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Original Research Article

Impact of Malnutrition on TB Development in BCG-Vaccinated Children Aged 2 Months to 12 Years

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Abstract

Aim: The aim of the present study was to assess the influence of malnutrition in development of tuberculosis in BCG vaccinated children in age group of 2 months to 12 years.

Methods: The Present study was a prospective study carried out at Nalanda Medical College and Hospital, Patna, Bihar, India. Study population was children in the age group of 2 months to 12 years with symptoms suggestive of tuberculosis. In our study, we studied 100 patients.

Results: Majority of the patients belong to 1 to 5 years (40%) followed by 6 to 10 years (26%). Patients less than 1 year were 17%. In our study, positive history was shown by 22% population and 78% showed negative history for tuberculosis. The predominant symptoms of presentation are Fever 66 (66%) and cough 59 (59%). 37 (37%) had initial presentation as seizures. 36% had weight loss or poor weight gain, significant lymphadenopathy was observed in 25 (25%) cases and 14 (14%) had wheezing. 21 (21%) had Grade I, 16 (16%) had Grade II PEM, 14 (14%) had Grade III PEM and 5 (5%) had Grade IV PEM according to IAP Classification of Malnutrition. 44 (44%) cases had normal nutritional status. Disseminated and Milliary TB was more in children with Grade III and Grade IV malnutrition. 5 cases of TBM had normal nutrition whereas 3 cases each had grade I and grade III malnutrition. 1 case of abdominal tuberculosis had normal nutrition and 1 case had grade I malnutrition.

Conclusion: Protective benefit of BCG vaccine against the dissemination of tuberculosis is children in possible only if they have normal nutrition.

Keywords: malnutrition, development of tuberculosis, BCG vaccinated children

Introduction

Tuberculosis remains a significant source of morbidity and mortality among children in resource-limited settings. Of the 9 million new tuberculosis infections each year, 11% are in children. [1] Malnutrition is also highly prevalent in children living in tuberculosis endemic countries and contributes to 2.2 million deaths in children under 5 years of age globally. [2] Poverty, overcrowding, food insecurity, and human immunodeficiency virus (HIV) further set the stage for both malnutrition and poor infection control.

Although the World Health Organization (WHO) states that malnutrition is a significant risk factor for childhood tuberculosis [1], there are limited studies to explain the mechanisms underlying this association. This may be due to the challenges in diagnosing pediatric tuberculosis, difficulty in establishing a causal role of malnutrition on tuberculosis, and an overall low research priority because of the limited infectivity of children. The vitamin D receptor (VDR) is a soluble nuclear receptor found in many immune cells and is believed to play a role in cytokine secretion patterns, maturation of dendritic cells, and effector and regulatory T-cell function. [3] Several VDR gene polymorphisms have been found that can impact tuberculosis risk and outcomes, including BsmI, TaqI, and ApaI at the 3′ end of VDR, and FokI on exon site 2. The TaqI Tt and ApaI AA genotype are associated with improved response to therapy and faster time to sputum conversion in tuberculosis patients. On the other hand, TaqI tt, TaqI Bb, TaqI Ff, and BsmI bb have been associated with an increased risk of tuberculosis. [4] Risk or protection may be influenced by ethnic background; a recent meta-analysis was performed on a variety of populations and found that the FokI ff genotype was most significant in the Asian population, whereas there was no effect in Africans or South Americans. [5]

Defense against M. tuberculosis requires a complex immune response that involves both innate and adaptive immunity. [6] However, in newborns, it is important to appreciate that cell-mediated immunity is incomplete, and they depend mostly on innate immunity and maternal antibodies.[7] Yet, even innate immunity is impaired; evidence suggests that newborns have reduced function in antigen-presenting cells (APCs), neutrophils, and TLRs, and decreased blood complement levels. [7] Moreover, adaptive immunity is thought to be skewed to a helper T cell 2 type response, potentially as a way to reduce a proinflammatory reaction, decrease an allo-immune response against the mother, and promote tolerance of harmless new antigens such as gut flora and food. [7] However, this also places them at considerable risk against intracellular organisms, including tuberculosis, that depend on a Th1 response. [6,7] Nutrition plays an essential role to develop the appropriate innate and Th1 immune responses against tuberculosis. [8]

The aim of the present study was to assess the influence of malnutrition in development of tuberculosis in BCG vaccinated children in age group of 2 months to 12 years.

