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Original Research Article

Association of Nutritional status and BCG vaccination with Tuberculosis in Children in a Tertiary care centre: A Case Control study

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Abstract:

Background: India reported 2.82 million TB cases in 2022. Paediatric tuberculosis continues to be a significant contributor to illness and death. Malnutrition has a significant impact on the development, treatment outcomes and cure of Tuberculosis (TB). BCG vaccination is effective in preventing the complications of TB and its spread. This study tried to find out the association between nutritional status and BCG vaccination status with childhood tuberculosis.

Material and Methods: A Hospital based Observational Case Control study was conducted in the Department of Paediatrics, Mahatma Gandhi Medical College & Hospital, Jaipur among tuberculosis patients who were between 1-18 years (cases) and they were compared with non-TB children attending OPD (control). Nutritional status and BCG vaccination status were noted and compared.

Results: Cases of TB had a significant higher prevalence of moderate and severe malnutrition compared to controls, who predominantly have normal nutritional status ($p<0.01$) suggesting malnutrition being a critical factor for the occurrence of TB. Even BCG vaccination coverage among controls (non TB study subjects) was significantly higher compared to TB cases. ($p<0.05$) suggesting that BCG vaccination may provide a protective effect against the disease.

Conclusion: Tuberculosis is more prevalent in severely malnourished patients and those without BCG vaccination coverage. Hence nutritional improvement and wider BCG vaccination coverage among paediatric population must be stressed upon in tuberculosis endemic areas to prevent and control the spread of tuberculosis.

Keywords: Tuberculosis, Nutritional Status, BCG

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Introduction

In 2022, India reported 2.82 million TB cases, with 12% (approximately 342,000 people) succumbing to the disease. In 2022, tuberculosis (TB) was the world's second leading cause of death from a single infectious agent, following COVID19. [1] Paediatric tuberculosis continues to be a significant yet often overlooked contributor to illness and death in regions where TB is endemic. Approximately 10-20% of all TB cases are reported in children. [2]

Tuberculosis is mostly caused by bacteria Mycobacterium tuberculosis followed by The Mycobacterium tuberculosis complex includes Mycobacterium tuberculosis, Mycobacterium bovis, and Mycobacterium africanum. The virulence of the organism and the immune response of the host are the two major determinants of the progression from TB infection to active disease [3,4]. Malnutrition is both an etiological risk factor for TB and a clinical consequence of the disease [5]. Furthermore, nutritional deficiencies may impair host immunity and increase susceptibility to the development and progression of tuberculosis. Starvation-related malnutrition has been demonstrated to increase the incidence of TB by six

to eight times. [6] Other risk factors associated with TB include poor nutrition, traditional or cultural practices, tobacco smoking, exposure to sputum smear-positive patients etc. [3]

Bacillus-Calmette-Guérin (BCG) is the live attenuated vaccine form of Mycobacterium bovis used to prevent tuberculosis and other mycobacterial infections. The vaccine was developed by Calmette and Guérin and was first administered to human beings in 1921. [7] Protection against tuberculosis infection is usually due to the immune response to mycobacterial antigens. Prior contained latent infection with Mycobacterium tuberculosis can provide up to 80% protection against disease with subsequent exposure. [8] BCG vaccination is highly effective at preventing TB-meningitis and extra-pulmonary disseminated TB; however, its efficacy against pulmonary TB (PTB) in different human populations (children, youth, adult, and elderly) varies. [9]

Although tuberculosis disease typically reactivates in adulthood, most primary infections occur during childhood. Therefore, preventing the acquisition of latent tuberculosis infection in children will be essential for achieving the desired reductions in tuberculosis incidence. [10] Hence, this study was done to study the effect of nutritional status and BCG vaccination on prevalence of tuberculosis in children (cases) and comparing it with other children coming in OPD and not suffering from tuberculosis (control).

