Heliyon

Received:
30 May 2018
Accepted:
20 June 2018

Cite as: Nabila Benamrouche, Hassiba Tali Maamar, Samia Chemli, Houria Senouci, Kheira Rahal. Immune responses to vaccine-preventable diseases among toddlers and preschool children after primary immunization and first booster in Northwestern Algiers, Algeria.
Heliyon 4 (2018) e00664.
doi: 10.1016/j.heliyon.2018.e00664

Immune responses to vaccine-preventable diseases among toddlers and preschool children after primary immunization and first booster in Northwestern Algiers, Algeria

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Abstract

Objectives: To determine immune responses to selected vaccine-preventable communicable diseases: pertussis, diphtheria and *Haemophilus influenzae* type b (Hib[1]) in Algerian toddlers and preschool children after primary vaccination and first booster, recruited from three local healthcare facilities in Northwestern Algiers.
Methods: The information of demographic characteristics and vaccination status were collected for each subject by questionnaire. Specific antibody levels and Hib antibody avidity were determined using commercial ELISA kits.
Results: A total of eighty-one subjects aged between 19 and 55 months were studied. Almost all subjects were fully protected against diphtheria (76/81;

[1] Hib: *Haemophilus influenzae* type b.

https://doi.org/10.1016/j.heliyon.2018.e00664

93.83%; 95% CI[2]: 86.35−97.33) and invasive Hib disease (29/30; 96.67%; 95% CI: 83.33−99.41), while only 20/78 (25.64%; 95% CI: 17.26−36.31) had anti-PT[3] (pertussis toxin) antibody levels above 25 IU/ml. A significant decrease of anti-PT antibody levels was observed until the age of 36 months ($p = 0.02$). GMTs[4] (geometric mean titers) of anti-PT antibodies were low, but remain significantly higher in children ≤36 months of age ($p = 0.02$). Both GMT and rates of ≥0.15 μg/ml, ≥1 μg/ml, and ≥5 μg/ml titers were significantly higher in Hib-vaccinated subjects ($p < 0.01$). Relative Hib-avidity index (≥50%) and GMAI[5] (geometric mean avidity index) were high in both Hib-vaccinated and -unvaccinated groups.

Conclusions: As shown in the present study, young children were fully protected against diphtheria and Hib, but showed low immunity to pertussis. Further sero-epidemiological studies including a large number of subjects with a wider range of age are needed to explore the immunity level in older children, adolescents and adults.

Keywords: Immunology, Infectious disease, Public health

1. Introduction

Pertussis, diphtheria and invasive *Haemophilus influenzae* type b infection, are vaccine-preventable communicable diseases. Algeria has adopted the WHO[6] (World Health Organization) EPI[7] (Expanded Program on Immunization) since 1969 with the use of combined DTwP[8] (diphtheria, tetanus, whole-cell pertussis) vaccine. The immunization schedule recommended includes 3 doses of primary vaccination at 3, 4, and 5 months of age, followed by the booster dose at 18 months of age and one dose of diphtheria, tetanus vaccine at 6 years of age. The Sanofi Pasteur combined DTwP-Hib[9] (diphtheria, tetanus, whole-cell pertussis, *Haemophilus influenzae* type b) vaccine replaced the Serum Institute of India (SII[10]) combined DTwP vaccine since the introduction of *Haemophilus influenzae* type b vaccination into the national childhood immunization schedule in 2008. Since 2016, the immunization schedule has adjusted including 2 doses at 2 and 4 months of age, followed by the booster doses of DTwP at the age of 12 months and 6 years.

