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Anti-diphtheria immunity in Nigerian mothers and their newborns

Henry Cummings, Ayebo Evawere Sadoh*, Osawaru Oviawe, Wilson Ehidiamen Sadoh

Department of Child Health, University of Benin Teaching Hospital, Benin City, Nigeria

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ABSTRACT

Background: Immunity to diphtheria has been noted to wane with age such that previous studies have shown that a significant proportion of females with characteristics comparable to those of Nigerian women of reproductive age have inadequate levels of immunity to diphtheria. Thus, it is envisaged that Nigerian newborns may inherit inadequate levels of immunity to diphtheria from their mothers.
Methods: Cord blood and peripheral maternal blood samples were collected from 231 mother–infant pairs at delivery. Anti-diphtheria antibody titres were assayed using Enzyme-linked immunosorbent assay (ELISA) technique. Recruited babies were those born at term with normal birth weight.
Results: As much as 29.9% of both mothers and their babies had no protection (antibody titre < 0.01 IU/ml) from diphtheria. Ninety (39.0% CI 33%,45%) mothers and 107 (46.3% CI 40%,52%) babies were inadequately protected (antibody titre < 0.1 IU/ml) from diphtheria. The difference in the geometric mean antibody titres of mothers and babies was statistically significant ($p < 0.0001$). There was a strong positive linear correlation between maternal and newborn antibody titres ("r" = 0.983, $p < 0.0001$), such that, as mothers antibody titres increased those of their babies also increased.
Conclusion: Significant proportions of Nigerian mothers and newborns are at risk of developing diphtheria. Vaccination of parturient women with booster doses of diphtheria toxoid vaccine is recommended.

1. Introduction

Diphtheria is a disease caused by the bacterium *Corynebacterium diphtheriae* and its highly potent toxin which is associated with high case fatality [1]. It was one of the earliest infectious diseases that were controlled on the basis of principles of microbiology, immunology and public health [1]. As a result of effective vaccination campaigns, diphtheria was reduced from a major cause of childhood death in the western hemisphere in the early 20th century to a medical rarity (less than 2 cases per annum) [1].

More recently, re-emergence of diphtheria has been noted in several countries in Eastern Europe including Russia and other parts of the former Soviet Union [2–4]. Outbreaks have also been recorded in Afghanistan, Lesotho, Sudan, India and Algeria [5–9]. There has not been any recent report of diphtheria epidemic in most parts of sub-Saharan Africa. In Nigeria reported cases had been reducing with 5039 cases reported in 1989, 3995 in 2000, 2468 in 2001, 790 in 2002 and 312 in 2006 [10]. However, recent reports of clusters of diphtheria cases in Katsina, Lagos and Edo states, have led to speculations of possible resurgence of diphtheria in Nigeria [11–13].

A serological survey conducted in Nigeria in 1967 indicated that about 90% of older children and adults had protective levels of anti-diphtheria immunity [14]. The high level of immunity was attributed to high frequency of natural infections (especially cutaneous diphtheria) which maintained immunity to diphtheria. The findings of this survey may no longer be applicable to present day Nigeria as there has been reported improvement in the level of personal and environmental hygiene in the country [15]. It has been shown that improvement in the level of personal and environmental hygiene results in reduced frequency of cutaneous diphtheria infection with resultant decrease in boosts to immunity [16].

Furthermore, the Nigerian serological survey was carried out before formal immunization programme was initiated in the country [14]. In Nigeria, the Expanded Programme on Immunization (EPI) was launched in 1979 [17]. It has been reported that, increasing immunization coverage with the third dose of the diphtheria-pertusis-tetanus vaccine (DPT3), results in reduction of the frequency of diphtheria infection in the populace and hence reduction in the immunity boosting effects derived from natural infections [16]. According to the WHO [18], DPT3 coverage has progressively increased in Nigeria, from 5% in 1984 to 74% in the year 2010.

* Corresponding author.
E-mail address: ayebosadoh@yahoo.com (A.E. Sadoh).

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It is thus possible that the older population in Nigeria may have inadequate immunity to diphtheria due to a combined effect of waning of immunity over time and the lack of boosting due to lack of continuous exposure to natural infections. Therefore, there is a need to assess the current status of immunity to diphtheria in the older population and more importantly, that of a vulnerable group of children – newborns, whose immunity is solely dependent on that of an older population – their mothers (whose immunity may be suboptimal). This is especially important due to the recent reports of outbreaks [11–13] and an epidemic [19] from various parts of Nigeria. Also in reports of some of the outbreaks in the other countries more female than males were affected [20]. Furthermore, cases of diphtheria have been reported during pregnancy and the post-partum period [21–24] as well as in the neonatal and early infancy periods [25–28].

