DOI: https://doi.org/10.53350/pjmhs221661071

ORIGINAL ARTICLE

Incidence of Several Forms of Tuberculosis (TB) and Their Bacillus Calamette Guerin (BCG) Vaccination Status among Children

OMAIR MAZHAR[1], SHER ALAM KHAN[2], MUHAMMAD ARSALAN QAISAR[3], ZAFAR IQBAL BHATTI[4], MAHWISH AKHTAR QURESHI[5], IBRAHIM[6]

[1]*MBBS, FCPS Pediatrics, Consultant Pediatrician, THQ Kel, Azad Kashmir*
[2]*Senior Registrar Paediatrics, Combined Military Hospital, Abbottabad, Pakistan*
[3]*Medical Officer at Rehab Medical Clinic/ Ex House Officer Jinnah hospital, Lahore*
[4]*Associate Professor Pediatrics, Central Park Medical College, Lahore/ Consultant Pediatrics, Bahria International Hospital, Lahore*
[5]*Assistant Professor Department of Community Medicine Fazaia Medical College, Islamabad*
[6]*Assistant Professor, Peads Medicine, Swat Medical College / Swat Medical Complex Teaching Hospital, Saidu Sharif Swat*
Corresponding author: Sher Alam Khan, Email: drsheralamkhan7.dsk@gmail.com

ABSTRACT

Aim: The purpose of the study was to govern the incidence of various forms of tuberculosis and the status of BCG vaccination in children.

Study design: A Cross-sectional study.

Place and Duration of the Study: In the Pediatrics department of Jinnah hospital, Lahore for one-year duration from January 2021 to December 2021.

Methods: A total of 200 patients with various forms of tuberculosis were recruited who met the inclusion and exclusion criteria. A demographic profile including age, gender and hospital registration numbers is recorded. Informed oral consent was obtained from the parents of each child. BCG scar present or absent. Form of tuberculosis, pulmonary tuberculosis (fever> 14 days, ESR> 50, sputum positive for AFB, x-ray results), tuberculous meningitis (fever with focal neurological symptoms lasting longer than 14 days, CT results according to inclusion criteria, CSF pleocytosis), tuberculous lymphadenitis (detection of tuberculosis by histopathology on excisional lymph node biopsy), abdominal tuberculosis (fever longer than 14 days, previous weight loss and anorexia, mesenteric lymphadenitis, biopsy of the lesion suggestive of tuberculosis), description and labelling of the vaccinated and unvaccinated patient with the presence or absence of BCG scar.

Results: During this period, 200 patients who met the exclusion and inclusion criteria were selected in the study. Of the 200 patients included, 110 (55%) were males and 90 (45%) were females (Table 1), their age varies from 1 to 14 years, with 7.22 ± 3.78 years of an average age. Out of 200 enrolled patients, the four most common types of tuberculosis were examined. Out of 200 cases, 95 (47.5%) were pulmonary tuberculosis, 50 (25%) tuberculous meningitis, 35 (17.5%) tuberculous lymphadenitis, and 25 (12.5%) abdominal tuberculosis. Of the 200 patients enrolled, 85 (42.5%) were vaccinated (with BCG scarring) and 115 (57.5%) were unvaccinated.

Keywords: Tuberculosis, BCG, Pulmonary tuberculosis

INTRODUCTION

Tuberculosis is an infectious disease instigated by M. tuberculosis and is a serious health problem. It can affect any body system, but the most common organs involved are the lungs, brain, lymphatic system, abdomen, bones, and joints[1-2]. In the 20th century last decade, the numeral of tuberculosis -cases has augmented globally. Today, tuberculosis cases happen about 95% among the emerging world where AIDS/ HIV epidemics have the highest influence and where incomes are frequently lacking to adequately identify and treat these diseases[3]. Tuberculosis (TB) is currently the main reason of demise from a treatable infectious illness. The WHO guesses that in 2004 there were 9.1 million new tuberculosis cases (3.9 million of which were spread), although public health systems report only half of that number[4]. Prevention and treatment of TB in children is usually has less importance in countries where endemic of TB is common. Though, while childhood TB patients are hardly accurately documented, children subsidise significantly to the global burden of tuberculosis[5]. In Asia, fighting tuberculosis is a daunting challenge in low-income countries like Pakistan. Pakistan contributes 10% of the global burden of new TB cases[6-7]. Tuberculosis in children remains a serious public health problem, especially as severe forms of the disease are frequent and the accurate diagnosis of tuberculosis in children is associated with many difficulties[8]. The BCG vaccine is a key component of the Extended Immunization Program (EPI) in Pakistan and is administered at birth. However, the role of the BCG vaccine in preventing tuberculosis transmission among children and thus fighting tuberculosis remains controversial[9-10]. Numerous studies with BCG in various countries have shown that the protection provided by the BCG vaccine against tuberculosis disease ranges from 0% to 80%[11]. The aim of the study was to determine the frequency of various forms of tuberculosis and the status of BCG vaccination in children.