[2] CI: confidence intervals.
[3] PT: pertussis toxin.
[4] GMT: geometric mean titer.
[5] GMAI: geometric mean avidity index.
[6] WHO: World Health Organization.
[7] EPI: Expanded Program on Immunization.
[8] DTwP: diphtheria, tetanus, whole-cell pertussis.
[9] DTwP-Hib: diphtheria, tetanus, whole-cell pertussis, *Haemophilus influenzae* type b.
[10] SII: Serum Institute of India.

https://doi.org/10.1016/j.heliyon.2018.e00664

In 1969, following the introduction of mandatory vaccination, the incidence of pertussis in children decreased dramatically in Algeria, reaching the lowest level in 1994 [1]. However, even though the estimated immunization coverage maintained high [2], in the 2000s as many developed countries; the increase in the use of the biological diagnosis was followed by an increase of pertussis cases. In the 2011−2013, as everywhere around the world, a new cycle of pertussis occurred. The highest incidence of the disease has been reported in infants less than 3 months of age, which is life-threatening in these infants who are still too young to be vaccinated. Adults and adolescents are the main source of infection [3]. In Algeria, 134 laboratory-confirmed pertussis cases were reported in the 2012−2013, almost five times more than in 2011 (27 cases). One hundred and ten (82.09%) cases were infants under 6 months of age; among them 51.82% were less than 3 months old and were incompletely or not vaccinated. The primary source of exposure was mothers (54/66, 51.80%) [4]. As regards the diphtheria, after being well controlled in the 1980s, Algeria was experiencing an epidemic in the 1990s, more observed among adolescents and adults. The highest incidence of notified cases was reported in the 1994−95 with a rate above 3.5 per 100,000 inhabitants [1]. The main factors involved were waning immunity in adolescents and adults and socio-economic instability in this period. Mass vaccination campaigns and additional boosters introduced at 11−13 years of age, 16−18 years of age and every 10 years since 1997 had ensured control of the epidemic. Although the disease is currently controlled, as no cases of diphtheria have been recorded since 2007, resurgence of diphtheria remains possible and continued surveillance is required [5].

For the incidence of invasive *Haemophilus influenzae* type b disease, there is no available data before and after introduction of Hib vaccination, as in Algeria the notification system distinguish *Haemophilus influenzae* meningitis from other meningitis only since December, 2013 [6]. However, a study conducted between 2005 and 2012 in 301 infants mostly from Algiers revealed a remarkable decrease of *Heamophilus influenzae* meningitis rate, from over 15% in 2008 to around 1% in 2011 and no cases in 2012 [7]. Additionally, a decreasing number of invasive *Haemophilus influenzae* type b isolates (from 111 strains in 2008 to 07 strains in 2011), was recorded at the national level by the AARN[11] (Algerian Antimicrobial Resistance Network) reflecting the impact of the Hib vaccination on the decline of the incidence of the disease [8], which was consistent with the high estimated immunization coverage [9].

As no serosurveillance data are available in Algeria for pertussis, diphtheria and Hib, the present study was undertaken to investigate immune responses against selected

[11] AARN: Algerian Antimicrobial Resistance Network.

https://doi.org/10.1016/j.heliyon.2018.e00664

vaccine-preventable diseases among children under 5 years old who had completed the primary vaccination and the first booster in Northwestern Algiers.

2. Materials and methods

2.1. Study design

We conducted a descriptive study to assess immune responses to diphtheria, pertussis and *Haemophilus influenzae* type b antigens in healthy toddlers and preschool children who received the primary vaccine series and the first booster. Subjects were enrolled from three local public health facilities in Algiers, from November 2010 to January 2012. The study was approved by the Ethic Committee in Algiers. All parents gave their written informed consent. A questionnaire was completed for every child to provide information on date of birth, gender and vaccination status. All information were obtained from the parents and checked on children's immunization cards.

Children were eligible if they were (i) healthy, (ii) between 19 and 60 months of age and (iii) completing the primary vaccine series of three doses and first booster of the combined DTwP vaccine or combined DTwP-Hib as certified by their immunization card.

