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FREQUENCY OF BCG VACCINATION IN CHILDREN WITH TUBERCULOUS MENINGITIS AT LIAQUAT UNIVERSITY HOSPITAL HYDERABAD.

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ABSTRACT... Objectives: To determine the frequency of BCG vaccination in children with tuberculous meningitis of age 01 to 12 years at Liaquat University Hospital Hyderabad. **Study Design:** Cross sectional descriptive study. **Setting:** Department of Pediatrics, Liaquat University Hospital, Jamshoro / Hyderabad. **Period:** Six months from 20-08-2016 to 20-02-2017. **Material and Methods:** A total of 189 children with history of fever (axillary temperature >37.2°C) for ≥14 days duration with presentation, CT scan and CSF findings consistent with tuberculous meningitis were selected in this study. The data was collected on pre-structured proforma (attached). **Results:** There were 86(45.5%) male and 103(54.5%) female. Frequency of BCG vaccination in children with tuberculosis meningitis was found in 130(68.78%) cases. **Conclusion:** Our results show effectiveness of BCG vaccine in preventing TBM. Regardless of the protective efficacy of BCG in preventing pulmonary tuberculosis, in areas in which tuberculosis affects a significant percentage of the population, continued use of BCG may be warranted to prevent tuberculous meningitis.

Key words: Tuberculous Meningitis, BCG Vaccination, Pulmonary Tuberculosis.

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INTRODUCTION

Tuberculosis keeps on being a noteworthy general medical issue internationally while tuberculous meningitis (TBM) is the most perilous type of tuberculosis specifically observed in children.[1,2] TBM remains an essential reason for hospitalization, demise, and changeless neurological incapacity in kids in Pakistan.[3,4] Over the years there has been no critical decrease in the rate of this destructive ailment, notwithstanding the cases of high immunization inclusion with the Bacillus-Calmette-Guerin (BCG) antibody.[5]

Despite the fact that the BCG antibody has been utilized for more than 80 years, there remains a sorry excuse for uncertainty in regards to its incentive in insurance against tuberculosis.[6] Although the defensive adequacy of BCG immunization in grown-up types of the illness is dubious, it is held to be helpful in keeping the spread of and enhancing result of tubercular infection.[7] Vaccinated kids prepare their cell invulnerable reactions all the more viably when presented to regular tuberculous disease in spite of the fact that encountering haematogenous intricacies, for example, miliary tuberculosis and TBM.[8] However this insurance is just relative and might be defeated in nearness of an overwhelming contaminating portion from a family contact, within the sight of extreme hunger and as a result of winding down insusceptibility numerous years after vaccination.[9] There are few reports in the writing that depict particular clinical range of TBM in BCG immunized children[10,11], while the revealed commonness for BCG immunization in youngsters with tuberculous meningitis was 77% in the investigation by Thilothammal N, et al.[12]

Therefore, it is important to recognize the frequency of BCG vaccination in children with TBM of 1 to 12 years of age, so that early protective parameters can be achieved. The data regarding the BCG vaccination in children with TBM is scarce in our population while the study

was supportive for primary care pediatrician and health care providers for the evaluation of BCG vaccination in children presented with tuberculous meningitis because early screening was helpful to take appropriate measures whereas the decision for management plan can be taken according to the results of the study.

MATERIAL AND METHODS

The Cross sectional descriptive study was conducted in the department of Pediatrics, Liaquat University Hospital, Jamshoro / Hyderabad (20-08-2016 to 20-02-2017). Total 189 children with tuberculous meningitis was taken by non-probability consecutive sampling. The inclusion criteria were the children of 01 to 12 years of age, of either gender have history of fever (axillary temperature >37.2°C) for≥14 days duration with presentation, CT scan and CSF findings consistent with tuberculous meningitis (mentioned in operational definition).

