthy children to be 100% and in malnourished children to be 82% while the Mantoux was positive in 44.5% and 18 % only in the same group of children Also similar results obtained in India [21,22]. Clinical diagnostic criteria include the WHO TB score chart depending on the duration of illness the decrease of weight for age and presence of family or other close contact past or present. Then scoring for other clinical or skin test features. A score of 7 or more is considered suggestive and treatment is recommended [23]. The presence of 3 main WHO criteria has a positive predictive value of 63% and in a study in Zambia on 75 tuberculous children the sensitivity of the WHO chart was found to be 88% while the specificity was low and is only 20% [24]. IUATLD formed a task group from 10 countries to develop a score model for childhood TB and 5 clinical criteria were adopted as the most relevant disease predictors in children: History of contact with a case of TB, Positive skin test, Persistent cough, Low weight for age and unexplained prolonged fever.

The model is of low specificity of less than 70% but good positive predictive value of (60%-77%) [25]. The objective of this study was to evaluate the use of the WHO clinical score criteria and accelerated BCG test reaction in the diagnosis of tuberculosis in malnourished children attending Kassala hospitals.

## MATERIALS AND METHODS

### Study design

This was across sectional hospital based study.

### Study area

Kassala State in Kassala Teaching and Kuwaiti paediatric hospitals and referred patients from peripheral refugee camps and rural hospitals.

### Study period

One year from January 2010 to December 2011.

### Sample size

84 patients.

### Inclusion criteria

All newly diagnosed children as cases of tuberculosis of age less than 60 months and were classified as malnutrition or underweight according to the clinical Welcome-Trust classification.

### Exclusion criteria

Neonates, age more than 60 months, parental or care giver refusal to enrol in the study, concomitant chronic medical disease.

### Research tools and techniques

A questionnaire was designed to contain full information about the nutritional social and medical history of the patient. Also examination findings anthropometric measurements and relevant investigation findings records for every patient were made. Anthropometric measurements done were the weight, height or length, and the head and mid-upper arm circumference and these were plotted against the suitable centile charts and the results were recorded. weight of every child as unclothed and in grams.

### Investigations include

The Mantoux testing (use of PPD of 5 TU strength to give an intradermal injection of 0.1 ml to produce a wheal of about 5 mm on upper third of flexor surface of left forearm. Results were read in 48 hours-72 hours), Radiology; chest x-ray, E.S.R (Westergren device), Haemoglobin concentration (calorimeter), and WBC count and differential using a haemocytometer, BCG test IN Mantoux negative patients giving freeze dried BCG of concentration 0.1 mg/0.1 ml to inject intradermal 0.1 ml on lateral aspect of upper left forearm. Test considered accelerated when papule appears within 2 days, pustule within the first week and/or scab within the first 2 weeks. ZN stain for gastric aspirate and some further investigations as relevant.

### Ethical consideration

Ethical approval from the hospital authority was requested and obtained prior to the start of the study (dated on 15.11.2009).

Also obtaining informed consent for each patient from parents or guardian direct interview for each patient performed by the author to fill the questionnaires.

### Data entry and statistics

Data obtained was entered in a computer program (SPSS) and appropriate tests for significance levels were used.

## RESULTS

A total of 84 tuberculosis malnourished children were enrolled in this cross sectional study. The males constituted 51.2% and the females 48.8%. They were of different local ethnic groups

and the mean age was 28.8 months ranging from 5 to 59 months. The different patterns of malnutrition classifications of study group are shown in Figure 1 and the different pattern of TB presentation in the study group is shown in Figure 2.

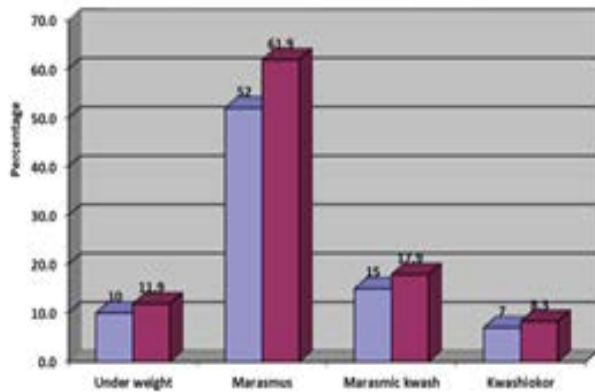


Fig. 1. The Welcome's classification of malnutrition in the study group (n = 84)

