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Prevalence of anti-measles antibodies in infants from 0 to 9 months: Case of three hospitals in the city of Douala (Cameroon)

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ABSTRACT

Background: Measles is an acute infection, usually occurring in childhood, caused by a virus of the *Paramyxoviridae* family. Infants born to mothers immunized against measles benefit from the transplacental transfer of anti-measles antibodies of the IgG type, and are in principle protected against infection in the first months of life. **Methods:** A cross-sectional study was carried out on infants born at term and not vaccinated against measles, in three hospitals in the city of Douala (General Hospital, Gynaecologic Obstetrics and Pediatrics Hospital and Laquintinie Hospital). The qualitative and quantitative research of type G immunoglobulins in serum or plasma was carried out by the ELISA technique using the "Measles Virus IgG^{TM}" kits, followed by a colorimetric reading. Sociodemographic and biological data were collected and analyzed. **Results:** A total of 178 infants were recruited of which 54.5% were male. The average age was 3 months ± 2.6 and the most common age group was 0 to 1 month. Antibody levels ranged from 8 to 5,700 mIU/ml and 39.9% of infants had protective levels against measles. The presence of antibodies based on age was 81.1% in 0-1 months infants, 51.1% 1-3 months, and 8.2% 3-6 months, respectively. Only one of them was protected in the 6 to 9 month age group. We observed a significant association between infant age, maternal history of measles and the rate of protected infants. **Conclusion:** The frequency of maternal antibodies in infants was low. Strategies should be put in place to strengthen the fight against this resurgent disease.

Introduction

Measles is an acute infection, usually occurring in childhood, caused by a virus of the *Paramyxoviridae* family [1]. Infants born to mothers who have already developed the disease benefit from the transplacental transfer of anti-measles IgG antibodies, and are normally protected against infection in the first months of life [2]. However, the presence of maternal antibodies can compromise the humoral response to vaccination, especially when a live vaccine is administered; This is the reason why the WHO recommends that the first dose of measles vaccine be given at 9 months of age in countries where the risk of death from measles remains high for infants, the vaccination reduced to 6 months in

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endemic countries with regular outbreaks [3]. In 2012, measles caused more than 120,000 deaths worldwide, the majority of cases in developing countries [4]. In 2013, **Waaijenborg et al.** estimated that in infants under one year of age, the risk and severity of measles were higher than in those over one year old, and in 2016, there was a resurgence of measles in Cameroon [5,6]. Our study aimed to determine the prevalence of maternal anti-measles antibodies in infants aged 0 to 9 months in three biggest hospitals in the city of Douala (Cameroon).

Material and Methods

A cross-sectional study was conducted from January to July 2018 at the Gynaecology Obstetrics and Pediatrics Hospital, Laquintinie Hospital and the Douala General Hospital for the recruitment of children; and at the clinical biology laboratory of the Douala General Hospital for sample analysis.

The study population consisted of infants aged 0 to 9 months of both sexes, born at term, received in the pediatric departments of the hospitals concerned, not vaccinated against measles and whose parents had agreed to participate in the study. Premature infants (born before 37 weeks of amenorrhea), children who had already had measles and those whose blood collection was difficult were excluded. After agreement and information of the investigation sheet by the parents, each infant included was subjected to a venous blood sample in a vacutainer tube without additives.

The samples were sent to the serology laboratory of the General Hospital of Douala where they were centrifuged at a speed of 3000 revolutions per minute for ten minutes, then aliquoted and stored at a temperature of -20 °C until the day of analysis. The qualitative and quantitative research of type G immunoglobulins in the serum was carried out by sandwich ELISA (Enzyme-Linked Immuno Sorbent Assay) using the Measles virus IgG^{TM} kit (IBL International), according to the manufacturer's recommendations. The sample-specific antibodies binding to the fixed antigens in the wells were detected by secondary antibodies conjugated to a specific enzyme for human IgG. After the substrate reaction, the intensity of the developed color proportional to the amount of specific IgG antibody was detected by measuring the optical density using a spectrophotometer with a wavelength of 450-630 nm. An IgG level <200 mIU/ml was considered non-protective.

Statistical analysis

The data were analyzed using Microsoft Word 2010, Excel 2010 and Epi info 7.2.2.6 softwares. Variables were presented as percent and mean ± standard deviation (SD) in tables and graphs. The distribution of protection status according to socio-demographic and clinical factors was assessed using the ki^2 test. A p-value less than 0.05 was considered statistically significant.