(I) TUBERCULOUS MENINGITIS

(a) Clinical presentation with fever (axillary temperature ≥ 37.2ºC) for 14 days
(b) Cranial / Brain CT scan
(c) Cerebrospinal fluid (CSF) shows raised protein (>400 mg/dl), decrease glucose (<40 mg/dl) and pleocytosis with predominant lymphocytes (>10 cells/mm^3).
The tuberculous meningitis was labeled when all of the above given parameters (a-c) are present.

(II) BCG VACCINATION

Was observed through gross physical examination (sign) by the presence of a scar with raised center on the left shoulder / arm

Exclusion Criteria

The children with history of congenital anomalies of CNS (encephalocele, microcephaly), brain tumors, cerebral malaria and abscess, the children already on anti-tuberculous therapy and the bacterial and viral meningitis.

The above mentioned disorders was evaluated by the specific history and relevant clinical examinations so that the effect modifiers can be controlled. Moreover, by the existence of previous medical record, hospitalization, laboratory investigations evidences and diagnosed slips given by consultant pediatrician mentioning such disorders as a diagnosis.

All children presenting in pediatric department of Liaquat University Hospital Hyderabad / Jamshoro with fulfillment of the inclusion criteria was recruited and enrolled in the study. The tuberculosis meningitis children were assessed for BCG vaccination scar according to the criteria and parameter mentioned in the operational definition. The senior consultant pediatrician of the ward was confirmed the scar while the written consent was taken from parents / guardians to participate in the study. The data was collected on pre-structured proforma (attached). Regarding financial compensation, all the expenditures of the study was bear by researcher and all the clinical maneuvers (history taking and clinical examinations) was performed by me under the supervision of senior consultant pediatrician (have ≥05 years clinical experience) in the pediatric department.

The data of all patients was analyzed in SPSS version 17.00. The frequency and percentage (%) was calculated for BCG vaccination in children with TBM and also for gender distribution. The qualitative variables are gender and BCG vaccinations while the mean ± standard deviation (SD) was calculated for numerical / quantitative variables (age, BMI and duration).

The stratification was done for age, gender, BMI (measure in kg/m^2), rural, urban, acute malnutrition and duration of disease to see the effect on outcome and the p-value ≤0.05 was considered as statistically significant.

RESULTS

A total of 189 children with history of fever (axillary temperature >37.2°C) for ≥14 days duration with presentation, CT scan and CSF findings consistent with tuberculous meningitis were selected in this study. Most of the children were 1 to 5 years of age as shown in Figure-1. There were 86(45.5%) male and 103(54.5%) female (Figure-2). Out of 189 children, 53.97% were belonged to urban

and 46.03% belong to rural as shown in Figure-3. An acute malnutrition observed in 77(40.74%) as shown in Figure-4.

Frequency of BCG vaccination in children with tuberculosis meningitis was found in 130(68.78%) cases as presented in Figure-5. Stratification analysis was performed and observed that there was no significant difference in frequency of BCG vaccination between age groups as shown in Table-I&II. Similarly this difference was not observed between male and female and urban and rural as shown in Table-III and IV respectively. Frequency of BCG vaccination was significant with BMI, duration of disease and acute malnutrition as shown in Table-V to VII.