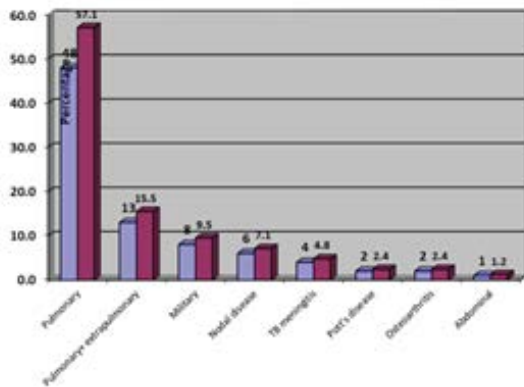


Fig. 2. The pattern of tuberculosis disease in the study group (n=84)

The positive chest x-ray features in the study group was seen 74 patients (88%) with hilar shadows in 22 patients (26.1%) consolidation in 10 patients (12%) miliary shadows in 7 children (8.3%) and consolidation-collapse shadows in 5 patients (6%)

as in Figure 3. There was no significant statistical association between x-ray features and either of the WHO clinical score (p value>0.811) nor with the IUATLD score (P value>0.775).

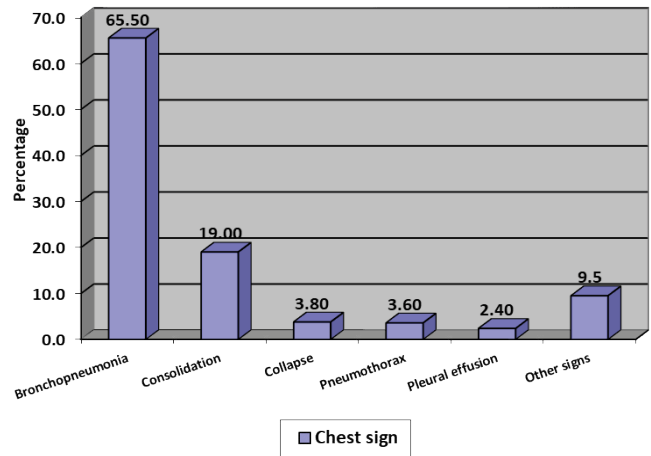


Fig. 3. The chest x-ray findings in the study group (n=84)

The reaction of Mantoux test was 10 mm and above in 18 patients (21.4%) as shown in Table 1 with no significant correlation with the type of TB disease but was significantly associated with the classification of malnutrition (P>0.001) (Table 2).

The BCG test was done in the 66 patients who were considered negative for Mantoux test (78.6% of the total patients) and the test was accelerated in 51 of these (60.7% of the total number of patients). This diagnostic BCG test showed no significant relation with

The classification of malnutrition, the WHO score chart, the IUATLD score test, nor with the age of the child in months. Statistical relationship to the age of the child is shown in Table 3.

The ESR was moderately or highly elevated in 67 patients (79.7%) and 40 of the children showed anaemia of less than 8 g/dl. ZN stain for gastric aspirate was done for 24 patients and positive results obtained in 3 of them (3.6% of total patients). The WHO TB score chart was positive of ≥ 7 in 66 patients

Mantoux size (in mm)	Frequency	Percentage
Zero	15	17.9
01-Sep	51	60.7
Oct-14	15	17.9
≥ 15	3	3.5
Total	84	100

PEM Classification	0 n(%)	1-9 n(%)	10-14 n(%)	<15 n(%)	Total n(%)
Kwashiorkor	03(3.6)	04(4.8)	00(00.0)	00(00.0)	07(8.4)
Marasmus	06(7.1)	36(42.9)	10(12)	00(00.0)	52(62)
Marasmic kwash	04(4.8)	09(9.7)	02(2.3)	00(00.0)	15(17.8)
Underweight	02(2.3)	02(2.4)	03(3.5)	03(3.6)	10(11.8)
Total	15(17.8)	51(69.8)	15(17.8)	03(3.6)	84(100.0)
p value >0.001					

**Tab. 3.** Co-relation between diagnostic BCG reaction and age in months in the study group (n=84)

Accelerated BCG TEST	Age in months			Total n(%)
	>12 n(%)	12>36 n(%)	<36 n(%)	
Non-reactive	03 (3.5)	03 (3.6)	02 (02.4)	08 (09.5)
Accelerated	10 (11.9)	21 (25)	20 (23.8)	51 (60.7)
Normal reaction	00 (00.0)	05 (06.0)	02 (2.4)	07 (08.4)
Not done	00 (00.0)	09 (10.7)	09 (10.7)	18 (21.4)
Total	13 (15.4)	38 (41.3)	33(39.3)	84 (100.0)

$\chi^2 = 11.9$ ; p value > 0.065

**Tab. 4.** The WHO tuberculosis score chart (TSC) in the study group (n=84)

Score	Frequency	Percentage
> 7	18	21.4
7-10	45	53.6
11-15	17	20.2
< 15	4	4.8
Total	84	100

(78.6%) shown in Table 4 and was statistically significantly associated with the chest x-ray features (p>0.027) but not associated significantly with type of TB, history of measles, nor the size of Mantoux test. The IUATLD clinical score was positive of  $\geq 5$  in 75 patients (89.3%). This score was significantly associated with the duration of symptoms, with presence of cough and with x-ray features of TB (p>0.001) but no significant association with type of TB disease, the positive BCG test, the Mantoux size nor the previous history of measles.