Results

Sociodemographic and clinical characteristics

A total of 178 infants were included in the study. The male sex was the more represented with (54.5%) and a sex ratio of 1.2. The age of the study population was between 0 and 9 months with a mean age of 3 ± 2.6 months. The 0 to 1 month and 1 to 2 month age groups were 29.8% and 16.9% of the total population, respectively. The ages of mothers of children ranged from 16 to 47 years old with an average of 30.4 years and the 25 to 30 age group represented 38.2%. Mothers with a higher level of education were the most represented at 53.4%, followed by those at secondary level with 42.7%. From a socio-professional standpoint, 27.5% of the mothers were students and 26.4% employed, traders and unemployed women each represented 23% **(Table I)**. Mothers of infants living in non-residential areas were the most numerous (83.1% compared to 16.9% for those in residential areas). Regarding the assessment of knowledge about measles and its routes of transmission, the majority (73.6%) of participating mothers of children had good knowledge. In addition, 14.6% of mothers declared having had a history of measles, and 47.7% did not know their status. Children born vaginally represented 72.5% of cases compared to 27.5% of children born by caesarean section. Mixed breastfeeding was practiced by 47.2% of mothers, exclusive breastfeeding by 39.8% and artificial breastfeeding by 14.1%. According to the birth order, 39.3% of infants were first born, 28.6% second of the siblings, 19.7% and 12.4% belonged to the third and fourth and higher rank respectively **(Table II)**.

Biological characteristics

The results of the serum analysis by the ELISA technique showed that the qualitative tests were positive on all of the samples and 81.1% of infants were protected by maternal antibodies between 0 to 1 month, 56.7% between 1 and 2 months, 40% between 2 and 3 months, 18.7% between 3 and 4

months, 5.5% between 4 and 5 months, no child was protected between the period between 5 and 7 months, only one infant protected between 7 and 9 months **(Figure 1)**. Quantitative ELISA tests revealed IgG levels ranging from 8 to 5,700 mIU / ml with an average level of 716.50 mIU / ml. Among infants below the threshold of protection (200 mIU / ml), 21.5% had a level below 50 mIU / ml, 22.4% a level varying from 50 to 100 mIU / ml and 56% a level of 100 to 200 mIU / ml. Among the protected infants, 22.5% had a level of 200 to 1000 mIU / ml, 45.1% had a level varying from 1000 to 2000 mIU / ml, 16.9% a rate of 2000 to 3000 mIU / ml, 14.1% a level of 3000 to 5000 mIU / ml and only one child had an antibody level greater than 5000 mIU / ml, or 1.4% **(Table III)**. The distribution of protection status according to socio-demographic factors revealed a significant association with the infant's age (p= 0.0) and the history of measles in the mother (p= 0.00001).

Table I. Distribution of protection status according to socio-demographic factors.

Variable		**Frequency n (%)**	**Protective IgG level n (%)**	***p-value***
Infant sex	Male	97 (54.5)	36 (0.37)	0.41
	Female	81 (45.5)	35 (0.43)	
Infant age (months)	0-1	53 (29.8)	43 (0.81)	0
	>1-2	30 (16.9)	17 (0.56)	
	>2-3	15 (8.4)	6 (0.40)	
	>3-4	16 (9.0)	3 (0.18)	
	>4-5	18 (10.1)	1 (0.05)	
	>5-6	15 (8.4)	0	
	>6-7	11 (6.2)	0	
	>7-9	20 (11.2)	1 (0.05)	
Mother's age (years)	15-20	8 (4.5)	6 (0.75)	0.09
	>20-25	25 (14.0)	12 (0.48)	
	>25-30	68 (38.2)	26 (0.38)	
	>30-35	48 (27.0)	17 (0.35)	
	>35-40	23 (12.9)	7 (0.30)	
	>40	6 (3.4)	3 (1)	
Mother's level of education	Primary	7 (3.9)	3 (0.43)	0.57
	Secondary	76 (42.7)	32 (0.42)	
	University	95 (53.4)	36 (0.38)	
Mother's occupation	Trader	41 (23.0)	12 (0.34)	0.15
	Employee	47 (26.4)	19 (0.40)	
	Student	49 (27.5)	22 (0.45)	
	Unemployed	41 (23.0)	18 (0.44)	
Living area	Residential	30 (16.9)	13 (0.43)	0.67
	Non residential	148 (83.1)	58 (0.39)	

