



ORIGINAL RESEARCH PAPER

Paediatrics

TUBERCULOUS MENINGITIS IN BCG VACCINATED AND UNVACCINATED CHILDREN A CLINICAL AND RADIOLOGICAL COMPARATIVE STUDY

KEY WORDS: TBM, BCG

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ABSTRACT

Tuberculous Meningitis is the most serious form of Tuberculosis in children the main aim of this study is to assess protective role of BCG vaccination in TBM and compare clinical and radiological features in BCG vaccinated and unvaccinated children. We have done a prospective study in Niloufer Hospital in the year 2016-17. Out of 108 children taken into study 66 were vaccinated 42 were unvaccinated.

Materials and Methods: Children who were taken into the study satisfied the pre-defined criteria for diagnosis of TBM provided they have not received anti tubercular treatment in the last three months.

Results: The analysis showed that the vaccinated children with BCG scar had more focal deficits compared to unvaccinated children. The CT findings show more children with basal enhancement in vaccinated children.

Conclusion: Our study indicates that the outcome of TBM was similar in both BCG vaccinated and unvaccinated children. The better outcome may in part be explained by better mobilization of cell mediated immune response to the infection as reflected in high mean CSF cell count in vaccinated children.

INTRODUCTION

Tuberculosis continues to be a major public health problem globally. India is a major contributor to this global burden, harbouring nearly a third of all cases,(1) Tuberculous meningitis (TBM) is the most dangerous form of tuberculosis and is, in particular, seen in children. TBM remains an important cause of hospitalisation, death, and permanent neurological disability in children in India. Over the years there has been no noteworthy decline in the incidence of this deadly disease, despite the claims of high vaccination coverage with the bacilli Calmette Guerin (BCG) vaccine.(2) Although the BCG vaccine has been used for over 80 years there remains a shadow of doubt regarding its value in protection against Tuberculosis.(8,9) Vaccinated children mobilize their cellular immune responses more effectively compared with unvaccinated children when exposed to natural tuberculous infection, thereby experiencing fewer haematogenous complications such as military tuberculosis and TBM.

It is important to recognize the full clinical spectrum of TBM in BCG vaccinated children so that the diagnosis is not delayed. With more children being vaccinated nowadays, the clinical spectrum of TBM may be changing. We therefore undertook this prospective study to compare the clinical and radiological features of TBM in BCG vaccinated and unvaccinated children.

AIMS AND OBJECTIVES:

- To assess the protective role of BCG vaccination in TBM.
- To compare the clinical and radiological features of TBM in BCG vaccinated and unvaccinated children.
- To compare the CSF finding in BCG vaccinated and unvaccinated children.
- To assess the morbidity and mortality in BCG vaccinated and unvaccinated children.
- To assess the outcome of the children.

MATERIALS AND METHODS:

108 children between one month and 14 years of age, who were admitted to Niloufer hospital and satisfied certain predefined criteria for diagnosis of TBM, provided they had not received antitubercular treatment in the last three months were taken into study. Detailed clinical history is taken and recorded in a written proforma. General physical examination is done for all cases giving on nutritional status. Children's nutritional status is assessed by weight for age percentage. Presence or absence of BCG scar on the left or right shoulder is recorded

Each child will be divided into two groups
 Group A – BCG vaccinated children
 Group B – BCG unvaccinated children
 Sensorium was assessed using Glasgow coma scale Vitals were recorded.

Detail neurological examination is done for all cases

Outcome of TBM is noted.

Diagnostic criteria to be followed is-

Modified Ahuja Criteria for Diagnosis of TBM in Children

Modified Ahuja Criteria for Diagnosis of TBM in Children

- Mandatory factors
- Fever lasting for more than 14 days
- Abnormal CSF findings (pleocytosis with more than 20 cells and more than 60% lymphocytes, proteins>100mg/dl, sugar<60% of corresponding blood sugar values)

Additional features:

- Evidence of extra neural TB
- Positive mantoux reaction (1TU)>10mm
- Abnormal CT scan findings (2 or more of following)
- Exudates in the basal cistern or in the Sylvian fissure
- Hydrocephalus
- Infarcts
- Gyral enhancement