In Algeria, the DTwP combined vaccine was used until September, 2008. On October, 2008, the DTwP-Hib combined vaccine was introduced. The first children eligible to receive a three month dose of this quadrivalent vaccine were born on July, 2008, and would have been eligible to receive their fourth dose on March, 2010. Thus, two different combined vaccines were used during the study period (transitional period): one (Diphtheria-Tetanus-Pertussis Vaccine Adsorbed) produced by the Serum Institute of India PVT. LTD. (Pune, India) and the other (TETRAct-HIB) produced by Sanofi Pasteur SA (Marcy l'Etoile, France).

Blood samples were collected and processed at the Medical Bacteriology Laboratory, Institut Pasteur of Algeria. One serum sample was collected from each child, and then divided into three aliquots and frozen at _20 °C until analysis.

2.2. Methods

Specific IgG to pertussis toxin (PT) was measured using Anti-*Bordetella pertussis* toxin ELISA IgG test kit (EUROIMMUN, Lübeck, Germany). Limits of quantification for this assay were 5−200 IU/ml. There is no correlate of protection; however, low levels of antibodies are highly correlated with susceptibility to

https://doi.org/10.1016/j.heliyon.2018.e00664

pertussis [10, 11]. Assay cutoffs were set at four times the minimum level of detection for antibodies to PT. So, anti-PT IgG antibody levels over than 25 IU/ml were considered as positive following the manufacturer instruction. DT[12] (diphtheria toxoid) specific IgG antibodies were measured using Anti-Diphtheria Toxoid ELISA IgG test kit (EUROIMMUN, Lübeck, Germany). Limits of quantification of the assay were 0.01−2 IU/ml. According to the international criteria, diphtheria antibodies levels below 0.01 IU/ml were considered to be not protective, 0.01 to <0.1 IU/ml concentrations confer basic protection while 0.1 to <1 IU/ml levels confer full protection. Levels of 1 IU/ml or higher are associated with long-term protection [12].

Levels of specific IgG antibodies against PRP[13] (polyribosylribitol phosphate), the Hib capsular polysaccharide were determined using the VaccZyme™ Human Anti-*Haemophilus influenzae* type b Enzyme Immunoassay Kit (The Binding Site, Birmingham, U.K). Limits of quantification of the assay were 0.11−9.00 μg/ml. In line with international recommendations, anti-PRP IgG titers ≥0.15 μg/ml were regarded to confer short-term protection, while concentrations ≥1 μg/ml were considered indicative of long-term protection. Anti-PRP IgG concentrations ≥5.0 μg/ml were considered to confer protection against upper respiratory tract colonization with Hib [13].

The IgG relative AI[14] (avidity index) to PRP was measured for subjects with Hib antibodies concentration ≥0.15 IU/ml, using commercial ELISA kit (VaccZyme™ Hib ELISA Accessory pack The Binding Site, Birmingham, U.K). A binding index ≥50% was considered as the relative avidity index for the tested serum.

Sera were diluted at 1:100 in sample buffer for all IgG-specific antibodies analyses. DT and PRP IgG-specific antibodies analyses were processed in 2012, while testing of PT antibodies were processed in 2016 since anti-PT ELISA kits were available.

2.3. Data management and statistical analysis

For pertussis and diphtheria analyses, the samples were classified into two groups, according to age: 19−36 and 37−55 months. Further, Hib-vaccinated subjects were compared to those -unvaccinated, designed as control group. For each group, the MTPV[15] was calculated. GMTs and GMAIs with 95% CI (confidence intervals) were calculated from the anti-log of the mean of log-transformed values. For the purpose of GMTs calculations, antibody concentrations below the lower limit of detection of the assay were given an arbitrary value of half the cut-off and antibody

[12] DT: diphtheria toxoid.
[13] PRP: polyribosylribitol phosphate.
[14] AI: avidity index.
[15] MTPV: mean time post-vaccination.

https://doi.org/10.1016/j.heliyon.2018.e00664

concentrations above the upper limit of detection of the assay were retested with additional dilutions until measurable value was obtained and then was multiplied according to the dilution factor to obtain the antibody concentration. The chi-square test or Ficher's exact test, as appropriate, was used to compare categorical variables between groups. The Mann-Whitney U test was used to compare the GMTs or GMAIs of specific IgG between two independent groups and the Spearman's rank order was used to assess correlations. For all analyses, a two-tailed *P* value of <0.05 was considered to be significant.