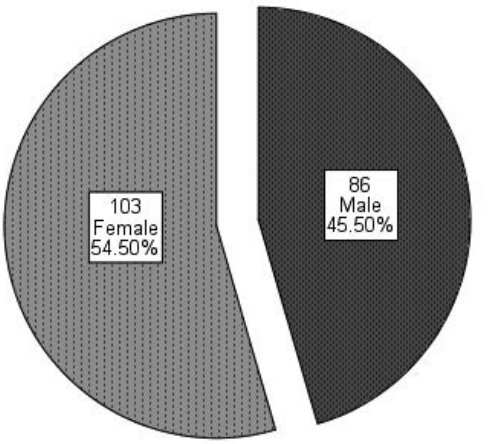

Figure-2. Gender distribution n=189

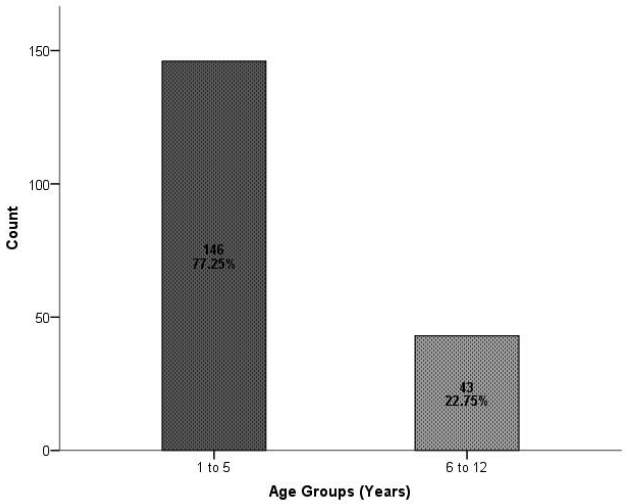

Figure-1. Age distribution of the patients n= 189

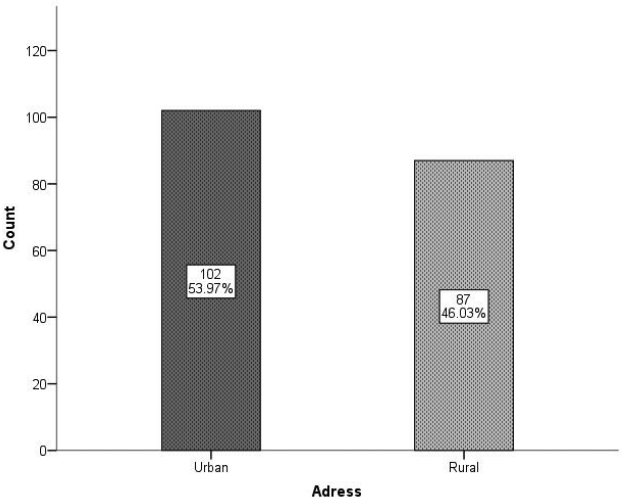

Figure-3. Rural distribution n=189

Statistics		Age (Years)	BMI (kg/m²)	Duration of Disease (Days)
Mean		4.77	20.06	5.84
Std. Deviation		2.55	3.44	1.53
95% Confidence Interval for Mean	Lower Bound	4.41	19.57	5.62
	Upper Bound	5.14	20.56	6.06
Median		4.20	20.76	6.00
Interquartile Range		2	6.6	2

Table-I. Demographic characteristics of patients n= 189

Age Groups (Years)	BCG Vaccination		Total	P-Value
	Yes	No		
1 to 5	104(71.2%)	42(28.8%)	146	0.180
6 to 12	26(60.5%)	17(39.5%)	43	

Table-II. Frequency of BCG vaccination in children with tuberculous meningitis by age groups n= 189 Chi-Square= 1.794

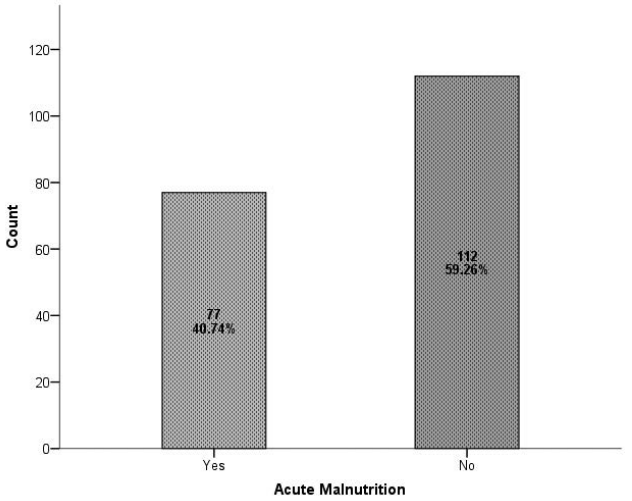

Figure-4. Acute malnutrition n=189

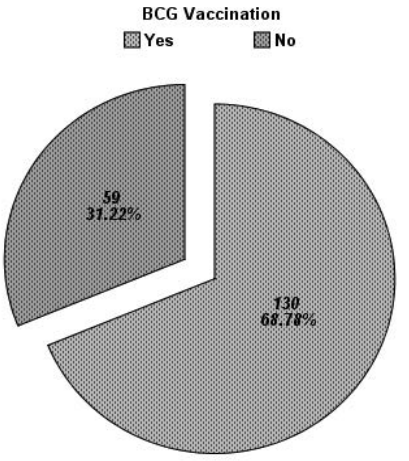

Figure-5. Frequency of BCG vaccination in children with tuberculous meningitis n= 189