Investigations done

1. CBP with ESR.
2. Tuberculin test with 5TU PPD.
3. Chest x-ray.
4. CSF examination for cells, proteins, sugars and bacterial growth.
5. Cranial contrast enhanced CT scan, done within 72 hours of admission.
6. Ventricular size is measured and graded as mild, moderate and severe.
7. Basal enhancement is also graded as mild, moderate and severe
8. Hydrocephalus is classified as communicating or non communicating

OBSERVATIONS AND RESULTS

Male Children	Female Children
59 (54.6%)	54 (45.4%)

Demography

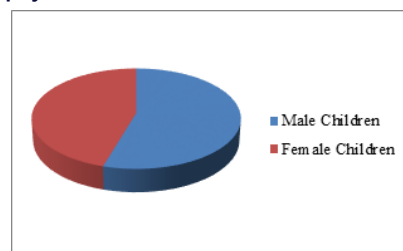


TABLE 1: Distribution of Symptoms in BCG Vaccinated and Unvaccinated Children with Tuberculous Meningitis

Symptoms	BCG scar present N = 66 (%)	BCG scar absent N = 42 (%)	p-value
Age (in years)	5.73 (4.12)	5.85 (4.29)	0.124
Duration of illness (in days)	19.06 (7.71)	21.62 (12.03)	0.18
H/O contact	14 (21.2)	16 (38)	0.056
Focal Seizures	16 (24.2)	8 (19)	0.526
Generalized Tonic Clonic Seizures	30 (45.4)	16 (38)	0.45
Fever	64 (98)	42 (100)	0.255
Headache	20 (30.3)	14 (33)	0.741
Vomiting	42 (63.6)	24 (57)	0.499
Altered Sensorium	50 (75.7)	28 (66.6)	0.305

TABLE 2: Comparison of Clinical Signs in BCG Vaccinated and Unvaccinated Children with Tuberculous Meningitis

Signs	BCG scar present (%)	BCG scar absent (%)	p-value
GCS	8.36 (3.19)	7.79 (3.99)	0.408
Meningial Signs	54 (82)	32 (76)	0.479
Focal Deficits	32 (48.4)	10 (23)	0.010 (sig)
Decerebration	6 (9)	4 (9.5)	0.939
Signs of Raised ICT	8 (12)	4 (9.5)	0.675

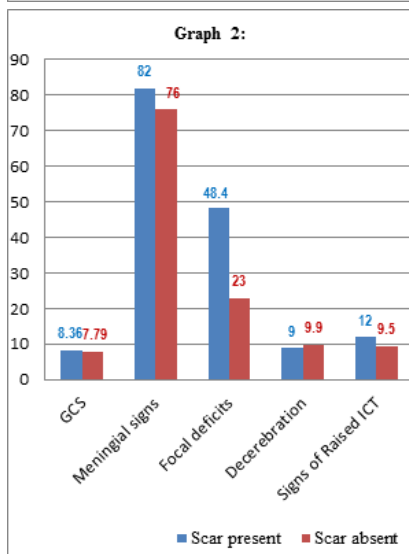
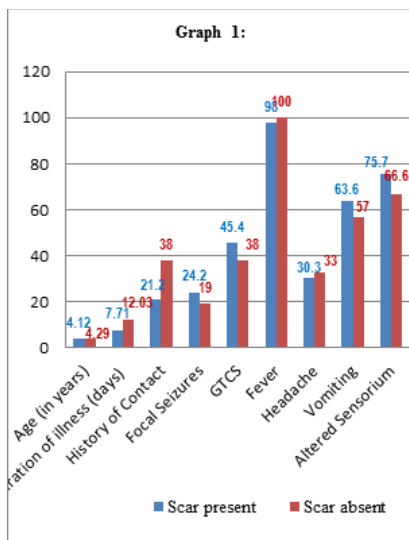


TABLE 3: Comparison of Computed Tomography Scan findings in BCG Vaccinated and Unvaccinated Children with Tuberculous Meningitis

Computed Tomography Scan Findings	BCG scar present (%)	BCG scar absent (%)	p-value
Hydrocephalous	62 (94)	38 (90.4)	0.502
Basal Enhancement	46 (69.7)	16 (38)	0.001 (sig)
Infarct	28 (42.4)	18 (42.8)	0.964
Tuberculoma	8 (15)	8 (24)	0.32