2.4. Ethical approval

This study was approved by the Ethic Committee of the Algiers University Medical School and the Algerian Ministry of Health.

3. Results

3.1. Study population

A total of one hundred and twenty-eight children were enrolled in the study. Forty one children were excluded because parents declined. A blood sample was not obtained for six toddlers, due to the difficulty of sampling. The final analyses for diphtheria, pertussis and Hib were therefore based on samples from 81 individuals. Anti-PT IgG antibodies were analyzed for 78 subjects (three subjects were not included as serum was insufficient). The IgG avidity index determination was assessed in 55/57 subjects who had anti-PRP IgG $\geq$0.15 μg/ml (two children were excluded as reagent was insufficient).

The 81 participants were aged between 19-55 months, with mean age at 36 months. Forty eight (59.26%) subjects were male and 33 (40.74%) were female. There was difference in the gender distribution among the groups.

Review of the children's vaccination cards revealed that 51 participants were vaccinated with the SII DTwP vaccine (Hib-unvaccinated group) while 30 participants were vaccinated with the Sanofi Pasteur DTwP-Hib vaccine (Hib-vaccinated group). The time elapsed between the collection of serum and the last vaccination ranged from 1 to 36 months. The overall MTPV was 17 months. The MTPV by age groups was 9 and 27 months in the 19−36 months and 37−55 months groups respectively and the MTPV in both Hib-vaccinated and −unvaccinated groups were 8 and 22 months respectively. Children received their first dose of vaccine at the mean age of 03 months of age (range 3−4), their second dose at 04 months (range 4−6), their third dose at 5 months (range 5−9) and their fourth dose at 19 months of age (range 18−27).

https://doi.org/10.1016/j.heliyon.2018.e00664

3.2. Immune responses

3.2.1. Pertussis

The distribution of antibody levels and geometric mean titers are presented in Table 1.

Among the 78 subjects studied, 20 (25.64%; 95% CI: 17.26−36.31) participants had anti-PT antibody concentration >25 IU/ml, significantly higher in 19−36 months group ($p = 0.020$). Five individuals had PT antibody concentration ≥100 IU/ml with no significant difference between groups. The time since their last vaccination was <18 months (range: 1−16 months).

The overall PT GMT was 12.02 IU/ml (95% CI: 10.80−13.24), significantly higher in 19−36 months age group ($p = 0.020$) (Fig. 1); while no significant difference was observed between males and females (14.12 IU/ml versus 12.59 IU/ml).

Although all participants received four doses of vaccine, the anti-PT IgG antibodies (20/78; 25.64%) were undetectable (<5 IU/ml), significantly higher in 37−55 months age group (14/37; 37.84%) ($p = 0.020$).

3.2.2. Diphtheria

As shown in Table 1, all the 81 participants had basic levels of anti-DT IgG antibodies ≥0.01 IU/ml. Seventy six (93.83%; 95% CI: 86.35−97.33) were fully protected with levels of anti-DT IgG antibodies above 0.1 IU/ml, with no significant difference between age groups. High levels of anti-DT IgG antibodies (>1.0 IU/ml), associated

Table 1. Levels of antibodies against diphtheria toxoid and pertussis toxin in the all participants and according to age groups.

