Short Communication

BIOMEDICAL Journal of Scientific & Technical Research

ISSN: 2574 -1241

DOI: 10.26717/BJSTR.2021.40.006448

# Frequency of Positive PPD Test After Inoculation of BCG Vaccine in 4-Month-Old Infants to 5-Year-Old Children

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**ARTICLE INFO**

**Received:** November 26, 2021

**Published:** December 07, 2021

**Citation:** Gholamreza Soleimani, Elham Shafighi Shahri, Maryam Nakhaee Moghadam, Elnaz Shafighi Shahri, Alireza Ganjali, et al. Frequency of Positive PPD Test After Inoculation of BCG Vaccine in 4-Month-Old Infants to 5-Year-Old Children. Biomed J Sci & Tech Res 40(3)-2021. BJSTR. MS.ID.006448.

**Keywords:** Tuberculin Test; BCG Vaccine; Tuberculosis

**ABSTRACT**

**Introduction:** Tuberculosis is an important cause of child mortality in developing countries. BCG vaccination of newborns has been shown to reduce the incidence and mortality of children with TB. Tuberculin skin test is used to identify people with a history of exposure to mycobacterial antigens. This test involves an intradermal injection of tuberculin, which causes delayed hypersensitivity due to T lymphocytes and occurs within 48 to 72 hours. In this study, we aimed to test the rate of positive tuberculin test after vaccination Test for infants 4 months to 5 years old in Zahedan.

**Materials and Methods:** This study was a cross-sectional study that was performed in 2020 in referral Hospital in Zahedan. In this study, 400 infants from 4 months to 5 years old children who were referred to the hospital were studied. Samples were selected sequentially and PPD test was performed on them. The bulge diameter between 48 and 72 hours after inoculation was assessed. Findings were analyzed and reported.

**Results:** the average protrusion diameter after inoculation was calculated to be 4.09 mm. Also, 60.8% of children had a bulge of 0 to 5 mm in diameter and 39.2% were more than 5 mm in diameter. Also, there was a statistically significant difference between increasing age and the probability of a positive test. ($P < 0.05$)

**Discussion:** PPD test is a valuable test for diagnosing tuberculosis. According to the results obtained and other studies, the positive rate of the test can indicate a high incidence of tuberculosis.

## Introduction

Tuberculosis is an important cause of child mortality in developing countries. BCG vaccination of newborns has been shown to reduce the incidence and mortality of children with TB. Protection against TB by BG vaccination has been observed shortly after birth in Canadian Indians (80%) and Chicago (75%) [1]. Bacillus Calmette Guerin (BCG) is a live bacterium of Mycobacterium bovis that was first used by Calmette and Green to immunize against tuberculosis and mycobacterial infections. The wax was first used for the general population in 1921 for tuberculosis. Since then, various vaccines against tuberculosis have been developed and various models of this vaccine have been developed to enhance the effectiveness of this vaccine [2,3]. The BCG vaccine is the most commonly prescribed vaccine worldwide. The vaccine has been administered to approximately 3 billion people worldwide to date and is one of the major vaccines in immunizing newborns [4]. Virtually, such as mycobacterial infections, this vaccine provides some degree of immunity against tuberculosis and, in some cases, mycobacterial infections [2]. History of natural infection with Mycobacterium tuberculosis and previous infection with non-tuberculosis mycobacteria provide immunity against tuberculosis [5,6]. Previous infection with Mycobacterium tuberculosis has been shown to increase immunity against recurrent infections in healthy individuals and in HIV-infected individuals, as well as in immunocompromised individuals who are susceptible to infection with other types of tuberculosis [7-11].

The duration of immunization of the BCG vaccine against tuberculosis is approximately 10 to 15 years. This period protects childhood against tuberculosis. Of course, this period can be different. A long-running clinical trial since 1930 of BCG vaccination among Native Americans and Alaskan Indians has shown that in some cases immunity may last up to 50 or 60 years [12]. The degree of usefulness of the BCG vaccine depends on three factors: the individual's own immunity before vaccination, a history of mycobacteria infection prior to vaccination, and the potential of the species used in the BCG vaccine [13]. So far, no agreement has been reached on which type of BCG is best for the vaccine, and different types of BCG are used to make the vaccine. There has also been no evidence that repeated BCG vaccination is more effective than a single dose against tuberculosis [14]. The standard dose of BCG vaccine is 0.1 microgram per milliliter. Other childhood vaccines can be given at the same time as the BCG vaccine. The vaccine can be given intravenously or multiple subcutaneously using the device. WHO prefers the subcutaneous method [15]. Skin reactions at the injection site are a common complication of vaccination. Other common complications include osteitis, osteomyelitis and diffuse infection. Factors that affect the incidence of complications include the dose of the vaccine, the type of vaccine and how the vaccine is administered [16].

