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Prevalence of BCG scar among BCG-vaccinated children in a southern Nigeria tertiary hospital

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Abstract: *Background*: The burden of tuberculosis is high in Nigeria as in other developing countries. The administration of BCG vaccine to neonates is essential in the control of tuberculosis. A scar usually develops 6 – 8 weeks later at the site of vaccination, which can be used clinically as a proof of vaccination. Not all vaccinated infants however, develop a BCG scar.
Objectives: To determine the prevalence of scar formation post-vaccination and to unravel, if present, any factors responsible for scar failure.
Methods: Two hundred and fourteen children were consecutively recruited from those who presented for immunization in the University of Benin Teaching Hospital, Benin. The bio-data and other relevant information were obtained using a proforma. The anthropometric measurements of the children were obtained and the children were examined for presence of a BCG scar.
Results: Two hundred and six subjects (96.3%) had a post-vaccination BCG scar. About 72% of the subjects were vaccinated within the first week of life. The age at vaccination was significantly affected by gestational maturation (P=0.003) and birth weight (P=0.0001). Gestational maturation is a strong predictor of BCG scar formation post-vaccination (P = 0.007)
Conclusion: There is high prevalence of BCG scar formation in this study and gestational maturation is a strong predictor of BCG scar formation.

Introduction

Tuberculosis is an infectious disease which is prevalent in developing countries. In 2011, there were an estimated 8.7million new cases of Tuberculosis in the general population (13% co-infected with HIV) and 1.4million people died from the disease[1]. There were an estimated 0.5million cases and 64000 deaths among children in 2011.Africa and Asia have the highest burden of tuberculosis[1]. The African Region has approximately one-quarter of the world's cases, and the highest rates of cases and deaths relative to population. Nigeria is one of the 22 countries with a high burden of tuberculosis, with an incidence of about between 90,000 to 330,000 cases per year[1].

As part of control measures to reduce the burden of tuberculosis especially in children, the World Health Organization recommends vaccination with BacilleCalmette-Guerin vaccine at birth or first contact with health services, especially in developing countries.[2] The World Health Organization has emphasized this policy in recent years, because of consistent evidence that BCG protects against serious childhood forms of tuberculosis, even where it may not protect to a high degree against adult pulmonary form of the disease[2]. In various clinical trials the estimates of effectiveness have ranged from 80% protection to no benefit[3]. Despite its limitations, the BCG vaccine is the only currently available vaccine for the prevention of tuberculosis. Overall, more than 80% of all neonates and infants in countries where the vaccine is part of the national childhood immunization programmereceive the vaccine[4]. The coverage however, varies from country to country. The estimated BCG coverage for the year 2011, reported by the World Health Organization, revealed levels ranging from 54% in Ethiopia and 60% in Nigeria, to 99.5% in India and China[5].

The BaccilleCalmette-Guerin contains a live attenuated strain of Mycobacterium bovis which is administered intra-dermally over the left deltoid muscle. After a period of 6 – 8 weeks post-vaccination a swelling appears which increases in size and ruptures leaving behind a life-long puckered scar after healing. The presence of a BCG scar and the tuberculin skin test are utilized in clinical settings to determine those who have been immunized with the BCG vaccine. The tuberculin skin test is usually positive in people who have received the vaccine. Considering the fact that the tuberculin test

is also positive in those with the disease and those exposed to non-tuberculous mycobacteria infection, it is not specific for identifying those who have received the vaccine. Moreover, the result is often negative in immunocompromised (HIV, disseminated tuberculosis, malignant conditions) individuals, even those who had previously been vaccinated, due to cutaneous anergy.

In the absence of a vaccination card the BCG scar may thus be the only option left to clinically determine vaccination status. It is however, noted that not all vaccinated children develop a scar.[6]Different studies world-wide have reported varying prevalence rates of the presence of BCG scar in vaccinated children. A study in Karachi, involving 250 infants, reported presence of scar in 80.4% of the infants.[6]However in this study, the age at vaccination, gestational age and other characteristics of the children were not evaluated in order to find the possible reason for the absence of scar formation. A study in Northern Nigeria reported a 95.1% prevalence of scar formation.[7]This study however, evaluated only 41 children. Another study in Northern Nigeria evaluated 296 children between the ages of 3 – 59months receiving immunization in a Teaching Hospital and two Primary Health Centers. Only 55.7% of the vaccinated children had a BCG scar.[8] This study is aimed at evaluating infants in Southern Nigeria to determine the prevalence of scar formation and to unravel, if present, any factors that may be associated with BCG scar formation.