**Tab. 4.** The WHO tuberculosis score chart (TSC) in the study group (n=84)

## DISCUSSION

Mantoux test was negative in 95.1% in the study of Adil, et al. but the test size had no significant association with the mortality [26]. Similar results to this study were obtained by Go CA, et al. in Turkey in their study on in which out of 22 malnourished tuberculosis children only 4 (18%) had a positive Mantoux test [21]. Studies on non-severely malnourished children suffering from tuberculosis on Sudanese children in Khartoum by Zien, et al., Magda, et al., and Moniem, et al. showed highly positive Mantoux of 88%, 92.8% and 81% respectively [27-29].

In a large Turkish study by Gocmen, et al. on 2205 62% have a positive Mantoux reaction [30].

BCG test was done in 66 patients in this study and was accelerated in 51 of them (77.3% of the total patients) several studies recommended the use of accelerated BCG as a simple method in the diagnosis of TB particularly in children [31].

Indian studies by Chanchuri, et al. and Chandra, et al. have shown that the positivity of accelerated BCG in diagnosing TB in is much higher than the Mantoux test [22,32]

Similar results were obtained by the studies done in other parts as in Turkey by Gocmen A et al and sonomez et al [12,30].

In my study the combined use of Mantoux test and of BCG in Mantoux negative patients gave a positive skin test reaction in 82.1% of the patients in the study.

In Sudanese studies on tuberculosis children radiography was

positive in in 75% to 88% of the cases similar to the results obtained in this study.

Microscopy and ZN staining of gastric aspirate usually gives a low yield in children as in this study (only 3 patients out of 24 tested that is 3.6% of the total patients). This was also the case in studies in Sudan and other African studies. The large study by Dias on 627 TB children showed positive AFB culture in only 5% of the patients [33].

All lymph node biopsies in previous studies on Sudanese children suspected for TB were suggestive as in my study [27,29].

Although the ESR was moderately or highly elevated in 78 patients (92.8) but prevalence of anaemia and associated infections may affect the results and their interpretation.

Sixty patients (78.6%) had a WHO TSC score of  $\geq 7$  and 75 patients (89.3%) had a positive IUATLD score of  $\geq 5$  indicating that the sensitivity of both scores is high, but their specificity evaluation needs further sophisticated diagnostic tools which are not feasible such as PCR. Criticism had been directed to the use of these scores in diagnosing paediatric TB in chronically debilitated children as in malnourished children [34].

A study by Rheenen in Zambia showed high rate of false positive WHO score chart for TB in malnourished children and in spite of the high sensitivity of the score of 88% the specificity was only 25% [24].

A large study to evaluate the IUATLD scoring criteria for TB diagnosis in children Done in India by Suryan on 607 children concluded that malnutrition gives large number of false positive results and recommended that objectivity increased by adding radiological evidence to the score, the cut off point for positivity fixed higher, the weight of symptoms scaled down and the test used for screening only [35].

## CONCLUSION AND RECOMMENDATIONS

From this study done on malnourished tuberculosis suffered children in Kassala hospitals, it was concluded that pulmonary TB was the prevalent form of disease in this tuberculosis malnourished group of children and that the Mantoux skin test is not of good diagnostic value in this group as it is only positive

in about one fifth of the patients, but the accelerated BCG test was of much help in these patients (was positive in near eighty percent of the tested children) the greatest skin test positivity and benefit to diagnosis could be obtained in these affected children when both tests used together.

The WHO score and the IUATLD score in tests were found to be sensitive in diagnosing these patients but nonspecific parameters are used in them and they generally appear non-specific

The followings are recommended:

- The use of BCG test in Mantoux negative malnourished children suspected for TB Will raise the skin test positivity

(82.1% in this study )

- Adoption of the recommended scores modifications for debilitated children including that the objectivity increased by adding radiological evidence to the score, the cut off point for positivity fixed higher, the weight of symptoms scaled down and the test used for screening only.
- Human development programmes and efforts in the area reinforced in improving education levels and better nutrition, housing conditions. Vaccination coverage and sanitation.

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