

Frequency of BCG Vaccination in Patients of Tuberculous Meningitis

Maryam Riaz and Abdul Basit

ABSTRACT

Objective; To determine frequency of BCG Vaccination in patients of tuberculous meningitis presenting at a tertiary care hospital.

Study Design: Descriptive study.

Place and Duration of Study: This study was conducted at the Department of Pediatric Medicine, Services Hospital Lahore from June 2016 to June 2017.

Materials and Methods; A total of 167 Patients were included in the study. Patients with Tuberculous meningitis (TBM) less than 5 years of age were included. Patients having acute onset of encephalopathy and those with lumbar puncture contraindicated were excluded from our study. Demographic bio data (patient name, father name, age, gender, date of admission) was taken. After that complete history regarding presenting complaints and vaccination were taken. Physical examination will be done. BCG scar mark was identified on examination. CSF examination, Chest X-ray, CT scan brain was done from single laboratory. Tuberculin test was applied and interpreted by experience pediatrician. Data was recorded on the specifically designed proforma.

Results; Of these 167 study cases, 106 (63.5%) were boys while 61 (36.5%) were girls. Mean age of our study cases was 3.31 ± 0.98 years. Mean duration of disease was noted to be 4.71 ± 1.49 weeks. History of contact with index TB patients was positive in 114 (68.3%) of our study cases, 68 (40.7%) were from rural areas and 99 (59.3%) from urban areas and majority of them i.e. 90 (53.9%) belonged to poor families with majority of mothers i.e. 129 (77.2%) were uneducated. BCG vaccination was positive in 94 (56.3 %) of our study cases.

Conclusion; Our study results support the use of BCG vaccination as it has some protective role against TB. Very high frequency of history of contact with positive index case was observed in our study. BCG vaccination was significantly associated with gender, history of contact with index case and socioeconomic status.

Key Words; BCG vaccination, tuberculous meningitis, frequency.

Citation of article: Riaz M, Basit A. Frequency of BCG Vaccination in Patients of Tuberculous Meningitis. Med Forum 2017;28(11):97-100.

INTRODUCTION

Tuberculosis (TB) is one of the leading causes of mortalities occurring due to infectious diseases all over the world although there has been dramatic advancements in the fields of diagnosis and treatment¹⁻³. World Health Organization (WHO) reported approximately 10 million new patients with TB in 2010 and around 2 million mortalities every year, even though it is a curable infection⁴⁻⁶. Tuberculous meningitis (TBM) is generally more prevalent in developing countries where it is more common in different population subsets and increased proportion of the human immunodeficiency virus (HIV) harbors the onset of higher numbers of new cases⁷.

However in recent years tuberculosis is also commonly seen in developed countries as a result of immigrations of infected people¹ because of escalation of violence

in certain regions and also due to excessive use of certain biological agents which favor TB spread.^{8,9}

Children are more vulnerable of all who are at increased risk of suffering from TBM as a result of their inability to combat the primary infection in their lungs.^{1,9} TBM is highly devastating infectious disease having approximately 30% mortality rates in case of most severe forms. Additionally other 50% of cases who survive develop neurological sequelae even after administration of appropriate intake of antibiotics.^{10,11}

BCG (Bacillus Calmette–Guérin) is a vaccine against tuberculosis that is prepared from a strain of the attenuated (virulence-reduced) live bovine tuberculosis bacillus, *Mycobacterium bovis*. The BCG vaccination and its protective effect appears to vary according to geography. BCG vaccination is recommended to be given intradermally by a nurse skilled in the technique after birth.¹² BCG is very efficacious against tuberculous meningitis in the pediatric age group, but its efficacy against pulmonary tuberculosis appears to be variable. BCG seems to have its greatest effect in preventing military TB or TB meningitis, so it is still extensively used even in countries where efficacy against pulmonary tuberculosis is negligible¹³.

Frequency of BCG vaccination was noted in 83.4% of the Tuberculous meningitis children¹⁴ and in another

Department of Pediatric Medicine, Services Hospital Lahore.