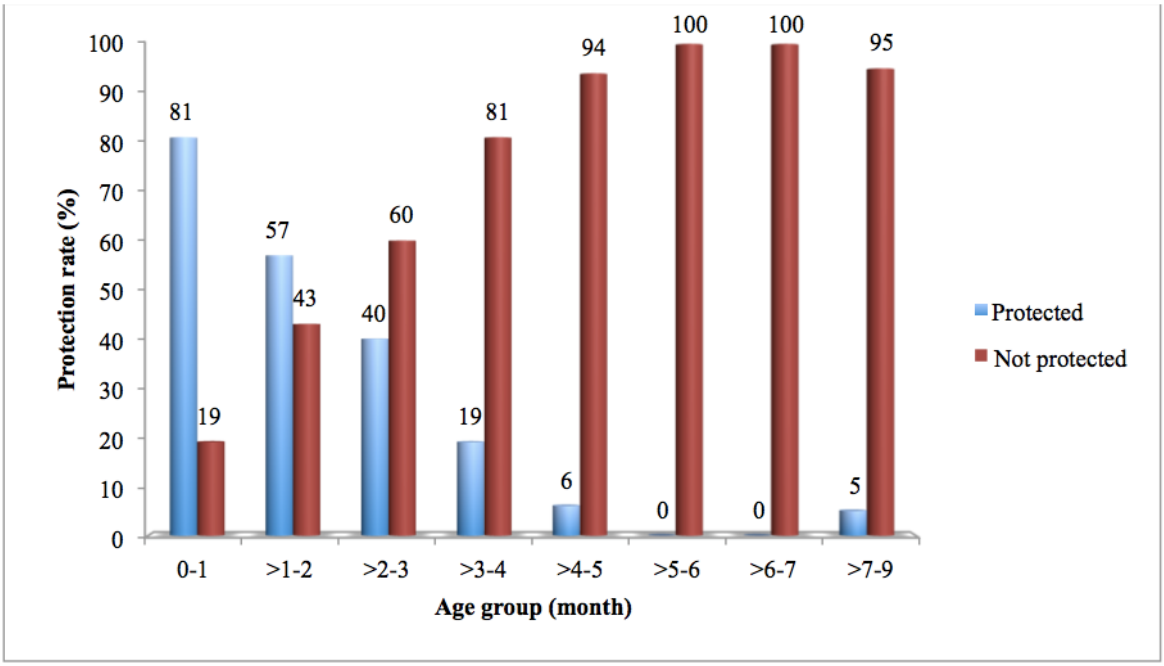
Table II. Distribution of protection status according to clinical factors and history.

Variable		**Frequency n (%)**	**Protective IgG level n (%)**	***p-value***
Type of delivery	Normal	129 (72.5)	55 (0.42)	0.22
	C-section	49 (27.5)	16 (0.33)	
Feeding type	Mixed	84 (47.2)	25 (0.24)	0.07
	Artificial	35 (19.7)	16 (0.45)	
	Breastfeeding	69 (38.8)	30 (0.43)	
Birth rank	1st	70 (39.3)	33 (0.47)	0.26
	2nd	51 (28.7)	18 (0.35)	
	3rd	35 (19.7)	11 (0.35)	
	4th and above	22 (12.4)	9 (0.40)	
Birth weight (kg)	2-2,6	43 (24.2)	19 (0.44)	0.51
	>2,6-4	135 (75.8)	52 (0.38)	
Size at birth (cm)	45-50	102 (57.3)	46 (0.45)	0.10
	>50-55	76 (42.7)	25 (0.33)	
Mother's history of measles	Yes	26 (14.6)	19 (0.73)	0.00001
	No	67 (37.6)	15 (0.29)	

Table III. Variation in the anti-measles IgG antibodies level according to age.

IgG rate (mIU /ml)		**Age group (month)**								**Total**
		0-1	**>1-2**	**>2-3**	**>3-4**	**>4-5**	**>5-6**	**>6-7**	**>7-9]**	**n (%)**
Non protective	<50	0	0	0	0	0	1	7	15	23 (12.9)
	50 -100	1	0	2	3	5	6	3	4	24 (13.5)
	100 - 200	9	13	7	10	12	8	1	0	60 (33.7)
	Total	**10**	**13**	**9**	**13**	**17**	**15**	**11**	**19**	**107 (60.1)**
Protective	200 - 1000	1	6	5	3	1	0	0	0	16 (9.0)
	1000 - 2000	23	8	1	0	0	0	0	0	32 (18.0)
	2000 - 3000	9	3	0	0	0	0	0	0	12 (6.7)
	3000 - 5000	10	0	0	0	0	0	0	0	10 (5.6)
	>5000	0	0	0	0	0	0	0	1	1 (0.6)
	Total	**43**	**17**	**6**	**3**	**1**	**0**	**0**	**1**	**71 (39.9)**

Figure 1. Distribution of children by protection status.