Materials and Methods

A Hospital based Observational Case-Control study was conducted in the Department of Paediatrics, Mahatma Gandhi Medical College & Hospital, Jaipur from August 2022 to December 2023 among patients between 1-18 years diagnosed with tuberculosis (pulmonary and extra pulmonary) which included 52 cases and equal number of age matched non-tubercular paediatric patients (52) attending OPD were taken as control.

Inclusion criteria for cases included 1 to 18 year patients of either clinically diagnosed or microbiologically confirmed involving lungs (Pulmonary TB) or involving organs other than lungs (Extra pulmonary TB). Patients of chronic renal diseases, chronic liver diseases, on antiepileptic drugs etc. were excluded from study. Due ethical clearance and consent was taken from parents or guardians.

A detailed medical history was taken and physical examination was done. Necessary tests such as sputum for AFB/ NAAT, Mantoux test, chest X ray, CSF examination, lymph node biopsy etc. necessary for diagnosis of P TB or Extra Pulmonary TB was done. Data was collected in MS Excel and analysed by statistical analysis (Statistical Package for the Social Sciences version 20). The student's T test and Pearson Chi-square were done and the level of significance was set at $p < 0.05$.

Results

In this study a larger proportion of cases (61.53%) reside in urban areas compared to controls (46.15%). Conversely, a larger proportion of controls (53.84%) reside in rural areas compared to cases (38.46%). There was no significant difference between cases and control regarding residence. ($p>0.05$).

Table 1 Comparison of Prevalence of Protein Energy Malnutrition among cases and control. (N=52)

Malnutrition	Cases N (%)	Control N (%)	P
No Malnutrition	5 (9.62)	43 (82.69)	**P<0.01 (Significant)**
Mild Malnutrition (Grade 1)	6 (11.54)	7 (13.46)	
Moderate Malnutrition (Grade 2)	22(42.31)	2 (3.85)	
Severe Malnutrition (Grade 3	19 (36.54)	0 (0.00)	
Total	52 (100)	52 (100)	

Nutritional status of subjects was assessed on basis of Gomez classification for protein energy malnutrition which takes into consideration standard weight for age. The table categorizes the participants based on their protein energy malnutrition status: normal, mild malnutrition (Grade 1), moderate malnutrition (Grade 2), and severe malnutrition (Grade 3). In case group, 5 (9.62%) subjects had no malnutrition, 6 (11.54%) had mild, 22 (42.31%) had moderate and 19 (36.54%) had severe malnutrition. In control group 43 (82.69%) had no malnutrition, 7 (13.46%) had mild and 2 (3.85%) had moderate malnutrition. There was no subject with severe malnutrition in control group. The table indicates a significant difference ($p< 0.01$) in the nutritional status between the cases and controls with cases having a much higher prevalence of moderate and severe malnutrition compared to controls, who predominantly have normal nutritional status. This suggests that the population classified as cases is at a higher risk of malnutrition, which could be a critical factor for the occurrence of TB. (Table 1, Figure 1)

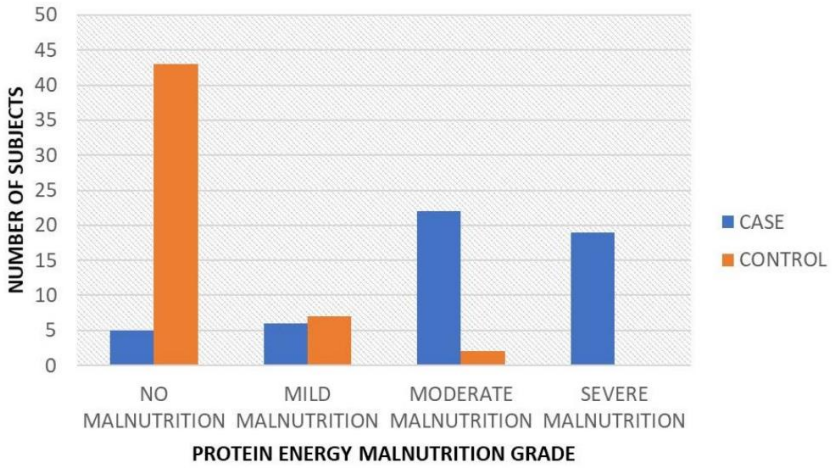

Figure 1. Bar Diagram Comparing Prevalence of Protein Energy Malnutrition among Cases and Control.