Materials and method

This is a cross-sectional study carried out between June and September, 2012 at the University of Benin Teaching Hospital, Benin-city, Edo State. The Hospital offers curative and preventive services to patients from Edo State and the neighbouring States of Delta, Ondo, Bayelsa, Ekiti and Kogi. Immunization services take place in the General Practice Clinic and the Institute of Child Health, on a daily basis from Monday to Friday, except on public holidays. The immunization units of the General Practice Clinic and Institute of Child Health vaccinate about 1000 children respectively annually.
Ethical clearance for the study was obtained from the Ethical Committee of the University of Benin Teaching Hospital. A verbal consent was obtained from the parents and caregivers of the subjects after explaining the objectives and the harmless nature of the study.

The subjects were consecutively recruited from children attending the General Practice Clinic, who had been previously vaccinated with BCG and have presently come for subsequent vaccines in the National Programme on Immunization schedule. Information on the bio data such as age, sex, and gestational age were obtained using a proforma. Information on birth weight, age at receipt of BCG vaccine and place of vaccination were also obtained. Subjects delivered before 37 completed weeks of gestation from the mothers last menstrual cycle were classified as preterm; those between 37 and 42 completed weeks of gestation as term while those delivered after 42 completed weeks were classified as post-term. The weight of the subjects was measured with an infant weighing scale, Way master^{R} made in England, calibrated to the nearest 50gm; the length was assessed with an infantiometer while the head circumference was measured with a non-elastic measuring tape. The left upper arm around the deltoid was examined for presence of a BCG scar. The subjects were classified nutritionally using the WHO weight for age z-score growth charts. Subjects with z-score of less than –3 were classified as severely under-nourished; between –3 and –2 as moderately under-nourished; between –2 and +2 as normal; while above+2 as overweight.[9]The data collected was recorded in Microsoft Excel spreadsheet and transported to SPSS version 19 for analysis. Univariate analysis was conducted for all variables to assess their distribution. Continuous variables were summarized using means and standard deviations while categorical variables were summarized using proportions.
Chi-square test was used to determine association between categorical variables. P-value of less than 0.05 was considered statistically significant.

Results

A total of two hundred and fourteen subjects comprising 117 (54.7%) males and 97 (45.3%) females were recruited for the study. The mean age of the subjects was 4.33 ± 2.54 months. The ages of the subjects ranged from 6weeks to 15months. The age group of 6weeks – 6 months formed the bulk (90.7%) of the study population. The general characteristics of the study population are as shown in table 1.

Table 1: General characteristics of the study population

Characteristic	n	%
Gender		
Male	117	54.7
Female	97	45.3
Age (in months)		
1.5 – 6	94	90.7
7 – 12	16	7.5
≥13	4	1.9
Age at vaccination (days)		
1 – 7	151	71.9
8 – 14	35	16.7
15 – 21	9	4.3
22 – 28	3	1.4
≥ 29	12	5.7
Gestational Maturation		
Pre-term	15	7.1
Term	186	88.6
Post-term	9	4.3
Birth weight category		
Low birth weight	13	7.6
Normal birth weight	137	80.1
High birth weight	21	12.3
Place of vaccination		
Private Hospitals	21	9.9
UBTH	180	84.9
Other Public Hospitals	11	5.2
Nutritional status		
Overweight	11	5.2
Normal	190	88.8
Underweight	8	3.7
Severe malnutrition	5	2.3