TABLE 4: Comparison of Outcomes of Vaccinated and Unvaccinated Children with TBM

Outcome	BCG scar present N = 66 (%)	BCG scar absent N = 42 (%)	p-value
Normal	14 (21.2)	8 (19)	0.271
Mild Sequelae	8 (12)	4 (9.5)	
Severe Sequelae	26 (39.3)	24 (57.1)	
Death	18 (27.2)	6 (14.2)	

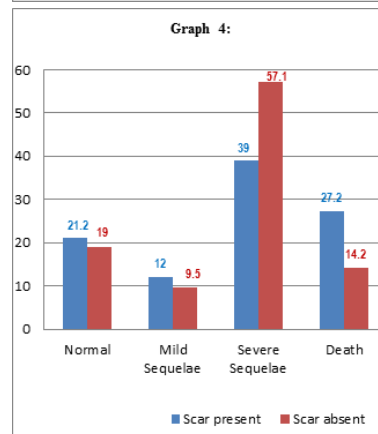
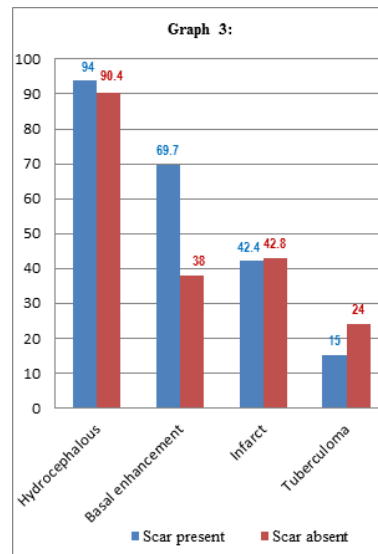


TABLE 5: Comparison of CSF findings of Vaccinated and Unvaccinated Children with TBM

CSF finding	BCG				p-value
	Scar Present		Scar Absent		
	Mean	SD	Mean	SD	
Cells	154.15	56.95	101.43	40.18	<0.001 (sig)
PML	35.26	28.81	19.02	12.57	<0.001 (sig)
Lympho-cytes	121.50	40.88	82.88	34.96	<0.001 (sig)
Protein	120.23	30.18	131.71	22.60	0.037 (sig)
Sugar	39.80	9.42	40.62	10.52	0.681

Independent sample t test

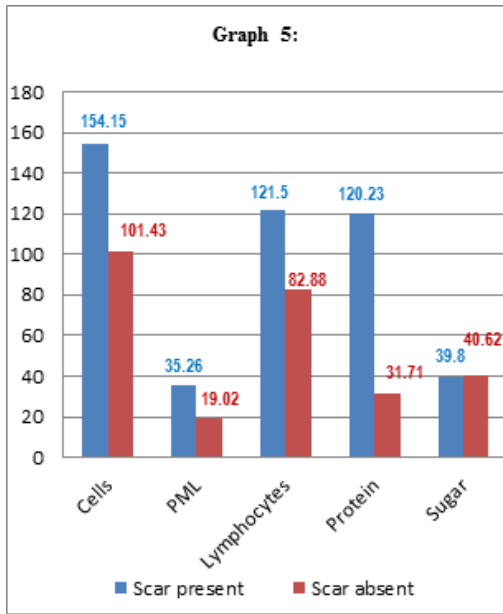
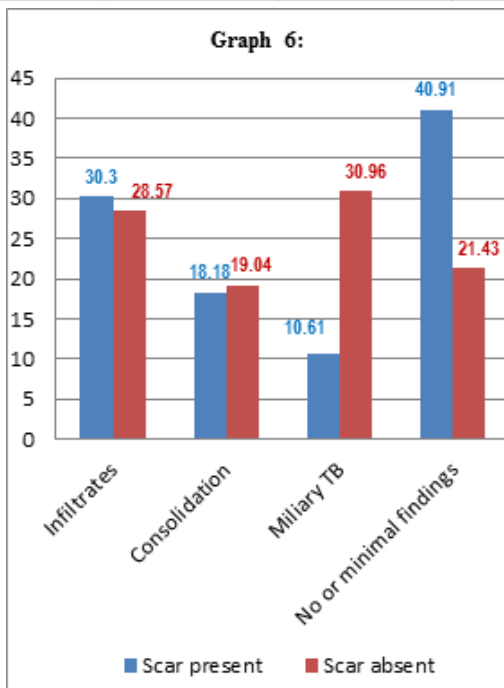


TABLE 6: Comparison of Chest X ray findings in BCG Vaccinated and Unvaccinated Children with Tuberculous Meningitis

Chest X ray findings	BCG Scar present N=66 (%)	BCG Scar absent N=42 (%)	p-value
Infiltrates	20	12	0.034 (sig)
Consolidation	12	8	
Miliary TB	7	13	
No or minimal findings	27	9	



DISCUSSION

Tuberculosis continues to be a major public health problem globally. India is a major contributor to this global burden, harbouring nearly a third of all cases(1). Tuberculous meningitis (TBM) is the most dangerous form of tuberculosis and is, in particular, seen in children.

