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Timeliness of Bacilli Calmette-Guérin vaccination among infants in a tertiary health facility in sub-Saharan Africa

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Abstract

Context: Administration of a single dose of Bacilli Calmette-Guérin (BCG) vaccine at birth is a key component of pillar one in the End Tuberculosis strategy and has been shown to be a cost effective tuberculosis preventive intervention. However, the proportion of children vaccinated at birth varies within and across countries.
Objective: To determine the proportion of infants vaccinated with BCG at birth, identify factors associated and barriers to vaccination at birth.
Materials and methods: A cross-sectional study carried out among infants aged 0 – 12 months attending the immunization clinic at a tertiary health facility in Abuja. Frequency tables, chi square and logistic regression were used in the statistical analysis.
Results: Among 414 caregiver participants, 100%, 75.8% and 97.1% were females, with tertiary education and married, respectively. Majority (53.1%) of infants were male. Almost all (99.5%) had received BCG but only 35.3% received at birth. No association was found between receipt of BCG at birth and socio-demographic factors or maternal obstetric history. The commonest barrier to receipt at birth was the vaccine not given to infants at health facilities on birth date (p = 0.0001 OR= 14.56 CI 8.077-26.248).
Conclusion: Majority of the infants had received the BCG vaccine, however, only a small proportion had received it at birth. There is an unmet need of ensuring infant vaccination with BCG occurs daily including weekends and public holidays while increasing public awareness especially through antenatal clinics. This may help reduce child mortality and morbidity from tuberculosis.

Key words: Timeliness, BCG, vaccine, infants, barriers.

Introduction

Tuberculosis (TB) is caused by *Mycobacterium tuberculosis* and is one of the 10 leading causes of mortality globally, responsible for about 1.4 million deaths and 1.2 million children ill health globally in 2019.[1] More than 95% of TB cases and deaths occur in developing countries.[1] Of the 87% of new TB cases that occurred in the 30 high burden countries in 2019, eight countries which include Nigeria were responsible for two-thirds of them. The seven other countries were Bangladesh, China, India, Indonesia, the Philippines, Pakistan and South Africa.[1] Populations at greater risk for tuberculosis are

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children aged less than five years, HIV-infected persons, migrants, refugees and incarcerated persons.[1]

One of the Sustainable Development Goals (SDG) target is to end TB epidemics by the year 2030. To achieve this, the End TB strategy was endorsed by the SDGs with the aim of reducing the number of deaths from TB by 95% by the year 2035 when compared with rates in 2015.[2] The administration of Bacilli Calmette-Guérin (BCG) vaccine at birth or thereafter, soonest after birth is one of the key components of pillar one of the End TB Strategy.[2]

At present, the BCG vaccine is the only vaccine in use for preventing TB.[3] The vaccine is derived from *M. bovis*. Several BCG vaccines containing different strains of *M. bovis* are available. The vaccine protects against the severe forms of tuberculosis in children and also confers protection against leprosy, Buruli ulcer and non-mycobaterium tuberculosis.[3] The protection from the vaccine is reported to last for 10 to 15 years[4] and so some have called for revaccination after this period. Available evidence for revaccination is not considered strong or cost effective, although some subgroups may benefit, there is however a need for further studies.[3]

The time at which BCG vaccine should be administered has generated some controversy. Some studies have shown that delaying administration of the vaccine may be more beneficial. It was reported that a delay of 10 weeks from birth in HIV-unexposed South African children resulted in an enhanced memory CD4 T-cell response.[5] Another study in South Africa demonstrated that delaying the BCG vaccine for eight weeks did not compromise immune response and may enhance immunity in TB.[6] However, this randomized controlled trial study had a small sample size with only 28 infants in each arm and was carried out among HIV-exposed children.