Majority of the subjects (71.9%) were vaccinated within the first week of life while 16.7% were vaccinated between the 8th and 14th day of life. Twelve (5.7%) subjects were vaccinated after one month of life. Among those vaccinated within the first week of life 9.3% and 10.6% were vaccinated on the 1st and 2nd day of life respectively. Majority of them (44.4%) were vaccinated on the 7th day of life. A greater proportion (26.7%) of pre-term infants were vaccinated after 4weeks of age in comparison to the term (9.3%) and post-term (0%) subjects as shown in table 2. This difference was statistically significant (P=0.003). Similarly, a greater proportion (30.8%) of the subjects with low birth weight were vaccinated after 4weeks in comparison to normal birth weight (0.7%) and high birth weight (4.8%) babies. This difference was also statistically significant (P=0.0001). The above findings indicate that prematurity and low birth weight are significantly associated with late presentation of the study population for BCG vaccination.

Table 2: Association between age of vaccination and gestational maturity and birth weight

	Age at vaccination (days)			χ^2	P-value
	0 – 14 n(%)	15 – 28 n(%)	≥29 n(%)		
Gestational maturity					
Pre-term	9(60)	2(13.3)	4(26.7)		
Term	165(90.7)	9(4.9)	8(4.4)	16.28	0.003
Post term	9(100)	0(0)	0(0)		
Birth weight category					
LBW	7(53.8)	2(15.4)	4(30.8)		
NBW	130(94.9)	6(4.4)	1(0.7)	35.93	0.0001
HBW	18(85.7)	2(9.5)	1(4.8)		

Evaluation of the nutritional status of the study population, as shown in table 3, showed normal nutrition in 190 (88.8%) subjects; 5.2% were overweight while 2.3% had severe malnutrition.

Presence of scar post-vaccination was observed in 206 of the subjects, giving a prevalence of 96.3%. There was absence of scar in 8 (3.7%).Evaluation of the factors related to scar formation showed a statistically significant difference (p = 0.011) among subjects in the various gestational age groups as shown in table 3. Absent scar formation was highest among the post-term (22.2%) in comparison to the term (3.2%) and pre-term (0%) subjects. The presence of BCG scar was not significantly associated with the place of vaccination; chronological age at vaccination, nutritional status, birth weight, and gender of the subjects.

Table 3: Association between BCG scar formation and some variables.

Variables	Presence of scar n(%)	Absence of scar n(%)	P-value
Gender			
Male	110(94)	7(6)	0.057
Female	96(99)	1(1)	
Gestational Maturity			
Pre-term	15(100)	0(0)	
Term	180(96.8)	6(3.2)	0.011
Post-term	7(77.8)	2(22.2)	
Age at vaccination (days)			
1 – 14	180(96.8)	6(3.2)	
15 – 28	11(91.7)	1(8.3)	0.509
≥29	12(100)	0(0)	
Birth weight categories			
Normal	134(95)	7(5)	
Low birth weight	13(100)	0 (0)	0.415
High birth weight	21(100)	0(0)	
Place of vaccination			
UBTH	173(96.1)	7(3.9)	
Other GovtHosp	10 (90.9)	1 (9.1)	0.619
Private Hospitals	21(100)	0(0)	
Nutritional status			
Over-weight	11(100)	0(0)	
Normal	182(95.8)	8(4.2)	0.789
Underweight	8(100)	0(0)	
Severe mal-nutrition	5(100)	0(0)	

Discussion

The WHO recommendations for routine use in EPI schedule and available data on BCG vaccine effectiveness indicate that the vaccine should be administered as soon as possible after birth and before 1 month of age for maximumprotection.[11]In this study, 71.9% of the subjects were vaccinated within the first week of life, while 5.7% were vaccinated after one month of age. Previous studies showed variable rates at reception of BCG vaccination. A study from Sri Lanka reported 99% reception of BCG within the first week of life[12]. The very high rate of vaccination within the first week of life in the Sri Lankan study may be due to high awareness of the need for BCG immunization which is reflected in the high BCG coverage of almost 100%[11] as against 49.7% in Nigeria where this study was carried out.[12]A similar study[7] from the Northern part of Nigeria reported a lower percentage (36.2%) of BCG vaccination within the first week of life. This difference might be due to a lower BCG coverage in the Northern part of Nigeria compared to Southern Nigeria, where our study was carried out, as shown in the National Demographic Health Survey in Nigeria[12].

