Original article

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Vaccination status in patients at risk for invasive disease with encapsulated bacteria at a children's hospital in the City of Buenos Aires

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ABSTRACT

Introduction. The Ministry of Health has established specific vaccines for people at high risk for invasive infections with encapsulated bacteria (EB). There is currently no information about compliance with the vaccination schedule.

Our objective was to assess EB vaccination status in subjects ≤ 18 years with risk factors.

Population and methods. Observational, analytical study with a survey to parents of subjects aged ≤ 18 years with HIV, asplenia and/or complement deficiency attending a vaccination center at a children's hospital between October 2020 and September 2021. Sociodemographic and clinical data were collected. Their vaccination status for the EB pneumococcus, meningococcus, and *Haemophilus influenzae* type b (Hib), their regular vaccination and flu vaccination schedules were assessed. The vaccine hesitancy scale (VHS) was administered: range 10–50. The association between the study variables and EB vaccination was analyzed using logistic regression (OR, 95% CI). The REDCap® database and the STATA® v.14 software were used.

Results. A total of 104 subjects participated; mean age: 9.9 years (SD: 4.4). Asplenia: 91.3%, HIV: 7.6%, and complement deficiency: 0.9%. Socioeconomic level: relative poverty: 38.4%, followed by middle class: 37.5%.

Complete vaccination status: meningococcal vaccine 45%, pneumococcal vaccine: 42%, Hib: 97%. The regular vaccination and flu vaccination schedules were up-to-date in 77.9% and 61.5% of cases, respectively. Mean VHS score: 41.9 (SD: 3.2). No significant associations were observed between variables and EB vaccination status.

Conclusions. A high percentage of subjects had not completed neither their EB vaccination nor their regular or their flu vaccination schedules. Caregivers' confidence in vaccines was high.

Key words: *HIV, spleen diseases, inherited complement deficiency, vaccination, confidence.*

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INTRODUCTION

Special hosts are a heterogeneous group of patients with a high susceptibility to develop infections and a higher morbidity and mortality than the general population. A personalized and timely vaccination is crucial in these individuals, including vaccines outside the national vaccination schedule, different vaccination times, secondary boosters, and, sometimes, a measurement of post-vaccination response.[3]

Within the group of special hosts, three entities account for a higher risk for invasive disease with encapsulated bacteria (EB): human immunodeficiency virus (HIV) infection, asplenia, and complement deficiency.[3–12]

In Argentina, between 1300 and 1500 children per year are exposed to HIV, and the perinatal transmission rate remains at 5%.[4] In relation to asplenia and complement deficiency, there are no data on their prevalence in our setting.

In HIV patients, the rate of *Streptococcus pneumoniae* (Sp) infections is estimated to be 30 to 100 times higher than in the general population.[5] For invasive *Neisseria meningitidis* (Nm) disease, there is a 60-fold increased risk[6] in untreated patients, especially in children with congenital infection.[7] For *Haemophilus influenzae* type b (Hib), the risk is 6 times higher.[8]

In relation to complement deficiency, specific deficiencies are considered a risk for invasive Hib and Nm disease, the latter includes even recurrent disease.[9,10]

In relation to asplenia, Sp, Hib, and Nm are the leading cause of fulminant sepsis after a splenectomy, with an incidence of 0.23–0.42% per year and a mortality rate of more than 50%.[11,12]

In 2014, the Ministry of Health implemented the national vaccination program for special hosts, which includes specific vaccines based on pathology;[5] to date, there is no information about adherence to this strategy. In addition, the COVID-19 pandemic caused a drop in vaccination coverage in our country[13] and may have had a negative impact on this group's vaccination.

The objective of this study was to assess the EB vaccination status in individuals ≤ 18 years who had a diagnosis of HIV, asplenia and/or complement deficiency.

POPULATION AND METHODS

This was an observational, cross-sectional, analytical study.

A survey was administered to the parents or caregivers of subjects ≤ 18 years of age with a diagnosis of HIV, asplenia and/or complement deficiency, who attended the vaccination center of Hospital de Niños Dr. Ricardo Gutiérrez between October 2020 and September 2021. Subjects who did not have a vaccination card at the time of the interview were excluded.

The following sociodemographic data were collected: age, sex, place of residence, and socioeconomic level as per Graffar's modified method;[14] clinical data: date and diagnosis of HIV, complement deficiency, and anatomical asplenia (congenital or surgical) or functional asplenia (impaired spleen function associated with hemoglobinopathies, idiopathic thrombocytopenia, collagen diseases, chronic inflammatory bowel disease, dermatitis herpetiformis, intestinal lymphangiectasia, chronic hepatitis, biliary cirrhosis, portal hypertension, hematopoietic stem cell transplantation, solid organ transplantation, high-dose steroids, amyloidosis).[3]

The EB vaccination status was assessed based on the following definitions:

- **Complete vaccination:** complete Sp, Hib, and Nm vaccines at the time of the interview after vaccination.[5]
- **Reasons for non-vaccination**: institutional, personal, clinical and/or COVID-19-pandemic.
- **Time between diagnosis and vaccination**: based on vaccine, age, and condition.[3,5]
- **Timely vaccination**: vaccine given within 30 days of the corresponding date (*Supplementary material 1: Data collection record*).

In relation to the visit, the following variables were investigated: referring professional (subspecialist or pediatrician), reason for the visit, request for consultation with the vaccination center medical team, and compliance with the regular vaccination schedule and flu vaccination schedule.

Finally, caregivers' confidence in vaccines was measured by means of a vaccine hesitancy scale (VHS), validated in our setting.[15,16]

The sample size was estimated based on the accessible population of 140 subjects in the study period, with a hypothetical frequency of 50% (±5) not having completed their EC vaccination and a 95% confidence level. A minimum of 103 subjects were required.