Table 2 Comparison of BCG vaccination and Prevalence of TB in Cases and Control. (N=52)

BCG Vaccination	Cases N (%)	Control N (%)	P
Yes	42 (80.76)	50 (96.15)	**P<0.05 (Significant)**
No	10 (19.23)	2 (3.84)	
Total	52 (100)	52 (100)	

In our study among the cases, 80.76% had received the BCG vaccination, while 19.23% were not vaccinated. In contrast, 96.15% of the controls were vaccinated with BCG, and only 3.84% were unvaccinated. The chi-square test revealed a statistically significant difference in BCG vaccination rates between cases and controls (p = 0.0317), suggesting that BCG vaccination may provide a protective effect against the disease. (Table 2, Figure 2)

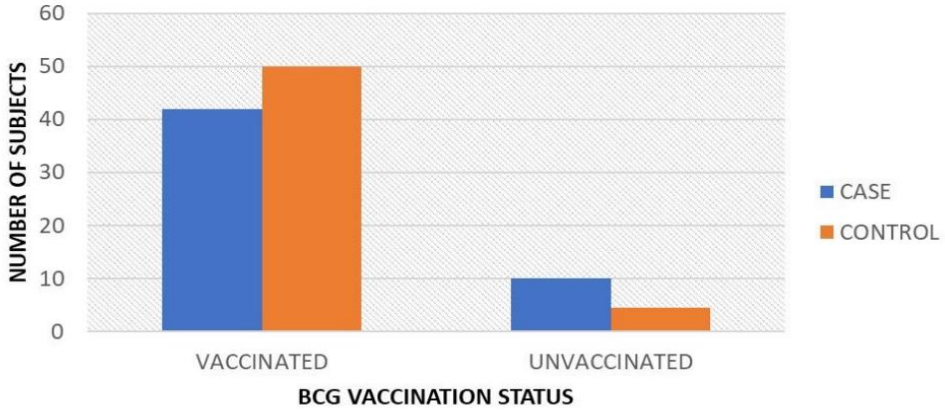

Figure 2 Comparison of BCG vaccination and Prevalence of TB in Cases and Control

Discussion

Tuberculosis being a multifactorial disease, this study emphasised the effect of immunity in the form of nutritional status in prevalence of TB and how it is different from non TB cases. Even how the BCG vaccination alters the immune response and affects the prevalence of TB among cases by comparing with non TB controls.

As per definition provided by census of India 2011 [11] study subjects were divided as per rural and urban residence. In our study, most cases were from urban areas (n=32, 61.53%), while 20 (38.46%) were from rural areas. Conversely, in the control group, a larger portion of patients were from rural areas (n=28, 53.84%), with 24 (46.15%) from urban areas showing no difference of variation in residential distribution between the case and control groups. (p>0.05)

Similar results were observed by Yani FF et al, (2017), [12] who found that there were no significant difference in case and control group according to belonging to urban or rural area (p= 0.402). Jain KS et al, (2013 in India) [13] performed his research and found 30% urban residence, 22.33% rural residence and the

maximum cases from Peri urban residence (47%). The above studies are aligning with our study. Ageeru K et al, (2023) [14] in their case-control study found a significant differences in rural and urban area distribution and malnutrition distribution between the groups, with a p-value of 0.001.

Similarly, Wu Rong Xi et al, (2010 in China) [15] performed his study and concluded the maximum cases from rural regions (67.6%). Since this study was done in a hospital and both the rural and urban population had a equal access so no urban rural difference was found.