Gender	BCG Vaccination		Total	P-Value
	Yes	No		
Male	60(69.8%)	26(30.2%)	86	0.790
Female	70(68%)	33(32%)	103	

Table-III. Frequency of BCG vaccination in children with tuberculous meningitis by gender n= 189
Chi-Square= 0.071

Residence	BCG Vaccination		Total	P-Value
	Yes	No		
Urban	66(64.7%)	36(35.3%)	102	0.190
Rural	64(73.6%)	23(26.4%)	87	

Table-IV. Frequency of BCG vaccination in children with tuberculous meningitis by residence n= 189
Chi-Square= 1.716

BMI	BCG Vaccination		Total	P-Value
	Yes	No		
< 18.5	71(89.9%)	8(10.1%)	79	0.0005
≥18.5	59(53.6%)	51(46.4%)	110	

Table-V. Frequency of BCG vaccination in children with tuberculous meningitis by BMI n= 189
Chi-Square= 28.18

Duration of Disease	BCG Vaccination		Total	P-Value
	Yes	No		
≤6 days	104(73.8%)	37(26.2%)	141	0.011
>6days	26(54.2%)	22(45.8%)	48	

Table-VI. Frequency of BCG vaccination in children with tuberculous meningitis by duration of disease n= 189
Chi-Square= 6.402

Acute Malnutrition	BCG Vaccination		Total	P-Value
	Yes	No		
Yes	69(89.6%)	8(10.4%)	77	0.0005
No	51(54.5%)	51(45.5%)	112	

Table-VII. Frequency of BCG vaccination in children with tuberculous meningitis by acute malnutrition n= 189
Chi-Square= 26.25

DISCUSSION

Tuberculosis keeps on being an across the board sickness particularly in creating nations. Tuberculous meningitis, a genuine inconvenience of this disease, happens in 7-12% of patients with tuberculosis and it is progressively regular in children. In youngsters, even with treatment, the mortality of tuberculous meningitis is 27% and changeless inability is assessed to be as high as 39%.[13] Tuberculosis (T.B) is in charge of real weight on wellbeing and financial matters low pay areas in which Pakistan is additionally included. Pakistan positions 6th on the planet having 1.5 million TB patients, with 250,000 new cases each year. Globally the malady is in charge of 26 percent avoidable passings. The rate of TB is 181/100000 and out of which half are AFB positive cases1. The precise figures of youth TB in Pakistan is obscure. Bacillus Calmette– Guérin (BCG) antibody is an immunization basically utilized against tuberculosis.[14] In nations where tuberculosis is normal, one portion is prescribed in sound infants as near the season of birth as possible. Rates of security against tuberculosis contamination fluctuate generally and assurance endures somewhere in the range of ten and twenty years. Among youngsters it keeps about 20% from getting tainted and among the individuals who do get contaminated it shields half from creating disease.[15] In this study to determine the frequency of BCG vaccination in children with tuberculous meningitis of age 01 to 12 years, A total of 189 children with history of fever (axillary temperature >37.2°C) for ≥14 days duration with presentation, CT scan and CSF findings consistent with tuberculous meningitis were selected. Children aged 6 months to 5 years are among the age groups most frequently suffering from TBM.[8,16] In our study out of 189 children, 77.2% were from 1 to 5 years of age reflecting most vulnerable age. So it is clear that children under the age of 5 years were vulnerable and these should be prevented from tuberculous infection. Our observation is supported by other studies. N Thilothammal et al in their prospective study reported the age of the 107 patients ranged from 6 months to 12 years. The number of children under 5 years was 69%.[17] Ailing health and tuberculosis are the two issues of extensive extent in the greater part of the immature areas of the world. Lack of healthy sustenance is a noteworthy wellbeing danger and mother of all issues in pediatric diseases.[18,19] It improves the dismalness as well as builds the death rate in kids. The term utilization has been for all intents and purposes synonymous with tuberculosis since the commencement[20] and the connection among tuberculosis and ailing health has for quite some time been perceived; hunger may incline individuals to the improvement of clinical sickness and tuberculosis can add to malnutrition.[21] In our examination intense lack of healthy sustenance youngster was seen in 77(40.74%).

