

Impact of Various Socio-Demographic Factors, BCG Scar and History of Contact on CBNAAT Detecting CNS Tuberculosis

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ABSTRACT

Aim: To evaluate the impact of various socio-demographic factors, BCG Scar and history of contact on CBNAAT detecting CNS tuberculosis

Material and method: The present was conducted from July 2017 to June 2018 in Department of Paediatrics, JLN Medical College and associated group of Hospitals, Ajmer. All the selected patients were subjected to detailed history, general physical examination, systemic examination, hematological investigations (level of hemoglobin, total leukocyte count, and differential leukocyte count, and erythrocyte sedimentation rate), radiological investigations (chest X-ray, USG cranium, cranial CT, and magnetic resonance imaging), tuberculin sensitivity test (performed by intradermal injection of 0.1 ml purified protein derivative [PPD] containing 5 tuberculin units [PPD-5] into the volar [ventral] surface of forearm by a disposable plastic tuberculin syringe), and CSF for culture and sensitivity (gold standard) and for CBNAAT (with use of quality controls).

Results: It was found that that rpoB gene of Mycobacterium tuberculosis was detected by Cartridge based nucleic acid amplification test in 66.7% of children among 0-5 yrs age group, in 40 % of females and 51.4 % of males. rpoB gene was detected by Cartridge based nucleic acid amplification test in 57.1% of patients with positive BCG scar and 42.9% of patients with absent BCG scar with a p-value of 0.02 which shows significant statistical difference.

Conclusion: It can be concluded that CBNAAT was affected by history of contact and BCG scar.

Keywords: CNS, Tuberculosis, Children

INTRODUCTION

Despite advances in the control of tuberculosis (TB) worldwide and in the United States, central nervous system (CNS) TB in children continues to have a high risk of death (~20%) and neurologic sequelae in more than one-half of survivors. In the United States, CNS TB affects ~1% to 3% of all pediatric patients with TB^{1,2}. It is most commonly diagnosed in children aged <5 years and may affect the same groups at high risk for pediatric TB. In children, CNS TB is often the result of recently acquired infection after close contact with an infectious TB case in an adult. Risk of dissemination to the CNS after TB exposure is influenced by age and immune status, including BCG vaccination³. In India, BCG vaccination is recommended in early childhood to decrease the risk of disseminated forms of TB such as miliary and CNS TB in children⁴.

At present, the diagnosis of CNS TB remains a complex issue because the most widely used conventional "gold standard" based on bacteriological detection methods such as direct smear and culture identification. The recent introduction of cartridge-based nucleic acid amplification

test (CBNAAT) has been bliss, as this assay is rapid and provides results within 2 h. It is a nucleic acid amplification test which simultaneously detects DNA of MTB complex and resistance to rifampicin (RIF) in <2 h⁵. Therefore, a planned study was conducted on the impact of various socio-demographic factors, BCG Scar and history of contact on CBNAAT detecting CNS tuberculosis.

MATERIAL AND METHOD

The present was conducted from July 2017 to June 2018 in Department of Paediatrics, JLN Medical College and associated group of Hospitals, Ajmer. The study was approved by the ethical committee of the institute. A written informed consent was obtained from the parents of the children. The subjects were included and excluded based on the following criteria's:

Inclusion Criteria: Subjects with suspected case of CNS TB either sex who met the following criteria:

1. Patient with clinically present with vague ill health lasting 2-8 weeks prior to the development of meningeal irritation. These non specific symptoms include malaise, anorexia, fatigue, fever, myalgia and headache.
2. Child may present with stiffness of neck along with :
 - a. Focal neurological deficits, behavioural changes and alteration in consciousness.
 - b. Fever with weight loss or no weight gain
 - c. History of contact in last two years
 - d. Tuberculin skin test positivity
 - e. Coexistence of precipitating illness
 - f. Abdominal USG suggestive of tuberculosis
 - g. CSF findings consistent with tubercular meningitis
 - h. Cranial CT suggestive of tuberculoma
 - i. Child present with taking history of Antiretroviral Treatment.

3. Patient who has not taken anti tuberculosis drugs.

Exclusion Criteria: Subjects already on Antitubercular therapy (ATT) were excluded.

All the selected patients were subjected to detailed history, general physical examination, systemic examination, hematological investigations (level of hemoglobin, total leukocyte count, and differential leukocyte count, and erythrocyte sedimentation rate), radiological investigations (chest X-ray, USG cranium, cranial CT, and magnetic resonance imaging), tuberculin sensitivity test (performed by intradermal injection of 0.1 ml purified protein derivative [PPD] containing 5 tuberculin units [PPD-5] into the volar [ventral] surface of forearm by a disposable plastic tuberculin syringe), and CBNAAT (with use of quality controls). Other relevant investigations were carried out wherever necessary to support the diagnosis. All the details of the examination were recorded on a specially designed pro forma with pre-tested information of study.

Statistical analysis: The data were coded and entered into Microsoft Excel spreadsheet. Analysis was done using SPSS version 24 (IBM SPSS Statistics Inc., Chicago, Illinois, USA) Windows software program.

RESULTS

Table no. 1 shows patients in the age group of 0-5 years are 37, 13 in the age group 5- 10 years and 15 in the age group 10-12 years. 55.4% of cases in our study were male while 44.6% of cases were females. Maximum number of cases belong to lower middle class with 38.5%, 33.8% were in upper lower and only 3.1% cases were of upper class. History of contact was present in 60% cases while absent in 40% of cases.