Parameter		Age groups		
		19−36 mo	37−55 mo	*P*
Anti-PT IgG titer (IU/ml); No. (%); (95% CI)				
No. of subjects	78	41	37	
>25	20 (25.64) (17.26−36.31)	15 (36.58) (23.59−51.88)	5 (13.51) (5.91−27.98)	0.020
GMT	12.02 (10.80−13.24)	17.78 (16.63−18.92)	14.79 (13.65−15.93)	0.020
Anti-DT IgG titer (IU/ml); No. (%); (95% CI)				
No. of subjects	81	44	37	
≥0.01	81 (100) (95.47−100)	44 (100) (91.97−100)	37 (100) (90.59−100)	
≥0.1	76 (93.83) (86.35−97.33)	43 (97.73) (88.19−99.60)	33 (89.19) (75.29−95.71)	0.173
≥1	18 (22.22) (14.54−32.42)	13 (29.54) (18.16−44.22)	5 (13.51) (5.91−27.98)	0.084
GMT	0.55 (0.44−0.65)	0.66 (0.51−0.81)	0.44 (0.29−0.59)	0.535

https://doi.org/10.1016/j.heliyon.2018.e00664

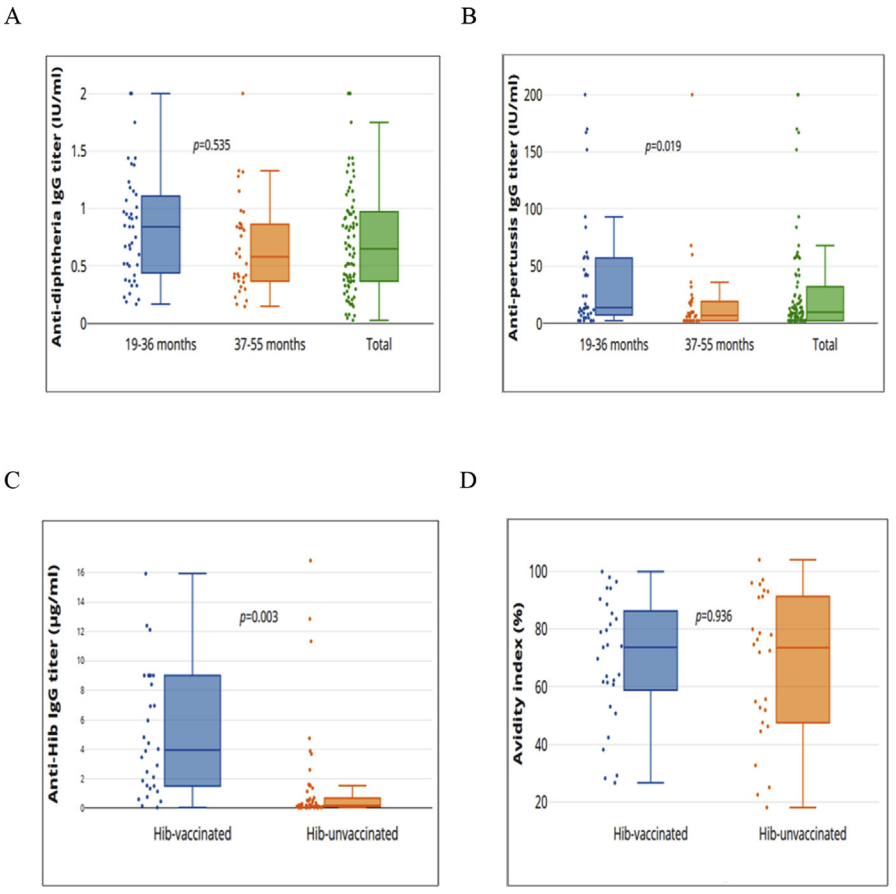

Fig. 1. Specific immune responses to selected vaccine-preventable diseases measured in toddlers and preschool children. A. Distribution of anti-diphtheria IgG titer by age groups. B. Distribution of anti-pertussis IgG titer by age groups. C. Anti-Hib IgG titer in Hib-vaccinated and -unvaccinated groups. D. Percentage of the avidity index in Hib-vaccinated and -unvaccinated groups. Specific antibody levels of DT, PT and Hib and avidity index of Hib are plotted as box-and-whisker-plots. The bottom and top of the box represent the first and third quartiles, respectively, and the horizontal band inside the box represents the median. The ends of the plots represent the minimum and maximum values, excluding outliers. Groups were compared using Mann-Whitney U test. A two-tailed *P* value of <0.05 was considered significant.

with long-term protection, were found in 18 (22.22%; 95% CI: 14.54−32.42) subjects with no significant difference between age groups.