Materials and Methods

The Present study was a prospective study carried out at department of Pediatrics, Nalanda Medical College and Hospital, Patna, Bihar, India from May 2023 to February 2024. Study population was children in the age group of 2 months to 12 years with symptoms suggestive of tuberculosis. In our study, we studied 100 patients.

Inclusion criteria: 1. Children vaccinated with BCG (presence of BCG scar) and admitted in paediatric ward or PICU with symptoms of tuberculosis 2. Children in age group of 2 months to 12 years of either sex 3. Children with Recurrent or prolonged fever, Recurrent respiratory infections and Recurrent wheezing 4. Children with Poor weight gain 5. Children with any of the symptoms /signs like Lymphadenopathy, Hepato splenomegaly, M Meningitis, Convulsions and Serous effusions 6. Babies not thriving well

Exclusion criteria: 1. Asymptomatic Mantoux positive children with no evidence of disease 2. Babies less than 2 months of age 3. Children with BCG adenitis 4. Children those without BCG vaccination or Scar 5. children on empirical anti-tubercular drugs were excluded from the study.

Study was approved by ethical committee of the institute. A valid written consent was taken from parents of children after explaining study to them. Data was collected with pre tested questionnaire. Data included sociodemographic data, clinical history and through clinical examination. Nutritional assessment was done according to IAP classification.12 All patients underwent Mantoux test, chest X-ray, Complete blood count and urine routine examination. Mantoux test was done with 0.1 ml of PPD (5TU PPD-S) injected on volar surface of forearm for all patients and induration exceeding 10mm after 48-72 hours was considered as positive reaction. In relevant cases gastric aspirate for AFB smear examination for three consecutive days. Lymph node biopsy, cerebrospinal, pleural and peritoneal fluid studies including adenosine deaminase test were done. Positive Mantoux test, positive X-ray findings, AFB positive in gastric aspirate, lymph node biopsy suggestive of tubercular pathology, CSF positive for tubercular meningitis and CT appearance of tuberculoma brain were used as diagnostic criteria in our study. All confirmed cases were treated according to IAP consensus for childhood TB. Data was entered in Excel sheet and analysed with SPSS version 22.0.

Results

Table 1: Distribution of patients according to age group

Age groups in years	N	%
< 1year	17	17
1 to 5 year	40	40
6 to 10 year	26	26
11 to 12 year	17	17
Total	100	100

Majority of the patients belong to 1 to 5 years (40%) followed by 6 to 10 years (26%). Patients less than 1 year were 17%.

Table 2: Distribution of patients according to positive history

History of contact	N	%
Positive history	22	22
Negative history	78	78
Total	100	100

In our study, positive history was shown by 22% population and 78% showed negative history for tuberculosis.

Table 3: Distribution of patients according to clinical presentation

Clinical presentation	N	%
Fever	66	66
Cough	59	59
Wt.Loss/Poor wt gain	36	36
Seizures	37	37
Lymphadenopathy	25	25
Wheeze	14	14

The predominant symptoms of presentation are Fever 66 (66%) and cough 59 (59%). 37 (37%) had initial presentation as seizures. 36% had weight loss or poor weight gain, significant lymphadenopathy was observed in 25 (25%) cases and 14 (14%) had wheezing.

Table 4: Distribution of patients according to nutritional status

Nutritional status	N	%
Normal	44	44
Grade I	21	21
Grade II	16	16
Grade III	14	14
Grade IV	5	5
Total	100	100

21 (21%) had Grade I, 16 (16%) had Grade II PEM, 14 (14%) had Grade III PEM and 5 (5%) had Grade IV PEM according to IAP Classification of Malnutrition. 44 (44%) cases had normal nutritional status.

Table 5: Distribution of patients according to nutritional status and type of tuberculosis

Types of TB	Normal	Grade I	Grade II	Grade III	Grade IV
PPC	28	10	7	3	1
LN	01	01	3	2	0
Diss. TB	-	-	00	00	2
Mill. TB	-	1	2	1	2
TBM	5	3	2	5	1
Tuberculoma	6	4	1	1	-
Abd. TB	01	1	-	-	-
PPC+LN	2	1	1	2	-
Cong. TB	1	-	-	-	-
Total	44	21	16	14	5

Disseminated and Miliary TB was more in children with Grade III and Grade IV malnutrition. 5 cases of TBM had normal nutrition whereas 3 cases each had grade I and grade III malnutrition. 1 case of abdominal tuberculosis had normal nutrition and 1 case had grade I malnutrition.