Out of 108 children taken into study 66 were vaccinated and 42 children were unvaccinated. Our statistical comparisons of the two groups included 31 variables, only 4 showed significant differences. It can be argued that the few significant differences

could have occurred by chance. However, it must be taken into account that the significant differences were found among related variables from the history and physical examination this shows a true association. The level of significance of p value had been taken as a standard 0.05 to assess if there is any significant difference.

Out of 108 children 59 children were male and 54 children were female as seen in the demography chart. It was found that there was no significant difference in the mean age of presentation.

The comparison of clinical symptoms in the vaccinated and unvaccinated groups revealed no significant difference as depicted in Table 1. The average duration of symptoms at admission was noted to be almost similar in both groups.

The comparison of clinical signs in the vaccinated and unvaccinated groups revealed a no significant difference in the focal deficits as depicted in Table 2. The commonly encountered cranial nerve palsies observed in both vaccinated and unvaccinated children was found to be 3, 6 & 7. Of these the facial nerve was the most commonly effected. However, the children recovered well after treatment.

Computed tomography scan was done for all patients as the facility is available in our centre. Table 3 represents the CT findings, which shows a statistical significant difference in the basal enhancement values. Hydrocephalous was found in CT findings of 95% of children of which communicating type was seen in 99% of children.

CSF analysis done, showed that the average number of cells were more in the vaccinated children when compared to unvaccinated children. There was statistically significant difference in the total cells as depicted in Table 5. This may reflect a better immune response and cellular reaction to the infection in this group. Similar findings were observed by R.Kumar et al in their study (7).

The chest X ray findings showed that features of either Miliary TB or Consolidation or infiltrates. Few children had no or minimal X ray findings. There was statistical significant noted in the X ray finding (Table 6). Most of the children with severe outcome and death had Miliary TB. Udani also stated that one of the most important factors effecting prognosis in TBM is BCG vaccination, and found that death rate due to military tuberculosis and TBM was twice as high in unvaccinated children (10).

On examination the Glasgow Coma Scale score was significantly lower in this group. In a study of 80 cases between 1973 and 1975, Udani et al observed that the "conscious" type of TBM was three times commoner in vaccinated children (10). They also found that localized forms of TBM occurred more commonly in BCG vaccinated children, whereas "classic" TBM was seen twice as often in the unvaccinated children studied. This may reflect a better immune response and cellular reaction to the infection we did not observe such brain stem syndromes or cranial nerve palsies more commonly in our Vaccinated group, our study supports Udani et al's observations that BCG vaccinated children have a significantly higher rate of conscious type TBM (10). We also found significantly higher rate of focal neurological deficits in the vaccinated group.

Comparison of outcomes of vaccinated and unvaccinated children with TBM showed that severe sequelae were found in more number of unvaccinated children. But the overall outcome showed no significant difference statistically as the p value was above 0.05. The severe sequelae included disabilities like frank motor deficits leading to inability to perform routine activities, blindness, deafness and rarely a complete vegetative state.

CONCLUSION

Our study indicates that outcome of TBM was similar in both BCG vaccinated and unvaccinated children in contrast to R.Kumar et al study who reported better outcome in the vaccinated children (7). However, we studied the short term outcome only.

R. Kumar et al reported that BCG vaccination does not totally prevent occurrence of TBM our results support earlier studies suggesting that children who have been vaccinated with BCG appear to maintain better mentation and ultimately have a better outcome than unvaccinated children (7).

Our study did not reveal any significant differences in neuroradiological features to explain this finding. The better outcome may in part be explained by the better mobilization of cell mediated immune response to infection as is reflected in the higher mean CSF cell count in vaccinated children in our study.

However a long term outcome and large number of children has to be studied to give a definitive conclusion.

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