The overall GMT was 0.55 IU/ml (95% CI: 0.44−0.65). No significant difference between age groups (0.66 IU/ml in 19−36 months versus 0.44 IU/ml in 37−55 months) or gender (0.59 IU/ml in males versus 0.49 IU/ml in females) was observed (Fig. 1).

3.2.3. Haemophilus influenzae type b

Among the 30 Hib-vaccinated subjects assessed, 29 (96.66%; 95% CI: 83.33−99.41) participants had Hib antibody concentration $\geq$0.15 IU/ml. Twenty five (83.33%;

https://doi.org/10.1016/j.heliyon.2018.e00664

95% CI: 66.44−92.66) had Hib antibody concentration ≥1 IU/ml and 12 (40%; 95% CI: 24.59−57.68) had Hib antibody concentration ≥5 IU/ml. These obtained antibody levels were significantly higher than levels measured in the 51 Hib-unvaccinated participants ($p < 0.001$) (Table 2). GMTs in Hib-vaccinated group were significantly higher ($p = 0.003$) than -unvaccinated group (2.95 μg/ml; 95% CI: 1.37−4.52 versus 0.35 μg/ml; 95% CI: 0.17−0.87) (Fig. 1). Only one Hib-vaccinated subject 19 months of age did not attain concentration ≥0.15 μg/ml.

Anti-PRP relative avidity index, considered as ≥50%, was positive for 24/29 Hib-vaccinated subjects and 19/26 Hib-unvaccinated participants, with no significant difference between the two groups (Fig. 1).

3.3. Association between time post-vaccination and immune responses

There was a negative correlation between time since last vaccination and specific antibody responses to pertussis ($r_s = -0.33$, $p = 0.003$) and diphtheria ($r_s = -0.36$, $p = 0.001$) with direction of effect for time since last vaccination for lower anti-PT and anti-DT antibody concentrations.

4. Discussion

The vaccine strategy in Algeria until 2015 recommended a primary vaccination at 3, 4 and 5 months of age followed by a booster dose at 18 months. Analysis of the vaccination booklet of the children included in our study indicates that the recommendations were followed during this period. In Algeria in 2008, the SII vaccine (DTwP) was replaced by the Sanofi Pasteur vaccine (DTwP Hib). However, no sero

Table 2. Anti-PRP antibody levels and avidity index in Hib-vaccinated and -unvaccinated groups.

	Hib-vaccinated	Hib-unvaccinated	*P*
Anti-PRP IgG titer (IU/ml); No. (%); (95% CI)			
No. of subjects	30	51	
≥0.15	29 (96.67) (83.33−99.41)	28 (54.90) (41.38−67.73)	<0.001
≥1.0	25 (83.33) (66.44−92.66)	12 (23.53) (14.00−36.76)	<0.001
≥5.0	12 (40.0) (24.59−57.68)	3 (5.88) (2.02−15.92)	<0.001
GMT	2.95 (1.37−4.52)	0.35 (0.17−0.87)	0.003
PRP Avidity index (%), No. (%); (95% CI)			
No. of subjects	29	26	
≥50%	24 (82.76) (65.45−92.40)	19 (73.08) (53.92−86.30)	0.385
GMAI	65.13 (56.88−73.37)	61.09 (50.73−71.45)	0.936

https://doi.org/10.1016/j.heliyon.2018.e00664

epidemiological studies were performed after the change of vaccine although it is known that immunogenicity of vaccine containing wP vaccines can vary [14, 15, 16].

