Prevalence of BCG Scar Formation Among BCG Vaccinated Apparently Healthy U-5 Children and its Correlation with Mantoux Skin Test Induration in Maiduguri, Nigeria.

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SUMMARY

Background: Tuberculosis (TB) is still a major public health problem world-wide. BCG scar is often used as an indicator of previous vaccination in clinical settings as well as in Immunization Surveys, although not all BCG-vaccinated children form scar.

Objective: This study was under-taken to determine the BCG scar rate formation among BCG-vaccinated children and the pattern of Mantoux test reactions among the children with and without BCG-scar in Maiduguri, Nigeria.

Methods: The study was descriptive and cross-sectional, conducted in Maiduguri, Nigeria, among 296 BCG-vaccinated apparently healthy 3-59 months old children who attended the child welfare clinics of the University of Maiduguri Teaching Hospital and two Primary Health Care centres from May to August 2008. Children who fulfilled the inclusion criteria were examined for BCG-scar and Mantoux tested.

Results: Out of 296 BCG-vaccinated children studied, 165 (55.7%) had BCG scar, while the remaining 131 (44.3%) had no scar. No significant statistical difference in relation to age at vaccination and BCG scar formation was noted, ($p = 0.376$). The mean Mantoux reactions between those vaccinated in the neonatal and post-neonatal period, ($p = 0.258$), was also not statistically significant. The vaccinated children with scar had a significant negative Mantoux test correlation with age; ($r = -0.39$, $p < 0.000$), compared to a non significant negative Mantoux correlation among the vaccinated children without scar; ($r = -0.193$, $p = 0.027$).

Conclusion: BCG scar formation among vaccinated children in Maiduguri is low. In spite of the difference in Mantoux readings between the children with and without BCG-scar, we recommend continued immunization with BCG at birth of all children in Maiduguri, as recommended by the Nigerian, National Programme on Immunization.

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INTRODUCTION

Tuberculosis (TB) is one of the major public health problems in the world, as one third of the population of the world are infected.[1] The World Health Organization (WHO) Expanded Programme on Immunization(EPI) recommends that BCG vaccine be given as a single dose as soon as possible after birth in all populations at high risk. The Nigerian National Programme on Immunization (NPI) also recommends Bacille Calmette-Guerin (BCG) immunization at birth as part of the routine immunization schedule. The presence or absence of a BCG scar is often used as an indicator of previous vaccination in clinical settings as well as surveys performed by health institutions such as the EPI to assess vaccine uptake. Failure to form a scar may be related to factors such as lack of maturation of the immune system, faulty technique, or use of a non-potent vaccine.[2,3]

Tuberculin skin test (TST), a delayed (Type IV) hypersensitivity reaction (DTH) is useful in diagnosis of TB infections. The TST is carried out by employing the Mantoux test, BCG-test or the multiple puncture test (MPT). Due to the short-comings of the MPTs, it is no longer recommended especially in children.[4,5] A Mantoux reaction of 10mm and above is generally considered positive, which denotes TB infection, although, a negative test does not exclude TB.[4-6] Several studies have emphasized that trained health care professionals must place, read, and interpret Mantoux tests.[7,8]

It is important to note that neither the presence of BCG scar nor size of the Mantoux test reaction predicts immunity to disease[9] nor protective efficacy[10] of BCG. The efficacy of BCG vaccine is thus estimated from prospective clinical trials and retrospective case-control studies, like the meta-analysis conducted by Colditz *et al*,[11] which showed that, on the average, BCG vaccine significantly reduces the risks of TB by 50%.

Studies from different parts of the World have assessed the relationship between the size of Mantoux test reactions and BCG immunization to determine the extent of false-positive reactions associated with BCG vaccine. Surveys conducted in Malawi[12] and Tanzania[13] found a higher prevalence of positive Mantoux tests (>10 mm) in children with a BCG scar when compared with children without a scar. However, in a study of 783 Botswana children aged 3–60 months, Lockman *et al*[14] noted that among those with documentation for BCG immunisation, 79% had non reactive Mantoux test (00 mm), 6% had a Mantoux test reaction between 1 and 4 mm and 8% had a Mantoux test reaction between 5 and 9 mm. Five per cent had a reaction between 10 and 14 mm, while only 2% had a reaction of >15 mm.