METHODS

It was a cross-sectional study conducted in the Pediatrics department of Jinnah hospital, Lahore for one-year duration from January 2021 to December 2021. Total of 200 children aged 2 to 14 years who met the inclusion and exclusion criteria (Inclusion criteria: Patients of any type of tuberculosis as noted, both genders, 2-14 years old.

The clinical examination or clinical history of bronchial asthma (recurrent episodes of wheezing, especially nocturnal dyspnea and hyperinflated lung area on chest X-ray), cystic fibrosis (chronic productive cough, haemoptysis, growth retardation and 2 positive sweat chloride tests), diagnosed with encephalitis and acute bacterial meningitis (cases of encephalitis and acute bacterial meningitis already proven in the cerebrospinal fluid where the CSF culture has shown bacteria other than tuberculosis) were excluded. A demographic profile including age, gender and hospital registration number was recorded. Informed oral consent was obtained from the parents of each child. BCG scar present or absent. Various forms of tuberculosis, pulmonary tuberculosis (fever greater than 14 days, ESR> 50, positive sputum for AFB, X-ray results), tuberculous meningitis (fever with focal neurological symptoms lasting more than 14 days, CT results according to inclusion criteria , pleocytosis of the cerebrospinal fluid), tuberculous lymphadenitis (histopathological examination of tuberculosis in a biopsy that excludes the lymph nodes), tuberculosis of the abdominal cavity (fever for more than 14 days, history of weight loss and anorexia, mesenteric lymphadenitis, biopsy of lesions suggestive of tuberculosis) were documented. The patient was marked as vaccinated and unvaccinated based on the presence or absence of BCG scar. The data was entered and analyzed using SPSS version 22.0. Age is presented as mean and standard deviation (SD). Gender and type of tuberculosis, e.g., pulmonary tuberculosis, tuberculous meningitis, tuberculous

lymphadenitis, abdominal tuberculosis, and vaccination status are presented as frequency and percentage.

RESULTS

During this period, 200 patients who met the exclusion and inclusion criteria were selected in the study. Of the 200 patients included, 110 (55%) were males and 90 (45%) were females (Table 1), their age varies from 1 to 14 years, with 7.22 ± 3.78 years of an average age. The age of the patients was divided into three groups, i.e., <5 years, 6 to 10 years and 11 to 14 years. 90 patients were <5 years of age, 80 patients were 6-10 years of age, and 30 patients were 11-14 years of age (Table-I).

Table 1: Distribution of patients by age and gender

Gender	Number	Percentage
Male	110	55
Female	90	45
Total	200	100.0
Age (Year) < 5	90	45
6-10	80	40
11-14	30	15

Out of 200 enrolled patients, the four most common types of tuberculosis were examined. Out of 200 cases, 95 (47.5%) were pulmonary tuberculosis, 50 (25%) tuberculous meningitis, 35 (17.5%) tuberculous lymphadenitis, and 25 (12.5%) abdominal tuberculosis (Tab-II).

Table-2: Frequency of various forms of tuberculosis

Type	Frequency	Percentage
Pulmonary TB	95	47.5
TBM	50	25
Tuberculous lymphadenitis	35	17.5
Abdominal tuberculosis	25	12.5
Total	200	100.0

We also analyzed the status of the BCG vaccination by checking the scar on the deltoid muscle. Of the 200 patients enrolled, 85 (42.5%) were vaccinated (with BCG scarring) and 115 (57.5%) were unvaccinated (Table-III).