The World Health Organisation (WHO) recommends that a single dose of the vaccine should be given at birth to all healthy newborn in countries or settings where there is a high incidence of TB, and/or leprosy and Buruli ulcer. Vaccination at birth has been shown to be a cost effective intervention for preventing TB.[2,3] If not given at birth, it should be administered at the closest possible time after birth.[3] The vaccine is given free in Nigeria under the Nigerian Programme on Immunisation in accordance to the WHO recommendation. However, the proportion of children vaccinated at birth varies within and outside the country, Nigeria. Considering that the vaccine is the only specific primary prevention method available for tuberculosis for now, it is pertinent that the recommended timeline guide for vaccination be adhered to. This study aims to determine the timeliness of receiving BCG vaccines among infants aged 0 – 12 months presenting to the immunization clinic at the University of Abuja Teaching Hospital, determine the factors associated with timeliness and the barriers associated with timeliness.

Method

Study design: A descriptive cross-sectional study design was used. The setting was the immunization clinic at UATH. The inclusion criteria were caregivers who gave their consent to participate, who presented with infants aged 0-12 months and the infant's immunization card containing their immunisation record. Caregivers who were sick, had sick infants or were less than 18 years old were excluded from participating in the study.

Recruitment of participants and study procedure: Random sampling method was used to select participants. They were then approached to participate and give consent. Every third caregiver who presented at the clinic was selected. If they refused consent, the next person was selected. They read through the participant information sheet first and signed the consent form if they accepted to participate after which they were given the questionnaire. Those who had difficulty reading or did not understand English were assisted by the researchers or trained research assistant who either read out the questionnaire or translated in Hausa, and then filled the questionnaire for them. Data collection lasted a period of three months from January to March, 2020.

The study instrument was a self-administered, structured questionnaire developed by the researchers which included questions obtained from previous studies.[7,8,9] A pre-test was done to determine the time it took to complete the questionnaire and identify difficulties participants may have in understanding and answering the questions. Subsequently, such questions were

modified. Questions asked were about the respondents' socio-demography, age and gender of the child and time of receiving BCG vaccine which were categorized into: at birth (within 24 hours of delivery), within two weeks of delivery, within two to four weeks of delivery and more than four weeks after delivery. There were also questions on maternal antenatal and delivery history and questions to determine the barriers to early receipt of the vaccine. After completion of the questionnaires, the participants put the completed questionnaires in a box in the clinic. Participation was totally anonymous as no names or identification numbers were written on the questionnaires. Confidentiality was maintained throughout and after the study.

Data analysis: The data was analysed using SPSS version 25. Frequency tables were used to show proportions while Chi square and logistic regression used to determine associations and strength of associations between timeliness of receiving BCG vaccine and various factors, as well as barriers to vaccine timeliness. Fisher's exact test was used to determine associations when the cells had a value of less than 5. A P value < 0.05 was taken as significant and the confidence interval set at 95%.

Ethical approval: This was obtained from the Health Research and Ethics Committee of the University of Abuja Teaching Hospital prior to commencement of the study. Standards of ethics practice was maintained all through the study according to the Helsinki Declaration of 1975 as revised in 2013. Participation in the study was voluntary. Participants were informed that they were free to decline consent at any point during the study without fear of repercussion. The researchers were responsible for the cost of the study.

Results

A total of 414 caregiver and child dyad participated in this study with 8 women declining, giving a response rate of 98.1%.

General characteristics of participants

All 414 (100%) caregivers were females with an age range of 19 years to 45 years, SD ± 4.279. Majority 413, (99.8%) were the infant's mother, had tertiary level of education (314; 75.8%), were married (402; and formally employed (109; 97.1%). The infants ages ranged between date of birth to 266 days (9 months) old, with 220 (53.1%) being males and 194 (46.9%) females. Majority of the children were > 28 days old. (Table 1).

Four (n= 4; 1%) mothers did not attend antenatal clinic. Of the majority that attended, most (n= 217; 52.4%) could not remember how often they attended the clinic. The attending personnel at the clinic were mainly skilled personnel (doctors n= 407; 98.3% and nurses/midwives n=301; 72.7%) and the location of the clinics, mainly government health facilities (n=395; 95.4%). The deliveries also, mostly occurred in government health facilities (n=377; 91.1%) with spontaneous vaginal deliveries being the commonest method (n=318; 76.8%). The source of information about immunization was mainly from government health facilities (n=370; 89.4%). Table 2 shows the maternal obstetric history. Totals may not add up to 100% as multiple answers were allowed in the questions on attendant personnel, place of antenatal care and source of information.