Inoculation during childbirth with BCG is generally connected as a feature of the Expanded Program on Immunization of the WHO.[22] Appraisals of its adequacy differ[23], attributable to an assortment of putative components.[24,25] The degree to which BCG immunization manages security against TBM is still discussed. As an ever increasing number of youngsters are being inoculated with BCG, the clinical range of the sickness (TBM) might change. A meta-examination of the distributed preliminaries on the viability of BCG inoculation proposed a defensive impact of 64% against TBM.[26] This figure is higher than that recommended for aspiratory TB (half), however may just reflect progressively precise case ascertainment of TBM given the all inclusive prerequisite for admission to clinic. Generally speaking, these and different investigations bolster the view that BCG immunization is defensive against TBM.

In our investigation Frequency of BCG immunization in kids with tuberculosis meningitis was found in 68.78% cases, appearing of BCG antibody in counteracting TBM. The outcomes from studies attempted to discover the adequacy of BCG in anticipating tuberculous meningitis have been empowering and the defensive viability has extended from 52-84%.[27,28,29] It is conceivable that BCG can forestall tuberculous meningitis by averting scattering of the tubercle bacillus inside the body regardless of whether passage isn't prevented.[30] In an investigation of 80 cases somewhere in the range of 1973 and 1975, Udani

et al saw that the ''cognizant'' sort of TBM was multiple times everyday citizen in inoculated children.[31] They additionally discovered that confined types of TBM happened all the more ordinarily in BCG immunized kids, while ''great'' TBM was considered twice to be regularly in the unvaccinated youngsters examined. Truly, Western nations that utilized BCG as a component of their TB control methodology did not encounter any more noteworthy decreases in the frequency or death rates from TB than nations that did not utilize BCG, for example, the Netherlands. In perspective of this, the estimation of BCG inoculation in controlling the transmission of Mycobacterium tuberculosis has been believed to be constrained. In any case, BCG is as yet viewed as helpful in lessening the frequency of tuberculous meningitis in youngsters.

CONCLUSION

Our outcomes show viability of BCG antibody in avoiding TBM. Notwithstanding the defensive adequacy of BCG in forestalling aspiratory tuberculosis, in zones in which tuberculosis influences a critical level of the populace, proceeded with utilization of BCG might be justified to counteract tuberculous meningitis. A noteworthy number of youngsters in our examination were discovered malnourished and as the connection among tuberculosis and lack of healthy sustenance has for quite some time been remembered, we suggest that in the TB destruction program the issue of Protein Calorie Malnutrition, particularly in youthful kids younger than 5 years, ought to likewise be managed. Each Health office should concentrate on giving BCG antibody during childbirth. The virus chain of BCG antibody ought to be required which results into the viability of the BCG immunization and it restraints the recurrence of TBM.

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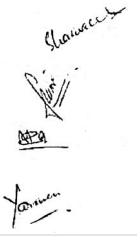
AUTHORSHIP AND CONTRIBUTION DECLARATION

Sr. #	Author-s Full Name	Contribution to the paper	Author's Signature
1	Shamaeel	Collected and interpreted data from pediatric department.	
2	Farzana Shaikh	Contribution for conception and design, Analysis and interpretation of data.	
3	Ghulam Shabbir Laghari	Collected and interpreted the data.	
4	Yasmeen Memon	Final reversion of data.	