Discussion

Among the infants included in this study, we observed a male predominance also noted by **Manirakiza et al**. in Bangui in 2011 (53%) [7]. The mean age of the children was 3 ± 2.6 months similar to that of **Hartter et al**. in Ibadan, Nigeria in 2000, which was 3.5 months [8]. The mothers who agreed to participate in the study were young, as already reported by in 2010 in Rwanda with an average age of 29.2 years [9]. Although the presence of specific neutralizing antibodies was found in all the samples with an average level of 716.5 mIU / ml, the level of protection was low (39.9%) with an antibody dosage between 200 and 5700 mIU / ml. **Oluseyi et al.** in 2005 in Nigeria had found a 42% protection rate with antibodies between 280 and 6950 mIU / ml [10]. This slight difference could be explained by the ELISA kits used, the specificity and sensitivity of the reagents may vary depending on the manufacturer. The transmission of anti-measles antibodies from mother to child and the duration of their persistence at protective levels are variable; in children at birth the concentration is proportional to maternal antibody levels and decreases steadily during the first months of life. The degree of protection depends on the maturity of the newborn, the total immunoglobulin level of the mother and the integrity of the placenta [2,11]. Just like anti-measles antibodies, the protective levels of maternal anti-rubella, anti-chickenpox, anti-tetanus and anti-diphtheria antibodies decrease or even disappear in infants from the 2nd month of birth; while protective levels of anti-pertussis toxin antibodies disappear at six weeks [12,13]. Thus in Korea in 2016, 98% of children under one month had protective titles, we obtained almost identical results [14]. In 1993 in Bangladesh at 2 months over 90% were protected, but in our study the rate of protection was only 56.7% [15]. **Dabis et al** in Congo-Brazzaville in 1986 showed that 19% of children aged 6 months were still protected by maternal antibodies [16].

Among children aged 4 to 8 months, only 1.5% were protected against measles in our study, this result is similar to that of Manirakiza in a study on the seroprevalence of anti-measles and anti-rubella antibodies in the Central African Republic where no children was no longer protected at this age group [7]. These two border countries could have similar epidemiological characteristics concerning childhood diseases. In Switzerland in 2000, 4% of children aged 6-9 were protected [17]. Of the 7-9 month old infants tested here, only one was protected, a 9 month old infant with an antibody titer of 5700 mIU / ml. This very high titer could be due to a previous vaccination which the mother could not remember, the child having been included in the study according to the parents' statements. **Markus et al.** in 2006 in Germany in their study observed an average post-vaccination measles antibody level of 6103.9 mIU / ml [18]. These data show that the transmission of fetal-maternal antibodies is low in our study population. Previous

studies had shown that the rate of transmission of maternal antibodies to newborns in developing countries was lower than in industrialized countries [8,19]. **Gendrel et al.** in a comparative study leads to the conclusions that maternal anti-measles antibody levels in European infants living in Europe are higher than those received by African infants living in Africa [20]. The distribution of protection status according to socio-demographic factors revealed a significant association with the age of the infant and the history of measles in the mother ($p < 0.05$). Indeed, the majority of younger children and those born to mothers with a history of measles were protected with high levels of antibodies, compared to those of mothers with no specific history.

Other factors including infant sex, mother's age, type of delivery and breastfeeding, birth order, infant birth weight and size at birth were not significantly associated with the presence of immunoglobulins in infant serum ($p > 0.05$). De **Francisco et al.**, **Zhang et al.** in their studies came to the same conclusion [15,21]. In contrast, HIV infection and malaria in mothers may be factors in reducing this transfer of antibodies to the fetus [22,23]. The age of vaccination must therefore take into account the ability of the immune system to react to the vaccine, and the disappearance of maternal antibodies, especially with regard to live attenuated vaccines such as those against measles-rubella-mumps; below the age of 6 months, the humoral response is insufficient to generate an adequate protective response [24]. This is why the first dose of the measles vaccine is given at the age of 9 months in Cameroon. As protective levels of maternal antibodies disappear from the second month of birth, infants become vulnerable until the age of the first vaccine. It would therefore be necessary for scientists to develop another vaccine that can protect children during their period of vulnerability to the measles virus, especially in developing countries.

Limitations

- During this study, the immunity status to measles virus of most mothers was unknown.
- The size of the sample does not allow us to interpret our results on a national level.
- Difficulties in convincing mothers to include their children in the study.

Conclusion

The frequency of maternal anti-measles antibodies in infants is low in the population studied. The distribution of protection status by socio-demographic and clinical factors revealed a significant association with infant age and maternal history of measles. The window of vulnerability for measles infection begins very early in infants in Douala from 2 months and lasts until 9 months, the recommended age for vaccination. Strategies should be put in place to protect these infants during the period of vulnerability from measles.

Ethics

This study obtained ethical clearance from the Institutional Ethics Committee of the University of Douala, and authorizations from the various directors of the hospitals concerned. The study was conducted in accordance with good clinical and laboratory practices.

Conflicts of interest

The authors declare no conflict of interest.

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