Table-3: Frequency of BCG vaccination in patients

Scar	Number	Percentage
Present	85	42.5
Absent	115	57.5
Total	200	100.0

We also investigated tuberculosis type and vaccination status from 200 patients, which helped us determine if BCG had a protective role. Of 95 patients with pulmonary tuberculosis, 45 (47.4%) were vaccinated (with scar BCG) and 50 (52.6%) were unvaccinated. Of the 50 patients with TB meningitis, 15 (30%) were vaccinated and 35 (70%) were unvaccinated. Of the 35 patients with tuberculous lymphadenitis, 20 (57.1%) were vaccinated and 15 (42.9%) were not. There were 25 patients with abdominal tuberculosis, of which 5 (20%) were vaccinated and 20 (80%) were unvaccinated (Table 4).

Table 4: Percentage and frequency of several forms of TB in BCG non-vaccinated and vaccinated

Type	No.	Vaccinated (%)	Non vaccinated (%)
Pulmonary TB	95	45 (47.4)	50 (52.6)
TBM	50	15 (30)	35 (70)
Tuberculous lymphadenitis	35	20 (57.1)	15 (42.9)
Abdominal tuberculosis	25	5 (20)	20 (80)
Total	200	85 (42.5)	115 (57.5)

DISCUSSION

Tuberculosis (TB) is an infectious ailment sourced primarily by M. tuberculosis. It mainly affects the lungs (pulmonary tuberculosis) but can affect any body system (extrapulmonary tuberculosis). Tuberculosis (TB) is currently the main reason of mortality from a treatable infectious disease[13-14]. The WHO estimations in 2004 was that there were 9.1 million new tuberculosis cases (3.9 million of which were spread), although public health systems report only half of that number[15]. BCG has been proven to provide high resistance to common and miliary forms of tuberculosis (80% of cases). In pulmonary tuberculosis, protection is much less (50% of cases)[16]. International studies show that the BCG vaccine is very beneficial in preventing childhood tuberculosis. Contrary to international data, local reports have shown controversy over the role of the BCG vaccine[17]. However, the effectiveness of the BCG vaccine has been heavily questioned. Studies of older children and adults showed 77% protection in the UK, only 14% in the southern US, and no protection in Madras[18]. The Birmingham study found that 62 of 108 cases (57%) received BCG and 336 of 432 (78%) controls received BCG. The estimated protective efficacy of the vaccines was 64% (95%, 43% and 77% confidence limits)[19]. Routine BCG vaccination in Asian infants provides useful protection against the development of tuberculosis in infancy. The study showed that the first dose of BCG vaccine had a strong protective effect against miliary and meningeal tuberculosis[20]. However, outcomes vary with the pulmonary form of the disease, with some showing a null effect and others close to 80%. In the study conducted at the Bahawal Victoria Hospital Pediatric Unit II in Bahawalpur, 76 of the 100 tuberculosis patients admitted during this period were vaccinated and 24 were unvaccinated[21]. Of the 35 cases of pulmonary tuberculosis, 27 (77%) were vaccinated and 8 (22.8%) were unvaccinated. The results of our study clearly showed that pulmonary tuberculosis is the most common and common form of tuberculosis in children compared to other studies. Since pulmonary tuberculosis is more common in vaccinated children, BCG prevention of pulmonary tuberculosis was not included in our study, but since meningeal tuberculosis and abdominal tuberculosis are less common in vaccinated children, BCG is more protective against meningeal tuberculosis, as does meningeal tuberculosis[22-23]. International data showing that BCG has a greater preventive effect in meningeal tuberculosis and less in pulmonary tuberculosis. Therefore, BCG vaccination was significantly associated with the reduction of extrapulmonary disease[24-25]. Data collection from one tertiary hospital was a limitation of the study and a larger study is needed to assess the actual effectiveness and preventive effect of the BCG vaccine. More work is needed on new tuberculosis vaccines that are equally effective against all forms of tuberculosis. Since tuberculosis is very common in our world, the BCG vaccine should be given right after birth.

CONCLUSION

Our study shows that the incidence of pulmonary tuberculosis is higher in all types of tuberculosis and that BCG protects against most forms of tuberculosis, especially meningeal tuberculosis and abdominal tuberculosis, but is less effective against pulmonary tuberculosis.