The mean age of receipt of BCG = 4.07 ± 4.7 days. Majority of the children had received their BCG vaccine (n=412; 99.5%). Only 2 (0.5%) had not received it. One-third (n= 146; 35.3%) had received BCG at birth as recommended while majority (n=260; 62.8%) received the vaccine within 2 weeks of delivery. Most children had received the vaccine mainly from government health facilities. This is shown in Table 3.

The association between the socio-demographic factors and receipt of BCG at birth as well as between the maternal obstetric history and receipt of BCG at birth were not statistically significant: age of caregiver (X^2 =1.492, P= 0.99), educational level of caregiver (X^2= 1.89, P = 0.596), marital status (X^2 =0.721, P = 0.697), employment status of caregiver (X^2 =0.438, P = 0.508), gender of child (X^2 =0.104, P = 0.747), frequency of attendance at antenatal clinic (X^2 =6.79, P = 0.075) and place of delivery (X^2 = 4.33, P = 0.115).

Table 4 shows the barriers to the children receiving BCG at birth (Totals do not add up to 100% as multiple responses were allowed). The leading cause of children not receiving BCG on their day of birth was that the vaccine was not given on that day in the health centre (n=164; 39.6%). This included public holidays and weekends. The second and third leading barriers were non availability of the vaccine

Table 1: General characteristics of the participants

Characteristics	Number	Proportion (%)
Gender of caregiver		
Females	414	100
Relationship of caregiver with child		
Mother	413	99.8
Aunt	1	0.2
Age of caregiver		
18 - 20	2	0.5
21- 25	50	12.1
26 - 30	185	44.7
31 -35	131	31.6
>35	46	11.1
Level of education		
No formal	7	1.7
Primary	9	2.2
Secondary	84	20.3
Tertiary	314	75.8
Marital status		
Single	8	1.9
Married	404	97.6
Divorced	2	0.5
Employment status		
Employed	302	72.9
Unemployed	112	27.1
Gender of child		
Male	221	53.4
Female	193	46.6
Age of child (days)		
=1	9	2.2
2-14	38	9.2
15- 28	5	1.2
>28	362	87.4

on the day of birth (n=32; 7.7%) and lack of knowledge that the vaccine was supposed to be given on the day of birth (n=28; 6.8%).

Table 5 shows the association between barriers to receiving BCG vaccination at birth and the receipt of the vaccine at birth was significant for the following barriers: The vaccine not being given on birth date (p = 0.0001); I was not strong/well enough to take him/her for vaccination (p = 0.011); the babies at the centre were not enough to open a new vaccine (p = 0.002); my baby was not well (p = 0.009); and fear of side effects of the vaccine (p = 0.048).

Using bivariate analysis, the barriers "BCG vaccine not given at the health centre the day my baby was born" and "I was not strong/well enough to take him/her for vaccination" remained significant with OR 14. 56 CI 8.077-26.248 and OR 10.042 CI 2.193-45.995, respectively.

Table 2: Maternal obstetric history

Variable	Number	Proportion (%)
Frequency of attendance at antenatal clinic		
I cannot remember	217	52.4
1 to 3	4	1
4 t0 7	61	14.7
=8	131	31.6
Missing result	1	0.2
Attendant personnel at antenatal clinic		
Doctor	407	98.3
Nurse/midwife	301	72.7
Community health extension worker	53	12.8
Traditional birth attendant	0	0
Voluntary community/village health worker	0	0
Others	0	0
Place of antenatal clinic care		
Participant's home	3	72.5
Government health facility	395	95.4
Private health facility	30	7.2
Others	0	0
Place of delivery		
Participant's home	9	2.2
Government health facility	377	91.1
Private health facility	24	5.8
Others	4	1
Method of delivery		
Spontaneous vaginal delivery	318	76.8
Caesarian section	79	19.1
Assisted delivery (augmented, instrument, etc.)	17	4.1
Source of information about immunisation		
Government health facility	370	89.4
Family	97	23.4
Private clinic	64	15.5
Friends	54	13.0
Mass media	31	7.5
Others	30	7.2
Voluntary community health worker	29	7.0
Partner	20	4.8
Health extension worker	13	3.1
Non-governmental organization	8	1.9