4.1. Pertussis

Consistent with previous studies [13, 14, 15, 16, 17, 18, 19, 20], the GMTs of IgG-PT were low, significantly higher in children 19−36 months of age: 17.78 IU/ml versus in children 37−55 months of age: 14.79 IU/ml. Twenty-five (25.64%) subjects had titers >25 IU/ml, significantly higher in children 19−36 months of age. These data indicates that pertussis antibody levels decrease quickly in young children despite receiving four doses of whole-cell pertussis vaccine. Previous studies explored the low immunity to pertussis with its rapid waning over time and it has been demonstrated that the vaccine-induced antibodies began to wane 1−3 years after pertussis vaccination; children became probably more susceptible to infection at 4 years of age [17, 18, 19, 20, 21, 22, 23]. Although local epidemiology of pertussis and immunization schedule play a role in the duration of protection following immunization [4, 11], it has previously been demonstrated that the immunogenicity of whole-cell pertussis vaccines may differ considerably according to the manufacturer, as there are difficult to produce reproducibly [14, 15]. Another explanation might be a modest number of studied subjects.

In addition, undetectable or very low anti-PT antibody levels had been observed in an open serological follow-up study conducted in French children at year 3 and 6 follow-up demonstrating their rapid decay [18]. In our study, the proportion of subjects with undetectable level (<5 IU/ml) of anti-PT IgG increased significantly in 37−55 months age group (14/37; 37.84%) ($p = 0.020$), suggesting susceptibility to infection, and requiring to consider the administration of a booster dose as suggested by WHO and introduced in Europe and North America at 6 years of age.

4.2. Diphtheria

Consequently to receiving completely primary vaccination and first booster, almost all (76/81; 93.83%) study subjects demonstrated high antibody response to diphtheria toxoid (≥0.1 IU/ml) conferring full protection with no significant difference in age groups ($p < 0.05$). The overall GMT level was 0.55 IU/ml, with no significant difference according to age groups ($p < 0.05$). A previous Algerian serological study conducted in the year 1998 in 1755 subjects after mass vaccination campaigns and the introduction of boosters in adolescents and adults in the year 1997 following resurgence of diphtheria in the 1990s had shown that 87.06% subjects aged between 2 and 15 years had DT antibodies ≥0.1 IU/ml and a GMT level of 0.51 IU/ml [24]. The high rate of fully protected subjects against diphtheria had previously demonstrated by other studies. Indeed, these studies showed that 100% of children had DT antibody titers ≥0.1 IU/ml as well as in children who received the combined

https://doi.org/10.1016/j.heliyon.2018.e00664

SII or Sanofi Pasteur vaccine [16, 25]. Only five subjects had basic protection (<0.1 IU/ml) and need immediate booster.

Further serosurveillance studies including wider ranges of age (older children, adolescents and adults) are needed to extend our observations in the other age groups.

4.3. *Haemophilus influenzae* type b

As expected, in the Hib-vaccinated group, rates of anti-PRP antibodies levels associated with short-term and long-term protection were observed in 96.67% and 83.33% respectively, with significant difference for those observed in -unvaccinated group ($p < 0.001$). These data showed, in line with those reported in other studies in European and African countries, the high rate of long-term protection against Hib [26, 27, 28, 29, 30, 31, 32, 33]. Over 50% of subjects in the -unvaccinated group had anti-PRP antibodies concentration associated with short-term protection, while over 20% had antibodies concentration associated with long-term protection. This is most likely due to the carriage and/or previous exposure to natural infection to Hib in upper respiratory tract.

The GMT of anti-PRP antibodies in Hib-vaccinated group was 2.95 μg/ml, significantly higher than in -unvaccinated group (0.35 μg/ml) ($p = 0.010$). A similar high GMTs were reported in studies conducted in many developing countries [28, 29, 30, 31, 32], unlike those from developed countries where lower protective levels were observed [26, 27]. The stronger anti-PRP response observed in children in our study as well as in other developing countries could be explain by more extensive colonization with Hib or with other bacteria expressing polysaccharides that cross-react with PRP (e.g., *E. coli* expressing K100) [32], and the use of the more immunogenic whole-cell pertussis containing combination Hib conjugate vaccine [31]. These boosting factors would be diminished over time as the widespread Hib vaccination in our country would have gradually reduced carriage. They would also be lower if a switch from whole-cell pertussis vaccine to acellular pertussis vaccine, as in many developed countries, is adopted in the childhood combination vaccine and as whole-cell pertussis vaccines are less and less produced by vaccine manufacturers.