Similarly, Nottidge *et al*[15] found 96.6% of BCG vaccinated children in Saudi Arabia to have negative Mantoux test.

This study was therefore conducted to determine the BCG scar rate formation among BCG-vaccinated children and the pattern of Mantoux test reactions among BCG-vaccinated children with and without scar in Maiduguri, Nigeria.

METHODS

This descriptive cross-sectional study was conducted in Maiduguri, Nigeria, among 3-59 months old children attending the child welfare clinics of the UMTH and two of the four Primary Health Care (PHC) centres selected by simple random method (Yerwa and Gamboru), after obtaining parental or guardian informed verbal consent.. Lower age limit of 3 months was considered because tuberculin conversion occurs from 3 weeks to 3 months following contact with *Mycobacteria*.[6] Children vaccinated with BCG at a later date (not at birth) were recruited only if at least 3 months had elapsed since vaccination (also to allow for tuberculin conversion), and all recruited children were examined for a typical BCG scar.

Apparently healthy children was defined by; absence of fever (axillary temperature < 37.5^{0}C) or skin rash, normal general physical examination, including the spine, absence of significant peripheral lymphadenopathy, normal examination findings in the chest, abdomen, ears and throat, normal weight,[16] and normal length or height.[16] Children recently (< 6 weeks)[17] vaccinated with live-attenuated vaccine e.g measles and OPV, children treated for TB in the past or receiving treatment at the time of the study and those on steroids or cytotoxic agents were excluded. Other excluded children included those with recent Mantoux test(less than one year), to avoid boosting effect,[18] non-consent of parent /guardian and those aged < 3 months or > 59 months.

Purified protein derivative- Siebert (PPD-S) stabilized in *tween* 80 (0.005%), BB-NCIPD Ltd, Sofia, Bulgaria with Batch number 4240106 was used in all children studied. The manufacturer's instructions were strictly adhered to.

The injection of PPD and reading of the reaction was done by one of the authors (MGM) after undergoing training. An assistant helped in stabilizing the limb during injection of the PPD and reading of the reactions when necessary. The date and time of injection and reading of the reactions were all recorded. Investigator's TST readings were validated by the officer in charge of administration and reading of the Mantoux tests in the hospital, and found to be highly reproducible with a 98% degree of concordance.

Diameter of induration was measured along the transverse axis of the forearm 48 to 72hours[5,19] after injection using a plastic transparent meter rule and also employing the use of the "ball point pen" technique of Sokal[20] which helps to make measurements more accurate. Reading of the reaction was done in good light. The results were recorded using two digits in millimetre (mm). The Mantoux reaction of the subjects was greaded according to modified Egbebe *et al*,[21] as follows;

1. Negative, with induration of 00 - 04mm
2. Borderline, with induration of 05-09mm (intermediate)
3. Positive, with induration of 10-14mm
4. Moderately positive with induration of 15-20mm and
5. Strongly positive with induration of 21 - 30mm. Negative and borderline Mantoux reactions constitute non-positive Mantoux reactions.

Children with positive Mantoux test were followed up in the Paediatric out-patient clinic, where their history and physical examination were evaluated further. A chest radiograph, complete blood count and erythrocyte sedimentation rate, were also done for appropriate management.

Data Analysis: Data analysis was done using SPSS version 13.0. Frequencies were compared using chi-square(x^2) test, Yates' corrected chi-square test or Fisher's exact test as appropriate, and means were compared using Student t-test. A p-value of <0.01 was considered significant. Tables were used for data presentation where appropriate.

RESULTS

A total of 296 BCG vaccinated children aged 3-59 months were recruited from the 3 health facilities (UMTH, Yerwa and Gamboru PHCs) between May 2007 and August 2007. One hundred and sixty five (55.7%) of the 296 children had BCG scar, while the remaining 131 (44.3%) had no BCG scar. There was significant statistical difference in the mean Mantoux reactions of the children with BCG scar compared to the children without a BCG scar, (t = 4.887, p< 0.000). Significant statistical difference was also observed between the children with positive and non-positive Mantoux reactions among the vaccinated children with and without scar, (p < 0.000). The vaccinated children with scar had a stronger and significant negative Mantoux test correlation with age; (r = -0.39, p < 0.000), compared to a weaker and non significant negative Mantoux correlation among the vaccinated children without scar; (r = - 0.193, p = 0.027). While majority (72.5%) of the vaccinated children without scar had Mantoux induration in the range of 00-04mm, only 48.5% of the vaccinated children with BCG scar had Mantoux induration in that range (Table I).