Table 3: Receipt of BCG vaccine

Receipt of BCG	Number	Proportion (%)
Has your child received BCG		
Yes	412	99.5
No	2	0.5
Age child received BCG		
At birth	146	35.3
Within 2 weeks of delivery (2 – 14 days)	260	62.8
Within 2weeks to 4 weeks (15 – 28 days)	5	1.2
>4weeks after delivery	3	0.7
Place of receipt of BCG		
Government health facility	394	95.2
Private health facility	20	4.8
Others	0	0

Table 4: Barriers to receipt of BCG at birth

Barriers to receipt of BCG at birth	Number of women	Proportion (%)
BCG vaccine not given at the health centre the day my baby was born	164	39.6
The vaccine was not available in the health centre	32	7.7
I did not know it was to be given on the day of birth	28	6.8
I was not strong/well enough to take him/her for vaccination	21	5.1
The babies at the centre were not enough to open a new vaccine	17	4.1
My baby was not well	12	2.9
Fear of side effects of the vaccine	7	1.7
I did not take permission from my husband	6	1.4
Health centre too far from my house	5	1.2
I did not have money for transport	3	0.7

Table 5: Association between the barriers to vaccination at birth and receipt of BCG at birth (N= 412)

Barriers to BCG vaccination at birth	Receipt of BCG vaccination at birth				
	Yes n (%)	No n (%)	Total	X^2	P value
BCG vaccine not given at the health centre the day my baby was born					
Yes	16 (3.9)	148 (35.7)	164 (39.8)	78.54	**0.0001**
No	130 (31.6)	118 (28.6)	248 (60.2)		
The vaccine was not available in the health centre					
Yes	7 (1.7)	25 (6.1)	32 (7.8)	2.79	0.09
No	139 (33.7)	241 (58.5)	380		
I did not know it was to be given on the day of birth					
Yes	6 (1.5)	22 (5.3)	28 (6.8)	2.58	0.108
No	140 (34)	244 (59.2)	384 (93.2)		
I was not strong/well enough to take him/her for vaccination					
Yes	2 (0.5)	19 (4.6)	21 (5.1)	6.49	**0.011**
No	144 (35)	247 (60)	391 (95)		
The babies at the centre were not enough to open a new vaccine					
Yes	0	16 (3.9)	16 (3.9)	9.17	**0.002**
No	146 (35.4)	249	395 (95.9)		
My baby was not well					
Yes	0	12 (2.9)	12 (2.9)	6.78	**0.009**
No	146 (35.4)	254 (61.4)	400 (97.1)		
Fear of side effects of the vaccine					
Yes	0	7 (1.7)	7 (1.7)	3.91	**0.048**
No	146 (35.4)	259 (62.9)	405 (98.3)		
I did not take permission from my husband					
Yes	0	6 (1.5)	6 (1.5)	3.34	0.068
No	146 (35.4)	260 (62.8)	406 (98.5)		
Health centre too far from my house					
Yes	1 (0.2)	4 (1)	5 (1.2)	0.527	0.468
No	145 (35.2)	262	407		
I did not have money for transport					
Yes	0	3 (0.7)	3 (0.7)	1.66	0.198
No	146	263	409		

Discussion

All 414 caregivers who participated in the study were females with 413 of them being the infant's mother. This showed that male/spousal participation in routine childhood immunization services of their children was absent. Studies have shown that lack of male involvement reduces uptake, timeliness, commencement and completion of childhood immunisation schedules.[10,11,12]

The mean age of receipt of BCG at birth was much lower than reported in an older study in Nigeria.[7] This could be due to the general improvement in immunization services and coverage over the years[13,14] as these studies were conducted 12 years apart.