In preterm infants, it is recommended not to inject the vaccine because the risk of infection in this group is much higher than in term infants [17]. Among the tests currently used in clinical medicine is the PPD test, which has been developed in the last century. This long history of using this test indicates that the interpretation of this test is still controversial. However, it has been well shown that the tuberculin skin test reaction and immunity are in fact independent phenomena. The rate of tuberculin reaction is often consistent with immune conditions [1]. Tuberculin skin test is used to identify people with a history of exposure to mycobacterial antigens. The test involves an intradermal injection of tuberculin, which causes delayed hypersensitivity due to T lymphocytes and occurs within 48 to 72 hours. Tuberculin is actually purified protein derivative (PPD) (the recommended dose in North America is 5 units of tuberculin (0.1 ml)). The standard dose is 2 units of tuberculin [18]. The only way to test for tuberculin skin is the Mantoux technique, which involves injecting tuberculin intravenously into the forearm. To read the test, the diameter of the swollen area should be recorded and expressed in millimeters. This measurement should be done within 48 to 72 hours [19]. In this study, we aimed to evaluate the positive rate of tuberculin test after inoculation of BCG vaccine in infants 4 months to 5 years old children in university referral Hospital in Zahedan-Iran.

## Methodology

The study was a descriptive study that included children between 4 months and 5 years old who were referred to Hospital in Zahedan who were vaccinated with BCG at birth. Inclusion criteria included having informed consent, age between 4 months to 5 years and history of BCG vaccination. Exclusion criteria also included congenital anomalies, cancer, immune disorders (acquired and congenital), history of infection during vaccination, palpable adenopathy, malnutrition, immunosuppressive drugs and concomitant viral diseases have been. At the beginning of the project, informed consent was obtained from all parents or legal guardians of the children. All children's information is kept confidential. Sampling was performed through available and sequential samples. Then, for all these patients, a questionnaire form containing all the mentioned variables was filled out. Then PPD test was performed for all subjects and then after 48 hours to 72 hours later the bulge diameter was measured and then the data were entered into the computer and analyzed. To analyze and describe the data, descriptive statistics were used to describe the data including frequency - percentage - mean and standard deviation. Chi-square test was used to compare the frequency of qualitative variables between the two groups.

## Results

In this study, 400 infants from 4 months to 5 years old children referred to university referral Hospital were evaluated. 173 (43.25%) were girls and 227 (56.27) were boys. In the age study, 128 subjects (32%) were 4 months to 1 year old. Also, 272 people (68%) were 1 to 5 years old. According to the positive and negative criteria of the test mentioned at the Introduction, 243 people (60.8%) were 0 to 5 mm. 157 patients (39.2%) were more than 5 mm in diameter, which indicates that this test is positive. In terms of protrusion diameter after inoculation, the mean protrusion diameter was 4.09 mm with a standard deviation of 2.88. The lowest was 0 mm and the highest was 17 mm. Among people aged 4 months to 5 years, 68% were 0 to 5 mm in diameter and 32% were more than 5 mm in diameter. Also, between 1 and 5 years old, 57% were 0 to 5 mm, 43 more than 5 mm in diameter. (Table 1) Chi-square test was used to evaluate the relationship between age and the possibility of a positive PPD test. After statistical analysis, P valuation was calculated to be 0.026 and there is a statistically significant relationship between age and the probability of positive PPD test. (P<0.05).

**Table 1:** Frequency of positive PPD test after inoculation of BCG vaccine in 4-month-old infants to 5-year-old.

| Amounts/ Age | Frequency | Percentage | PPD Test result | |
|---|---|---|---|---|
| | | | 0 - 5 mm | > 5 mm |
| 4 – 12 months | 128 | 32 | 68% | 32% |
| 1 – 5 year | 272 | 68 | 57% | 43% |

## Discussion

In our study, the bulge diameter was reported to be 4.09 88 2.88 after inoculation. Also, 61% of people had a negative test result and 39% had a positive PPD test result. Another goal of this study was to investigate the relationship between age and the probability of positive PPD test. In data analysis, there was a significant relationship between age and the probability of positive test (P <0.05), ie with these interpretations with increasing age of the child. The probability of a positive PPD test increase. In different studies, the percentage of PPD test positive in different communities, different results have been reported. Which, of course, is related to different conditions such as the prevalence of tuberculosis, the percentage of vaccination coverage, and so on. In a meta-analysis conducted by Dr. Rezai et al. In 2017, which analyzed the last 14 studies, among 26,281 Iranian children (CI: 95%), 8.5% reacted more than 10 mm, 29.9% reacted between 5 They had 9 mm and 60% less than 5 mm. In this study, it was shown that with increasing age, the percentage of positive test decreases. On the contrary, in our study, the test was more positive with age, which is most likely due to the wider age range selected by Dr. Rezaei. On the other hand, in our study, the rate of positive tests was 39%, but in Dr. Rezaei's study, only 8.5% of cases above 10 mm reacted [20]. In the study of Alavi SM et al. In 2001 in Ahvaz, the percentage of positive test results was reported to be 2%, which was about 1% less than the amount obtained in our study. However, in this study, 90% of people in the first week after birth They had received the BCG vaccine [21]. In a study by Sleiman R in Saudi Arabia in 2007, the positive rate was much higher than our study and Mr. Alavi's study in Ahwaz, which was reported to be 8%. About 62% of people were also vaccinated with BCG [22]. In 2008, Araujo Z et al reported a positive rate of 28%, which is very high. This high percentage can be due to the reasons mentioned above [23]. In a study published in Uganda, this study also reported a very high rate of positive testing. In this study, the prevalence of positive PPD test was 32%, which is due to factors such as the prevalence of tuberculosis and the percentage of vaccination coverage, etc. As a result of this study.

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**ISSN: 2574-1241**

DOI: 10.26717/BJSTR.2021.40.006448

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