Anti-PRP antibody levels ≥5 μg/ml considered to confer protection against Hib upper respiratory tract colonization were significantly higher (12/30; 40%) in Hib-vaccinated group ($p < 0.001$). This may provide indirect (herd) protection to older children and adults, caused by decreased transmission of Hib.

The relative avidity index (≥50%) as well as GMAI (as marker of immunological memory), were high both in Hib-vaccinated and -unvaccinated group.

Only one toddler 19 months old had concentration of anti-PRP antibodies <0.15 μg/ml, despite of being fully vaccinated with 4 doses. As demonstrated in previous

https://doi.org/10.1016/j.heliyon.2018.e00664

studies, this may represent vaccine failure, breach in the cold chain during transportation and storage or delay in immune response [34, 35, 36, 37].

4.4. Time post-vaccination and immune responses

The negative correlation observed between time post-vaccination and specific antibodies against pertussis and diphtheria is expected and is in line with previous studies [18, 20, 21].

The strengths of this study that it provides first data on immune responses in Algerian toddlers and preschool children to selected vaccine-preventable diseases (pertussis, diphtheria, and Hib). Our findings highlight that the need of population-based serosurveillance studies to guide the national immunization program is relevant and timely. Our study has a number of limitations: (i) enrollment of a modest number of subjects with specific groups in unequal numbers and different gender distribution, (ii) variable interval between the blood sampling and the time since last vaccination, (iii) long interval between the blood sampling and PT analysis that may have an impact on the results, (iv) the absence of Hib carriage data, that may be an important mechanism for maintaining protective immunity and (v) collection of samples from one particular geographical area of Algiers, which might not truly reflective of the situation in the rest of the country.

5. Conclusion

Our results support the recently introduced booster dose of pertussis vaccine in children 6 years old. Further sero-epidemiological studies including large numbers of subjects and wider age ranges (including older children, adolescents and adults) are needed to guide the national immunization program before recommending the introduction of more immunogenic vaccines and/or improvement of immunization schedules. Ongoing evaluation of the effectiveness of these measures on carriage and herd immunity would be required. In addition, there is a need to strengthening the notification of laboratory-confirmed cases for vaccine-preventable diseases more than clinically diagnosed cases. Finally, it is essential for our country to have reference laboratories for specific diseases having diagnostic and monitoring facilities when setting up a surveillance system.

Declarations

Author contribution statement

Nabila Benamrouche: Conceived and designed the experiments; Performed the experiments; Analyzed and interpreted the data; Contributed reagents, materials, analysis tools or data; Wrote the paper.

https://doi.org/10.1016/j.heliyon.2018.e00664

Hassiba Tali Maamar: Performed the experiments; Contributed reagents, materials, analysis tools or data.

Samia Chemli, Houria Senouci: Performed the experiments.

Kheira Rahal: Conceived and designed the experiments.

Funding statement

This research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors.

Competing interest statement

The authors declare no conflict of interest.

Additional information

No additional information is available for this paper.

Acknowledgements

The authors express their gratitude to children and parents who participated to the study and all colleagues from the local public health facilities of Cherraga, Draria and Bouzareah in Algiers for contacting the families and assistance in collecting blood samples.

The authors would like to thank specifically Dr. Nicole Guiso, Institut Pasteur, France for reviewing the manuscript and Dr. Djohar Hannoun, from the National Institute of Public Health, Algeria for the discussion about statistical analysis.

The authors also thank Sanofi Pasteur for providing VaccZyme™ Human Anti-*Haemophilus influenzae* type b Enzyme Immunoassay kit and Hib ELISA VaccZyme™ accessory pack used for PRP antibody testing.

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