Discussion

Globally it has been estimated that 1.9 billion people (1/3 of world's population) are infected and 5000 people die of TB Globally each day. [9] Out of which 95% are in the developing world. About 3 million cases die every year with an addition of 4-5 million new cases every year. [10] The majority of infected individuals live in South East Asian region. More than 90% of deaths are reported to occur in low-income countries. In India 1.8 million new cases annually accounting for one fifth of new cases two of every 5 persons (>400 million) in general population have latent tuberculosis. [11] Tuberculosis long known to be a major cause of morbidity and mortality throughout the world has for the several decades been a neglected disease in both industrialized and developing countries specially in children because of the difficulty of confirming the diagnosis. The Global burden of childhood Tuberculosis in the world is unclear. Another important reason is that children do not make a significant contribution to the spread of tuberculosis. [12]

Majority of the patients belong to 1 to 5 years (40%) followed by 6 to 10 years (26%). Patients less than 1 year were 17%. Bhakku et al [13] reported 71% under 5 years of age and 22.9% in 5–12 years. In our study, positive history was shown by 22% population and 78% showed negative history for tuberculosis. The predominant symptoms of presentation are Fever 66 (66%) and cough 59 (59%). 37 (37%) had initial presentation as seizures.

36% had weight loss or poor weight gain, significant lymphadenopathy was observed in 25 (25%) cases and 14 (14%) had wheezing. 21 (21%) had Grade I, 16 (16%) had Grade II PEM, 14 (14%) had Grade III PEM and 5 (5%) had Grade IV PEM according to IAP Classification of Malnutrition. 44 (44%) cases had normal nutritional status. The ICMR BCG trials in Chingleput also report that BCG offers no protection against primary tubercular infection or its progression to severe forms. [14]

It is stated that BCG vaccine has protective value against dissemination of tuberculosis because T cells in vaccinated children are highly sensitized preventing hematogenous spread.16 In under-nourished children, cell mediated immunity is greatly impaired and hence the vaccine fails in preventing dissemination of tuberculosis. [15] Disseminated and Milliary TB was more in children with Grade III and Grade IV malnutrition. 5 cases of TBM had normal nutrition whereas 3 cases each had grade I and grade III malnutrition. 1 case of abdominal tuberculosis had normal nutrition and 1 case had grade I malnutrition. Presently, BCG vaccination is advised to be continued in infants and children to reduce the risk of primary tubercular infection disseminating to severe forms. [16]

In younger individuals the progression to disease is earlier and is more disseminated. Pulmonary tuberculosis (PTB) is usually smear negative. PTB to extra-pulmonary TB (EPTB) ratio is usually around 3:14. In infants, the time span between infection and disease can be as little as 6-8 weeks. Untreated adults pass the disease on to 43% of children under one and to 16% of children from 11-15 years old. Only 5-10% of adults in similar contact would contract the disease. Scientific data on the burden of all forms of TB amongst children in India are not available. Most surveys conducted have focused on pulmonary TB and no significant population based studies on extrapulmonary TB are available. Pulmonary TB is primarily and adult disease and it has been estimated that in 0-19 year old population PTB is only 7%. [17] After the implementation of expanded and universal immunization programmes in India, there is substantial improvement in BCG vaccination coverage reaching up to 90% in urban areas. [18]

Conclusion

Protective benefit of BCG vaccine against the dissemination of tuberculosis in children is possible only if they have normal nutrition. However, the mechanisms underlying the association between malnutrition and childhood tuberculosis remain unclear. However, it is equally important to recognize the severe gaps in our knowledge. We require greater prospective studies that evaluate how nutritional status impacts the risk of tuberculosis, while conducting further randomized controlled trials on the use of supplementation in tuberculosis therapy. As our basic understanding of the interaction between tuberculosis and malnutrition grows, it is important that we seek to apply these advances to the welfare of this vulnerable population.

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