REFERENCES

1. Berendsen ML, Øland CB, Bles P, Jensen AK, Kofoed PE, Whittle H, de Bree LC, Netea MG, Martins C, Benn CS, Aaby P. Maternal priming: Bacillus Calmette-Guérin (BCG) vaccine scarring in mothers enhances the survival of their child with a BCG vaccine scar. Journal of the Pediatric Infectious Diseases Society. 2020 Jun;9(2):166-72.
2. Rahman MH, Cox AB, Mills SL. A missed opportunity: birth registration coverage is lagging behind Bacillus Calmette–Guérin (BCG) immunization coverage and maternal health services utilization in low-and lower middle-income countries. Journal of Health, Population and Nutrition. 2019 Oct;38(1):1-4.
3. Mangtani P, Nguipdop-Djomo P, Keogh RH, Trinder L, Smith PG, Fine PE, Sterne J, Abubakar I, Vynnycky E, Watson J, Elliman D. Observational study to estimate the changes in the effectiveness of bacillus Calmette-Guerin (BCG) vaccination with time since

vaccination for preventing tuberculosis in the UK. Health technology assessment. 2017 Jul 1;21(39):7-.
4. Berendsen ML, Van Gijzel SW, Smits J, De Mast Q, Aaby P, Benn CS, Netea MG, Van Der Ven AJ. BCG vaccination is associated with reduced malaria prevalence in children under the age of 5 years in sub-Saharan Africa. BMJ global health. 2019 Nov 1;4(6):e001862.
5. Berg MK, Yu Q, Salvador CE, Melani I, Kitayama S. Mandated Bacillus Calmette-Guérin (BCG) vaccination predicts flattened curves for the spread of COVID-19. Science advances. 2020 Aug 5;6(32):eabc1463.
6. Chimoyi L, Velen K, Churchyard GJ, Wallis R, Lewis JJ, Charalambous S. An ecological study to evaluate the association of Bacillus Calmette-Guerin (BCG) vaccination on cases of SARS-CoV2 infection and mortality from COVID-19. PLoS One. 2020 Dec 17;15(12):e0243707.
7. Nissen TN, Birk NM, Smits G, Jeppesen DL, Stensballe LG, Netea MG, van der Klis F, Benn CS, Pryds O, Andersen A, Kjærgaard J. Bacille Calmette-Guérin (BCG) vaccination at birth and antibody responses to childhood vaccines. A randomised clinical trial. Vaccine. 2017 Apr 11;35(16):2084-91.
8. Nissen TN, Birk NM, Blok BA, Arts RJ, Andersen A, Kjærgaard J, Thøstesen LM, Hoffmann T, Jeppesen DL, Nielsen SD, Kofoed PE. Bacillus Calmette-Guérin vaccination at birth and in vitro cytokine responses to non-specific stimulation. A randomized clinical trial. European Journal of Clinical Microbiology & Infectious Diseases. 2018 Jan;37(1):29-41.
9. Thøstesen LM, Kjaergaard J, Pihl GT, Birk NM, Nissen TN, Aaby P, Jensen AK, Olesen AW, Stensballe LG, Jeppesen DL, Benn CS. Neonatal BCG vaccination and atopic dermatitis before 13 months of age: a randomized clinical trial. Allergy. 2018 Feb;73(2):498-504.
10. Amanati A, Pouladfar G, Kadivar MR, Dashti AS, Jafarpour Z, Haghpanah S, Alborzi A. A 25-year surveillance of disseminated Bacillus Calmette–Guérin disease treatment in children in Southern Iran. Medicine. 2017 Dec;96(52).
11. Du Preez K, Seddon JA, Schaaf HS, Hesseling AC, Starke JR, Osman M, Lombard CJ, Solomons R. Global shortages of BCG vaccine and tuberculous meningitis in children. The Lancet Global Health. 2019 Jan 1;7(1):e28-9.
12. Shah I, Kathwate J, Shetty NS. Comparison of tuberculin skin test and QuantiFERON-TB Gold In-Tube test in Bacillus Calmette–Guerin-vaccinated children. Lung India: Official Organ of Indian Chest Society. 2020 Jan;37(1):24.