This study assessed the current status of anti-diphtheria immunity in Nigerian mothers and newborns. In addition the relationship between maternal and newborn anti-diphtheria immunity was evaluated.

1.1. Study subjects

The study subjects were parturient women (and their babies) who had registered in University of Benin Teaching Hospital (UBTH) for antenatal care (ANC) and had vaginal delivery in the UBTH. Written informed consent was obtained from the mothers during the last trimester of pregnancy. Ethical approval for the study was obtained from the University of Benin Teaching Hospital Ethical Review Committee. The babies were apparently healthy term newborns whose gestational ages at delivery were within 37–41 completed weeks and who had birth weights between 2500 g and 3999 g. Mothers who received blood or blood products during the index pregnancy and those with cardio-pulmonary diseases, hypertensive diseases, HIV/AIDS infection, malignancies, diabetes mellitus and Sickle cell anaemia were excluded as these are conditions that are known to affect materno-foetal transfer of antibodies [29–32].

Babies who had perinatal asphyxia and those who were products of multiple gestations were also excluded.

Mother's bio-data, socio-demographic data as well as maternal childhood vaccination history were recorded in a proforma.

1.2. Clinical evaluation

Each baby recruited for the study was examined. For each baby, the gestational age at birth was determined from both the date of the mothers' Last Menstrual Period and the Dubowitz and Dubowitz gestational age estimation chart. The weight, length and occipitofrontal circumference of the babies were measured according to standard procedures [33].

1.3. Specimen collection

3 ml of blood was collected from all enrolled mothers (immediately after delivery) using aseptic procedure, into a plain universal bottle. 3 ml of cord blood was also collected from babies immediately following birth.

1.4. Laboratory methods

All sera were transported to the laboratory at a temperature of 4 °C. Anti-diphtheria antibody titres were determined by senior laboratory scientists at the University of Benin Teaching Hospital Chemical Pathology Laboratory using Diphtherie IgG ELISA kit, manufactured by IBL – International, batch no. RE56191. Assays were carried out according to manufacturer instructions.

Table 1
Socio-demographic characteristics of the mothers.

Characteristics	*n*	%
Place of abode		
Rural	23	10.0
Urban	208	90.0
Total	231	100.0
Family size (persons/household)		
≤5	215	93.1
≥6	16	6.9
Total	231	100.0
Socio-economic status		
I & II (Upper class)	103	44.6
III (Middle class)	79	34.2
IV & V (Lower class)	49	21.2
Total	231	100.0

2. Interpretation of result

Subjects' immunity to diphtheria as determined from the laboratory tests was classified using WHO guidelines [34].

Serum anti-diphtheria antibodies (IU/ml)	Evaluation
• <0.01	No protection
• 0.01–<0.1	Minimal protection
• 0.1–<1.0	Safe protection
• >1.0	Long term protection

3. Data analysis

Data analysis was carried out using Statistical Package for Social Sciences (SPSS) version 13.0. A serum antibody titre of at least 0.1 IU/ml was the cut off for protective anti-diphtheria immunity in the study since safe and/or long term protection is achieved at titres ≥0.1 IU/ml [34]. Serum antibody titres of <0.1 IU/ml were classified as inadequate protection while those ≥0.1 IU/ml were classified as adequate protection. The proportion of mothers and babies with different levels of immunity was recorded as percentages. The antibody titres were transformed logarithmically and used to calculate geometric mean titres and 95% confidence intervals. Differences between means were assessed using the Student's *t* test (and Analysis of Variance, ANOVA where appropriate). The paired *t* test was used to test differences in the mean antibody titres of mother–baby pairs. Correlation between maternal and newborn antibody titres was determined using Pearson's correlation test. In all statistical tests, *p*-value <0.05 was considered statistically significant.

4. Results

The study was carried out over a period of 8 months (September 2010–April 2011). One thousand two hundred and eighty-four women received antenatal care during the study period. Of these, 684 eligible women in their third trimester were followed up till delivery. Only 572 of those followed up gave birth to their babies in the study centre during the study period. Of these, 240 mother-baby pairs met the inclusion criteria and were recruited. However, 9(3.8%) mother-baby pairs were excluded from analysis on account of spillage during laboratory analysis. Thus, a total of 231 mother-baby pairs were analyzed in the study.

The mean ± SD age of the mothers was 29.6 ± 4.5 years with a range of 16–46 years. Of the 231 babies 97(42%) were males. The mean gestational age of the babies was 38.7 ± 1.2 weeks. The mean weight, length and occipitofrontal circumferences of the babies were 3.24 ± 0.41 kg, 49.57 ± 1.94 cm and 34.39 ± 1.42 cm