Table 2 shows that rpoB gene of Mycobacterium tuberculosis was detected by Cartridge based nucleic acid amplification test in 66.7% of children in 0-

5 yrs age group while detection among age group 5-10 & 10-12 years was 16.7% each with insignificant statistically. Mycobacterium tuberculosis was detected by Cartridge based nucleic acid amplification test in 40 % of females and 51.4 % of males with p-value of 0.42 which shows no statistical significant difference.

Graph 1 shows that rpoB gene was detected by Cartridge based nucleic acid amplification test maximum in both class III and class IV children with a percentage of 33.3% with p-value of 0.76 which shows no significant statistical difference.

Table 3 shows that rpoB gene was detected by Cartridge based nucleic acid amplification test in 57.1% of patients with positive BCG scar and 42.9% of patients with absent BCG scar with a p-value of 0.02(S) which shows significant statistical difference. Table 3 also shows percentage of children in our study with positive history of contact were 46.7% while 53.3% had no history of contact rpoB gene was detected by Cartridge based nucleic acid amplification test with P-value of 0.04 which is statistically significant.

Discussion: Our findings on the characteristics of CNS TB patients are broadly similar to those found in other studies. The young age at diagnosis has been well documented^{1,2,6} and highlights how susceptible these youngest children are to developing CNS TB.

It was observed that the positivity rate of CBNAAT in patients with a history

of TB contact was significantly higher (p=0.04) than in those with no history of contact. Furthermore, the positivity of CBNAAT was higher in lower socioeconomic groups (Class III and Class IV). Gupta et al⁷ obtained a significant association between positive history of contact and positive Xpert assay (p=0.03). Yin et al⁸ demonstrated positivity of Xpert associated significantly with a history of contact with TB in patients (p=0.010).

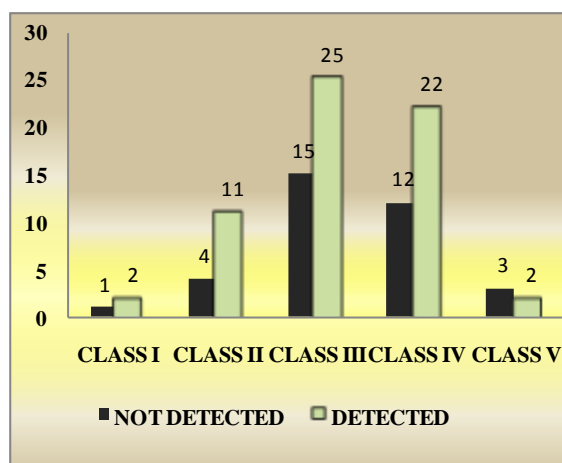
Positive CBNAAT results were obtained in 57.1% of cases which had BCG scar and in 42.9% of cases with absent BCG scar which shows the statistical difference (p=0.02). Yin et al⁸ demonstrated that positivity rate of Xpert MTB/RIF assay in patients with no BCG scar was significantly higher than in those with BCG scar (p=0.001).

Table 1: Age, gender, socioeconomic status and history of contact distribution among the study subjects

Age Group	N	%
0-5 Years	37	56.9
5-10 Years	13	20
10-12 Years	15	23.1
Gender		
Male	36	55.4
Female	29	44.6
Socioeconomic Status		
Upper	2	3.1
Upper Middle	11	16.9
Lower Middle	25	38.5
Upper Lower	22	33.8
Lower	5	7.7
Total	65	100
History of Contact		
Yes	39	60
No	26	40

Table 2: Distribution of cartridge based nucleic acid amplification test based on age and gender

			Age (Years)			p value
			0-5	5-10	10-12	
CBNAAT	Not Detected	N	17	8	10	0.32
		%	48.6%	22.9%	28.6%	
	Detected	N	20	5	5	
		%	66.7%	16.7%	16.7%	
Total		N	37	13	15	
		%	56.9%	20.0%	23.1%	
			Gender			
			Female	Male		
CBNAAT	Not Detected	N	17	18	0.42	
		%	48.6%	51.4%		
	Detected	N	12	18		
		%	40%	51.4%		
Total		N	29	36		
		%	44.6%	55.4%		



Graph 1: Distribution of cases according to CB-NAAT & socioeconomic status

Table 3: Distribution of CBNAAT based on BCG Scar and history of contact

		BCG Scar		p value
		Present	Absent	
CBNAAT	Not Detected	N 25	5	0.02*
		% 83.3%	16.7%	
Detected	N 20	15		
	% 57.1%	42.9%		
Total		N 45	20	
		% 69.2%	30.8%	
		History of Contact		
		No	Yes	
CBNAAT	Not Detected	N 10	25	0.04*
		% 28.6%	71.4%	
Detected	N 16	14		
	% 53.3%	46.7%		
Total		N 26	39	
		% 40.0%	60.0%	

*: statistically significant

Due to lack of literature, the findings of current study can't be compared at vast. Still the results of the present study revealed the importance of CBNAAT in detecting CNS tuberculosis.

Conclusion: From the results of the present study, it can be concluded that CBNAAT was affected by history of contact and BCG scar but not by age, gender and socio-economic status.

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