Majority of the children studied had received the BCG vaccine which was similar to findings reported in other studies.[7,15,16,17] However, only about a third of infants received the vaccine within 24 hours of delivery. This was much higher than the findings reported in a cross-sectional study in southern Nigeria[8] carried out almost a decade ago and a more recent study in the Philippines[17] where the data was collected retrospectively. The cross-sectional study in southern Nigeria was among 153 children, only 2 (1.3%) of the children received the vaccine at birth while 66 (43.1%) received it within one week of delivery.[8] In a much older study also carried out in the same place in southern Nigeria, 208 (42.2%) of 512 children received BCG vaccine within 14 days of delivery.[7] This much older study was a retrospective study in which data was obtained from hospital records.[7] A disadvantage of retrospective studies using hospital records is the high probability of inadequate and incomplete records. In Ghana, a hospital-based, cross sectional study showed that 88.9% (230/259) of study participants received their BCG vaccine within two weeks of delivery.9 While in a study in China, 88.3% of 1,393 children sampled had received BCG vaccine within 28 days of delivery.[18] No absolute figures were reported for those who received at birth or within two weeks of delivery. This suggests that although there has been an improvement in the number of children who receive BCG at birth, much work still needs to be done. Reports from studies including this, show that majority of infants received the vaccine within the first 2 weeks of life.[7,8,15,17]

Studies in Nigeria have reported that most infants received their vaccines in government (public) facilities.[8,15] Also, most mothers sampled attended antenatal care and gave birth in health facilities, as well as obtained their information about childhood immunization from health facilities especially government-owned facilities. There is therefore a need to create more awareness on the childhood immunization schedule, the importance of adhering to it and to ensure that the correct information is passed across to mothers and other caregivers.

No association was found between the receipt of BCG at birth and caregiver socio-demographic and obstetric history factors. A study in southern Nigeria reported that socioeconomic class, place of delivery and maternal education was associated with vaccine receipt within one week of birth[8] while another in China, reported that delivery in a hospital, higher maternal level of education, a mother without a job and a resident child were positively associated with higher BCG vaccination coverage and timely administration of BCG vaccines.[18] Another in western Nigeria found that maternal education, occupation, delivery place and delivery mode was significantly associated with vaccine receipt within 14 days of birth using bivariate analyses but was no longer significant with further analyses.[15] A larger, multicentre, study, with emphasis on vaccine receipt on date of birth may assist in obtaining a more conclusive result.

The reasons for delay in the vaccine receipt was consistent with previous reports. The leading cause of delay was that it was not given at the health centre the day the infants were born. The birth date included public holidays, weekends and days of the week when BCG vaccine was not scheduled to be given to children. This was consistent with other findings.[8] Reasons such as none availability of the vaccine as a barrier should be brought to the appropriate authorities as early as possible. The proportion of caregivers who stated ignorance of recommended BCG vaccine schedule shows that more counselling and health education is required during antenatal and peripartum period as majority of the mothers attended antenatal care and delivered in health care facilities. This also suggests missed opportunities for early vaccination of infants born in health facilities.

A worrisome reason was that the babies were not enough to open a vial of the vaccine as this is no

longer supposed to be in practice. An opened, reconstituted, multidose vial of BCG vaccine is supposed to be discarded after six hours. Those giving the vaccines may want to preserve their stock if there are not enough children to use up a vial. However, the current guideline states that health workers should open vials regardless of the number of children present for vaccination .[19]

A limitation of this study was that there was reliance on caregiver recall and truthfulness in obtaining the reasons for infants not receiving the BCG vaccine at birth even though the immunisation card records were used in ascertaining receipt of the vaccine.

In conclusion, although most infants had received the BCG vaccine, only a small proportion had received it at birth. The major reason being that the vaccine was not given at the health facilities on the birth date. It is therefore recommended that the Nigerian government ensure infant vaccination for BCG occurs daily including weekends and public holidays while increasing public awareness on the importance of timely vaccination of infants especially through antenatal clinics. This may help reduce child mortality and morbidity from tuberculosis. A change in strategy is therefore advocated.

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