13. Funch KM, Thysen SM, Rodrigues A, Martins CL, Aaby P, Benn CS, Fisker AB. Determinants of BCG scarification among children in rural Guinea-Bissau: a prospective cohort study. Human vaccines & immunotherapeutics. 2018 Oct 3;14(10):2434-42.
14. Pelzer PT, Mutayoba B, Cobelens FG. BCG vaccination protects against infection with Mycobacterium tuberculosis ascertained by tuberculin skin testing. Journal of Infection. 2018 Oct 1;77(4):335-40.
15. Stensballe LG, Ravn H, Birk NM, Kjærgaard J, Nissen TN, Pihl GT, Thøstesen LM, Greisen G, Jeppesen DL, Kofoed PE, Pryds O. BCG vaccination at birth and rate of hospitalization for infection until 15 months of age in Danish children: a randomized clinical multicenter trial. Journal of the Pediatric Infectious Diseases Society. 2019 Jul;8(3):213-20.
16. Salmon C, Conus F, Parent MÉ, Benedetti A, Rousseau MC. Association between Bacillus Calmette–Guérin vaccination and lymphoma: a population-based birth cohort study. Journal of Internal Medicine. 2019 Nov;286(5):583-95.
17. Choi YY, Han MS, Lee HJ, Yun KW, Shin CH, Yoo WJ, Cho TJ, Cheon JE, Park KU, Choi EH. Mycobacterium bovis osteitis following immunization with Bacille Calmette-Guérin (BCG) in Korea. Journal of Korean medical science. 2019 Jan 7;34(1).
18. Salmon C, Conus F, Parent MÉ, Benedetti A, Rousseau MC. Association between Bacillus Calmette-Guerin (BCG) vaccination and lymphoma risk: A systematic review and meta-analysis. Cancer Epidemiology. 2020 Apr 1;65:101696.
19. Kusnanto K, Arifin H, Kurniawati Y. Determinant of BCG vaccine coverage among Indonesian children aged 0–2 months. Children and Youth Services Review. 2020 Sep 1;116:105238.
20. Cernuschi T, Malvolti S, Nickels E, Friede M. Bacillus Calmette-Guérin (BCG) vaccine: a global assessment of demand and supply balance. Vaccine. 2018 Jan 25;36(4):498-506.
21. Chacon-Cruz E, Arellano-Estrada JL, Lopatynsky-Reyes E, Alvelais-Palacios J, Becka C. Children with lymphadenitis associated with Bacillus Calmette-Guérin (BCG) vaccination do not experience more infections when compared with BCG-vaccinated children without lymphadenitis: a three years paired-cohort in Mexico. Therapeutic Advances in Vaccines. 2017 Aug;5(4-5):103-7.
22. Jayaraman K, Adhisivam B, Nallasivan S, Krishnan RG, Kamalarathnam C, Bharathi M, McSharry B, Namachivayam SP, Shann F, Boopalan SI, David P. Two randomized trials of the effect of the Russian strain of Bacillus Calmette-Guérin Alone or with oral polio vaccine on neonatal mortality in infants weighing< 2000 g in India. The Pediatric Infectious Disease Journal. 2019 Feb 1;38(2):198-202.
23. Mangtani P, Nguipdop-Djomo P, Keogh RH, Sterne JA, Abubakar I, Smith PG, Fine PE, Vynnycky E, Watson JM, Elliman D, Lipman M. The duration of protection of school-aged BCG vaccination in England: a population-based case–control study. International journal of epidemiology. 2018 Feb 1;47(1):193-201.
24. Khalid FA, Eldirdery MM, Mukhtar MM. Reactivity of tuberculin among Bacillus Calmette-Guérin vaccinated school children, Kassala State, Sudan Fatima A. Khalid1. Elderidiry MM2, MM Mukhta3.
25. Zimmermann P, Donath S, Perrett KP, Messina NL, Ritz N, Netea MG, Flanagan KL, van der Klis FR, Curtis N. The influence of neonatal Bacille Calmette-Guerin (BCG) immunisation on heterologous vaccine responses in infants. Vaccine. 2019 Jun 19;37(28):3735-44.