Correspondence: Dr. Abdul Basit, Ex-House Officer,
Department of Pediatric Medicine, Services Hospital Lahore.
Contact No: 0300-5393022
Email: info.basit@gmail.com

Received: July 17, 2017;

Accepted: September 09, 2017

study it was 57.4% of tuberculous meningitis paediatric patients¹⁵.

This study was done to monitor the efficacy of BCG vaccination in patients against tuberculous meningitis. With lack of good clinical evidence on the subject and the resulting practice variation additional data regarding this is needed. Moreover there is no such data and no clinical trials conducted on this issue is available here at in our local population.

MATERIALS AND METHODS

A total of 167 Patients were included in the study. Patients with Tuberculous meningitis (TBM) less than 5 years of age were included from department of pediatric medicine Services Hospital, Lahore. Patients having acute onset of encephalopathy and those with lumbar puncture contraindicated were excluded from our study. TBM was diagnosed as CSF showing predominant lymphocyte pleocytosis ≥ 50 cells/umm, proteins ≥ 60 mg/dl, sugar $< 2/3^{\text{rd}}$ of blood level plus supportive along with essential two or more present; History of fever of two weeks or more, positive family history of TB, tuberculin skin test of 10mm or more with 5 TU of PPD, superficial adenitis of tuberculosis etiology proved by histology/FNAC, positive radiological evidence of TB in chest, CT scan evidence of basal exudates and/or ventricular dilatation in CNS TB. Demographic bio data (patient name, father name, age, gender, date of admission) was taken. After that complete history regarding presenting complaints and vaccination were taken. Physical examination will be done. BCG scar mark was identified on examination. CSF examination, Chest X-ray, CT scan brain was done from single laboratory. Tuberculin test was applied and interpreted by experience pediatrician. Data was recorded on the specifically designed proforma. Data was analyzed with statistical analysis program (SPSS version 20). Mean and standard deviation was calculated for quantitative variables like age of the patients. Frequency and percentages were computed for qualitative variables like gender, history of contact with TB patients and BCG vaccination status. Confounders like age and gender were controlled by stratification. Post stratification chi-square test was applied to see their effect on outcome at 0.05 level of significance.

RESULTS

Of these 167 study cases, 106 (63.5%) were boys while 61 (36.5%) were girls. Mean age of our study cases was 3.31 ± 0.98 years ranging from 2 – 5 years. Mean age of boys was 3.23 ± 0.95 years while that of girls was 3.46 ± 1.00 years ($p = 0.141$). Mean duration of disease was noted to be 4.71 ± 1.49 weeks. Mean duration of illness in boys was 5.00 ± 1.62 weeks while in girls was 4.20 ± 1.09 weeks ($p = 0.001$).

Table No. 1: Stratification of BCG vaccination with regards to gender. (n = 167)

Regards to Gender (n = 167)			
Gender	BCG Vaccination		P – value
	Yes (n=94)	No (n=73)	
Male (n=106)	49	57	0.001
Female (n=61)	45	16	
Total	167		

Table No. 2: Stratification of BCG vaccination with regards to age. (n = 167)

Age groups	BCG Vaccination		P – value
	Yes (n=94)	No (n=73)	
1 – 3 Years (n=99)	52	47	0.268
More than 3 Years (n=68)	42	26	
Total	167		

Table No. 3: Stratification of BCG vaccination with regards to disease duration. (n = 167)

regards to disease duration. (n = 167)			
Disease duration	BCG Vaccination		P – value
	Yes (n=94)	No (n=73)	
Less than 4 weeks (n=47)	30	17	0.231
4 – 8 weeks (n=120)	64	56	
Total	167		

Table No. 4: Stratification of BCG vaccination with regards to History of contact with TB patient.

regards to history of contact with TB patient.			
History of contact	BCG Vaccination		P – value
	Yes (n=94)	No (n=73)	
Yes (n=114)	55	59	0.002
No (n=53)	39	14	
Total	167		

Table No. 5: Stratification of BCG vaccination with regards to residential status. (n = 167)

Residential status	BCG Vaccination		P – value
	Yes (n=94)	No (n=73)	
Rural (n=68)	37	31	0.752
Urban (n=99)	57	42	
Total	167		

History of contact with index TB patients was positive in 114 (68.3%) of our study cases, 68 (40.7%) were from rural areas and 99 (59.3%) from urban areas and majority of them i.e. 90 (53.9%) belonged to poor families with majority of mothers i.e. 129 (77.2%) were

uneducated. BCG vaccination was positive in 94 (56.3%) of our study cases.