Two hundred and forty seven (83%) of the vaccinated children had neonatal BCG vaccination, while 49 (17%) were vaccinated after 28 days of life. No significant statistical difference in relation to age at vaccination and BCG scar formation was noted, (Yates corrected x^2 =0.785, p = 0.376). There was also no significant statistical difference in the mean Mantoux reactions between those vaccinated in the neonatal and post-neonatal period, (t =1.13, p=0.258).

Table I: Mantoux reaction groups of the study population

	MANTOUX GROUP(mm)				
BCG SCAR	**0-4**	**5-9**	**10-14**	**15-20**	**TOTAL**
YES	80	58	24	3	165
NO	95	33	3	0	131
TOTAL	**175**	**91**	**27**	**3**	**296**

DISCUSSION

The BCG scar rate of 55.7% found in this study, though higher than scar rate of 44% reported in Port Harcourt,[2] is however low compared to scar rates of 72% and 99% reported from other parts of the world.[22,23] Some of the reasons advanced

for the low scar rates include; altered vaccine potency as result of frequent power failure leading to poor cold chain maintenance, also the possibility of poor technique of vaccine administration especially in busy clinics was also entertained.[2] Therefore BCG scar may not be a good indicator of vaccine coverage in Maiduguri, as in Port Harcourt, contrary to Peru[23] where a BCG scar was reported to be a sensitive marker of vaccination status.

The finding in this study of significant proportion of vaccinated children with negative Mantoux reactions is similar to studies from Botswana[22] and The Gambia.[24] Likewise in Saudi Arabia, 96.6% of BCG vaccinated children had a negative Mantoux test.[25] Although the proportion of vaccinated children without BCG-scar among the children with negative Mantoux induration was significantly more than the children with scar, the possibility of anergy to Mantoux test among the study population was not considered, since all the subjects were apparently healthy. The reason why BCG-vaccinated children especially young ones may have a negative Mantoux test to such a large proportion may be difficult to state. The difference in numbers and proportions of viable and dead organisms according to dose of BCG given[19] in addition to microbiologic and genetic differences in various strains of the vaccine, could account for the variations in reactogenicity and immunogenicity of the vaccine.[23] Other possible explanations may include poor shipment and storage of the vaccines.

The significant difference found in the mean and positive Mantoux reactions between BCG vaccinated children with scar and those without scar in this study underscores the importance of the presence of scar in BCG conversion and as a screening tool for BCG immunization coverage. Similarly, Lockman *et al*[22] and Santiago *et al*[23] reported that, increased Mantoux reactions (but not = 10mm) are associated with the presence of BCG scar. Although, BCG conversion rates of 20-90% have been reported,[26] failure of BCG vaccine to induce skin sensitivity should not be taken as evidence of its failure to confer protection against TB.[11,26]

Age at immunisation was not significant in determining BCG scar formation, contrary to the findings of Anochie *et al*,[2] who compared BCG skin reactions of babies vaccinated in the first week of life and after one week of life. The difference with this study may be due to age groups studied. While the earlier study considered first week of life, in this study, neonatal BCG vaccination was compared with post-neonatal vaccination. The observation that, age at immunization was not found to be significant in determining the size of Mantoux reaction, is similar to a report from Nnewi, Nigeria, and a study by Santiago *et al* who compared Mantoux reaction of children vaccinated within 48 hours of birth and those vaccinated 3- 29 days after birth.[23,27] In spite of these findings, it is still important to give BCG vaccine at birth, so that protection against TB can be offered to children as early in life as possible.

Factors determining BCG scar formation and pattern of Mantoux skin reaction among different category of children greatly vary. In spite of these variations, we recommend continued immunization of children at birth with BCG in Nigeria, which currently ranks fifth among the countries with high TB burden.[28]

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