Nutritional status of subjects was assessed on the basis of Gomez classification for protein energy malnutrition. This takes into consideration standard weight for age. In case group, 5 (9.62%) subjects had no malnutrition, 6 (11.54%) had mild, 22 (42.31%) had moderate and 19 (36.54%) had severe malnutrition. In control group 43 (82.69%) had no malnutrition, 7 (13.46%) had mild and 2 (3.85%) had moderate malnutrition. There was no subject with severe malnutrition in control group. There was a highly statistically significant difference in nutrition status of subjects of case and control group ($p<0.01$) which means cases of tuberculosis were more suffering from severe malnutrition compared to controls.

This finding was concurrent with results of Ageeru K et al., (2023 in India) [14], who also found that among the cases, a total of 64 (91.4%) were malnourished, with 35 (50%) of them having severe malnutrition, 22 (31.4%) having moderate malnutrition, and 7 (10%) having mild malnutrition. While in the controls, 7 (10%) were mildly malnourished and four (5.7%) were moderately malnourished, with a p-value between both groups of 0.001.

Kannayan et al [16] (2024) in their systemic review and meta-analysis study, found the pooled prevalence estimates of malnutrition among Indian tribes living with TB to 514 per 1000 people, with 95% CI: 232-791. In another systemic review and meta-analysis by Li et al [17] (2023) it was concluded that that malnutrition was prevalent in patients with PTB, and bacterial positivity, low income, and those residing in rural areas were risk factors for malnutrition. They suggested that clinical workers should pay attention to screening the nutritional status of patients with PTB and identifying the risk factors to reduce the incidence of malnutrition and provide nutritional interventions early to improve the prognosis in patients with PTB.

The reason for higher prevalence of TB in malnourished is that lower immunity hampers the opsonizing capacity of complement factor C3 and the ability of phagocytes to eliminate pathogens. Basically, two principal mechanisms for the removal of pathogenic organisms from the body are phagocytosis and the complement cascade. In cases of undernutrition, both the opsonizing capacity of complement factor C3 and the ability of phagocytes to eliminate pathogens are significantly diminished. [18] Additionally, B-lymphocytes, macrophages, dendritic cells, and Kupffer cells are reduced in the presence of malnutrition. The mycobactericidal response, due to low zinc and copper levels, cell-based immunity, and cytokine secretion—which include tumour necrosis factor-alpha (TNF-α), interferon γ, and interleukin-12—are impaired. [19,20]

In our study we observed statistically significant difference ($p<0.05$) of BCG vaccination status, which showed higher vaccination rates in controls (96.15%) compared to cases (80.76%). Similar result was observed by Ageeru K et al., (2023) [14], who also found that BCG vaccination was taken in 85.7% cases in the case group and 95.7% cases in the control group. Both groups were statistically different with a p-value of 0.042. The findings support the protective role of BCG vaccination against TB in paediatric age group. Cai et al[21] (2025) in their systemic review and meta-analysis on effect of BCG vaccination on the progression of latent tuberculosis infection, concluded that BCG vaccination was associated with a significantly lower risk of latent tubercular infection progression to active TB, with the strength of this association varying by geographic region and age. These findings highlight the need to consider regional TB burden and age-specific factors when formulating vaccination policies. Jubulis J. et al, (2014 in India) [22] recorded 86% controls had received BCG vaccination and 85% of cases had received BCG vaccination.

It is well documented that immune response to mycobacterial antigens imparted by BCG vaccination provides protection against new tuberculosis infection. But if patient has contacted prior infection with Mycobacterium tuberculosis which has been contained , this latent infection with can provide up to 80% protection against disease with subsequent exposure. [8] Hence in developing country like India BCG vaccination has prevented the contact and spread of Tuberculosis.

Conclusion

In developing country like India nutritional improvement and BCG vaccination is an important tool for prevention and control of tuberculosis infection. In our study we found a significant presence of malnutrition in the tuberculosis cases compared to non-tubercular controls. Even controls were more covered with BCG vaccination

compared to cases emphasizing the protective role of BCG vaccination in prevention and control of spread of tuberculosis infection.

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