DISCUSSION

There exists controversy regarding protective efficacy of BCG vaccination among children against tuberculous meningitis (TBM). Various factors such as child age, dietary habits, family status and positive index case in the family play potential role in its protective efficacy but there is limited data from our population on this topic. So this study was done to ascertain protective role of BCG vaccination in pediatric population with TBM¹⁶.

Our study included a total of 167 children with tuberculous meningitis meeting inclusion/exclusion criteria of our study. Of these 167 study cases, 106 (63.5%) were boys while 61 (36.5%) were girls. Masood et al¹⁵ reported equal distribution of male to female gender but our study results have reported male gender predominance. Nabukeera-Barungi et al¹⁷ also reported 1:1 male to female ratio which is different from our study results.

Tuberculous meningitis has traditionally been reported to be more common in children of younger age groups¹⁵. Mean age of our study cases was 3.31 ± 0.98 years ranging from 2 – 5 years. Mean age of boys was 3.23 ± 0.95 years while that of girls was 3.46 ± 1.00 years ($p = 0.141$). Nabukeera-Barungi et al¹⁷ reported mean age 32 months which is close to our study results. Masood et al¹⁵ also reported that majority of the TBM patients were younger around 2 years of age which is similar to our study findings.

Mean duration of disease was noted to be 4.71 ± 1.49 weeks. Mean duration of illness in boys was 5.00 ± 1.62 weeks while in girls was 4.20 ± 1.09 weeks ($p = 0.001$). Our study results have indicated that majority of our study cases i.e. 120 (71.9%) presented with duration of 4 – 8 weeks of illness. Kumar et al¹⁸ reported mean duration of disease to be 35.1 days which is close to our study results.

History of contact with index TB patients was positive in 114 (68.3%) of our study cases, 68 (40.7%) were from rural areas and 99 (59.3%) from urban areas and majority of them i.e. 90 (53.9%) belonged to poor families with majority of mothers i.e. 129 (77.2%) were uneducated. Masood et al¹⁵ reported that 70.4 % of the children with TBM had history of contact with TB patients which is similar to our study results.

The reported efficiency of B.C.G. vaccine in prevention of primary childhood or sputum positive adult tuberculosis very widely but it is believed to offer significant protection against hematogenous forms of tuberculosis. BCG vaccination was positive in 94 (56.3%) of our study while a study conducted by Nabukeera-Barungi et al¹⁷ reported 50% BCG vaccination in children with TBM which is close to our findings. Masood et al¹⁵ reported 57.4 % patients with

TBM had BCG vaccination. Chavalittamrong et al¹⁹ from Thailand reported 52.1% BCG vaccination in children with TBM which is again in compliance with our study results. Similar results have been reported by Kumar et al¹⁸.

CONCLUSION

Our study results support the use of BCG vaccination as it has some protective role against TB. Very high frequency of history of contact with positive index case was observed in our study. BCG vaccination was significantly associated with gender, history of contact with index case and socioeconomic status.

Author's Contribution:

Concept & Design of Study:	Maryam Riaz
Drafting:	Abdul Basit
Data Analysis:	Maryam Riaz
Revisiting Critically:	Abdul Basit, Maryam Riaz
Final Approval of version:	Maryam Riaz

Conflict of Interest: The study has no conflict of interest to declare by any author.