It was observed from this study that birth weight and gestational age significantly influenced the age of BCG vaccination. These two factors are closely related as preterm neonates will most likely have a low birth weight. Weight is usually a limitation in the commencement of immunization in Nigeria since, from observation in most immunization centres, a minimum weight of 2kg is insisted upon by health workers before administration of BCG. The same practice of late vaccination of Low birth

weight infants have also been reported in Guinea-Bissau[13]. According to the World Health Organization, pre-term infants in developing countries should be vaccinated with BCG at a post-conceptional age of 40weeks. Since establishing the correct gestational age is a challenge in most developing countries, the birth weight rather than gestational maturity is utilized in defining when BCG is administered. This has varied implications for the low birth weight infant, since failure to vaccinate children with BCG at birth has been reported to contribute to lower BCG vaccination coverage among low birth weight children.[13]Early vaccination of Low Birth Weight infants with BCG has also been reported to reduce mortality rate by 17% in a randomized control trial in Guinea-Bissau[14]. Late reception of BCG in the few patients (1%) reported in Sri Lanka was ascribed to illness which resulted in the children being admitted in the Special Care Baby Unit[11]. The gestational age and birth weight may be contributory as both are common reasons for admission into the neonatal unit.

The prevalence of scar formation from our study indicate that the presence of a BCG scar can be utilized as a reliable clinical evidence of BCG vaccination, in the absence of immunization card, as most of the studied population (96.3%) developed a scar post-vaccination. This observation is comparable to the findings from Peru[14]and India[15]where the prevalence of scar formation was 99% and 90.2% respectively. This observation is, however, at variance with the study of Mustapha et al[8] in Northern Nigeria where the prevalence of scar formation was 55.7%. This difference might be accounted for by the different age groups in Mustapha's study and these other studies. Mustapha et al studied children between the ages of 3 – 59months as against 6weeks – 15months in our study, with children between the ages of 6weeks – 6months forming the bulk (90.7%) of the study population. The studies from India and Peru similarly studied younger children vaccinated from birth to 3months of age and were followed up until 6months.There has been documented evidence of waning of BCG scar post-vaccination in children followed up from infancy to fourteen years of age[17]. The possibility therefore, of disappearance of the BCG scar in the older children among the subjects in Mustapha's study could have contributed to the lower prevalence of scar formation reported. Other factors which include use of a non-potent vaccine, faulty vaccination techniques and lack of maturation of the immune system are documented factors that may contribute to failure of scar following vaccination[15]. It is difficult to ascertain if these factors contributed to the difference in the prevalence of scar formation.

Presence of BCG scar was not significantly affected by sex, birth weight, age at vaccination, nutritional status and centre of vaccination. Santiago et al[15], similarly, did not find any association between scar formation and sex, birth weight, age at vaccination and nutritional status. There was however, a significant association between development of BCG scar and gestational age in our study, as a higher proportion of the post-term infants showed absence of scar post-vaccination. The possible reason for this finding is not quite apparent as previous studies relating gestational age and scar formation post-vaccination are at variance. Preterm neonates are more likely to show absent scar formation compared to term and post-term neonates due to poor immune response as reported by Sedaghatianet al[18] in the United Arab Emirates. A study in India[19] among preterm babies delivered less than 35weeks gestation and vaccinated at birth and at 38 – 40 weeks post-conception did not show any statistically significant difference in scar formation. The small number of post-term infants in our study may affect the interpretation of this finding and thus affect the deductions made.

Limitations of the study

Mothers' information on birth weight and gestational age was utilized in absence of information from the case file. The accuracy of this information might not be completely reliable.

Conclusion

This study shows a high prevalence of BCG scar formation post vaccination in early childhood and gestational age is a strong predictor of BCG scar formation post-vaccination.

Author's contributions

AOA: Conceptualization, methodology, planning and data collection, analysis and writing of the manuscript.

OOW: Methodology, planning and data collection, analysis, proof reading of the manuscript.

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