REFERENCES

1. Kazemnejad A, Arsang Jang S, Amani F, Omid A. global epidemic trend of tuberculosis during 1990-2010: using segmented regression model. *J Res Health Sci* 2014;14(2):115-21.
2. Pereira L. Tuberculosis: role of etiologic diagnosis and tuberculin skin test. *PediatrPulmonol Suppl* 2004;26:240-2.
3. Drobac PC¹, Shin SS, Huamani P, Atwood S, Furin J, Franke MF, et al. Risk factors for in-hospital mortality among children with tuberculosis: the 25-year experience in Peru. *Pediatr* 2012;130:e373-9.
4. Targeted tuberculin testing and treatment of latent tuberculosis infection. American Thoracic Society. *MMWR Recomm Rep* 2000;49:1-51.
5. Hatherill M, Hawkrige T, Zar HJ, Whitelaw A, Tameris M, Workman L, et al. Induced sputum or gastric lavage for community-based diagnosis of childhood pulmonary tuberculosis? *Arch Dis Child* 2009;94:195-201.
6. van den Bos F, Terken M, Ypma L, Kimpen JL, Nel ED, Schaaf HS, Schoeman JF, et al. Tuberculous meningitis and miliary tuberculosis in young children. *Trop Med Int Health* 2004;9: 309-13.
7. Thampi N, Stephens D, Rea E, Kitai I. Unexplained deterioration during antituberculous therapy in children and adolescents: clinical presentation and risk factors. *Pediatr Infect Dis J* 2012;31:129-33.
8. Amanatidou V, Syridou G, Mavrikou M, Tsolia MN. Latent tuberculosis infection in children:

- diagnostic approaches. *Eur J Clin Microbiol Infect Dis* 2012;31(7):1285-94.
9. Sandhu GK. Tuberculosis: current situation, challenges and overview of its control programs in India. *J Glob Infect Dis* 2011;3(2):143-50.
 10. Farinha NJ, Razali KA, Holzel H, Morgan G, Novelli VM. Tuberculosis of the central nervous system in children: a 20-year survey. *J Infect* 2000; 41:61-8.
 11. Saitoh A, Pong A, Waecker Jr NJ, Leake JA, Nespeca MP, Bradley JS. Prediction of neurologic sequelae in childhood tuberculous meningitis: a review of 20 cases and proposal of a novel scoring system. *Pediatr Infect Dis J* 2005;24:207-12.
 12. Manjunatha MV, Michael FG, Andres B, John C, William RJ, Steven AP. In vitro culture medium influences the vaccine efficacy of *Mycobacterium bovis* BCG. *Vaccine* 2012;30(6): 1038-49.
 13. Rodrigues LC, Diwan VK, Wheeler JG. Protective effect of bcg against tuberculous meningitis and miliary tuberculosis: a meta-analysis. *Int J Epidemiol* 1993;22 (6):1154-8.
 14. Khichi GQK, Channar MS, Mannan MA. Tuberculosis in BCG vaccinated and non-vaccinated children under 15 years of age. *Pak Paed J* 2003;27(3):114-6.
 15. Masood N, Sharif M, Asghar R. Spectrum of tuberculosis in BCG vaccinated and unvaccinated children. *J Rawal Med Coll* 2010;14(2):60-3.
 16. Güneş A, Uluca Ü, Aktar F, Konca Ç, Şen V, Ece A, et al. Clinical, radiological and laboratory findings in 185 children with tuberculous meningitis at a single centre and relationship with the stage of the disease. *Ital J Pediatr* 2015;41:75.
 17. Nabukeera-Barungi N, Wilmshurst J, Rudzani M, Nuttall J. Presentation and outcome of tuberculous meningitis among children: experiences from a tertiary children's hospital. *Afr Health Sci* 2014; 14(1):143-9.
 18. Kumar R¹, Dwivedi A, Kumar P, Kohli N. Tuberculous meningitis in BCG vaccinated and unvaccinated children. *J Neurol Neurosurg Psychiatr* 2005;76(11):1550-4.
 19. Chavalittamrong B, Chearskul S, Tuchinda M. Protective value of BCG vaccination in children in Bangkok, Thailand. *Pediatr Pulmonol* 1986; 2(4):202-5.