The sample was selected by convenience in the presence of investigators.

A descriptive analysis was performed. For quantitative variables, the mean and standard deviation (SD) and/or the median with interquartile

range (IQR) were described according to data distribution; for categorical variables, percentages were described with their corresponding 95% confidence intervals (CIs).

The confidence scale was used to assess the percentage of response to each item according to the degree of agreement. Then, a numerical value was assigned to each item, from 1 to 5 (1: strongly disagree, 2: disagree, 3: neither agree nor disagree, 4: agree, and 5: strongly agree) and the values were summed into an overall score (mean and SD), where the higher score correlated to a higher confidence in vaccines, so negative questions were scored inversely (items 5 and 6). Scoring range: 50 (maximum) to 10 (minimum).

In order to establish whether there was an association between sociodemographic variables, vaccination variables (regular and flu vaccination schedules) and the VHS score and special hosts having a complete vaccination status, the odds ratio (OR) and its respective 95% CI was calculated.

The time, in months, of total delay and adjusted for the pandemic was described considering the date of announcement of the preventive and mandatory social isolation policy in Argentina.[17] If vaccination occurred after March 20th, 2020, the delay due to the pandemic was estimated from the difference between the vaccination date and the date the preventive and mandatory social isolation policy was implemented.

Using a Kaplan-Meier analysis, the delays for each vaccine were plotted and stratified according to the vaccination status of the regular and seasonal flu vaccination schedules.

The REDCap® 18 database and the STATA® v.14 software were used.

Ethical considerations

This study was approved by the Research and Teaching Committee and the Research Ethics Committee of Hospital de Niños Dr. Ricardo Gutiérrez. In all cases, a written informed assent or consent was obtained.

Table 1. Sociodemographic and clinical characteristics of subjects (N = 104)

Sociodemographic and clinical variables		N	%
Age (years)	Mean and SD	9.9 (4.4)	
Sex	Female	56	53.8
	Male	48	46.2
Place of residence	CABA	30	28.8
	Greater Buenos Aires	66	63.5
	Provinces	8	7.7
Socioeconomic status	High (4–6)	7	6.7
	Middle-high (7–9)	14	13.4
	Middle (10–12)	39	37.5
	Relative poverty (13–16)	40	38.4
	Critical poverty (17–20)	4	3.8
Diagnosis	Asplenia	95	91.3
	Anatomical:	16	16.8
	Congenital	1	
	Splenectomy	13	
	Planning surgery	2	
	Functional*	79	83.2
	HIV	8	7.7
	Complement deficiency	1	0.9

*Hemoglobinopathies (N = 17), idiopathic thrombocytopenia (N = 10), solid organ transplantation (N = 6), high-dose steroids (N = 39), chronic hepatitis (N = 11), portal hypertension (N = 5), hematopoietic stem cell transplantation (N = 6), collagen diseases (N = 29), congenital immune deficiencies (N = 3).

Socioeconomic status: classification according to the social characteristics of the family, the father's occupation, the level of education, the sources of family income, housing comfort, and the characteristics of the area where the family lives.

SD: standard deviation.

RESULTS

A total of 120 special hosts attended the vaccination center; 104 met the inclusion criteria and agreed to participate. The survey was administered to 92 mothers (88.5%), 10 fathers (9.6%), and 2 caregivers (1.9%). *Table 1* describes the sociodemographic and clinical characteristics of subjects.

It was observed that 76.9% (95% CI: 68.1–84.2) of subjects had not received all EB vaccines. The main reasons for non-vaccination mentioned by survey respondents were lack of medical indication: 75% (95% CI: 66–82.6), fear of getting COVID-19: 8% (95% CI: 3.6–14), lack of contact with the subspecialist due to the pandemic: 6.8% (95% CI: 3–12.8), delay in relation to other appointments: 4% (95% CI: 1.2–9), temporal vaccine shortage: 3.8% (95% CI: 0.7–7.6).

Table 2 describes EB vaccination status stratified by vaccine and by total delay, delay due to the pandemic, and delay adjusted for the pandemic.

Figure 1 shows vaccination delays in relation to Nm and Sp vaccines. The *Supplementary material* shows delays compared to the regular vaccination schedule and compliance with the corresponding seasonal flu vaccine.

The reasons for attending the vaccination center were administration of the flu vaccine in 54% of cases (95% CI: 41.3–60.4), followed by EB vaccination in 48% (95% CI: 37.6–56.7), and a vaccine from the regular vaccination schedule in 29% (95% CI: 20.7–38.1). In addition, 29.8% of subjects (95% CI: 21.6–39.1) attended with the medical prescription to get advice from the vaccination center team.

The referral to the vaccination center was made by a subspecialist in 75% of cases (95% CI: 66–82.6) and by the pediatrician in 19.2% (95% CI: 12.5–27.6); 5.8% (95% CI: 2.3–11.6) consulted on their own.

In relation to the status of the regular vaccination and flu vaccination schedules, 77.9% (95% CI: 69.1–85) and 61.5% (95% CI: 51.9–70.5) were complete, respectively.

The mean VHS score was 41.9 points (SD: 3.2). *Figure 2* describes the percentage of response to each item. In relation to the degree of agreement, 100% (95% CI: 97.2–100) and 99% (95% CI: 95.4–100) of survey respondents believed that vaccines were important and effective for their children (items 1 and 2), respectively, and 96% (95% CI: 90.9–98.7), that they were good for the community (item 3). Also, 100% (95% CI: 97.2–100) agreed with following their pediatrician's indications (item 8). It was observed that 53.4% of parents (95% CI: 43.2–62.3) feared adverse events (item 9), and 16.3% (95% CI: 10.1–24.3) believed that new vaccines carried more risks than older ones (item 5).

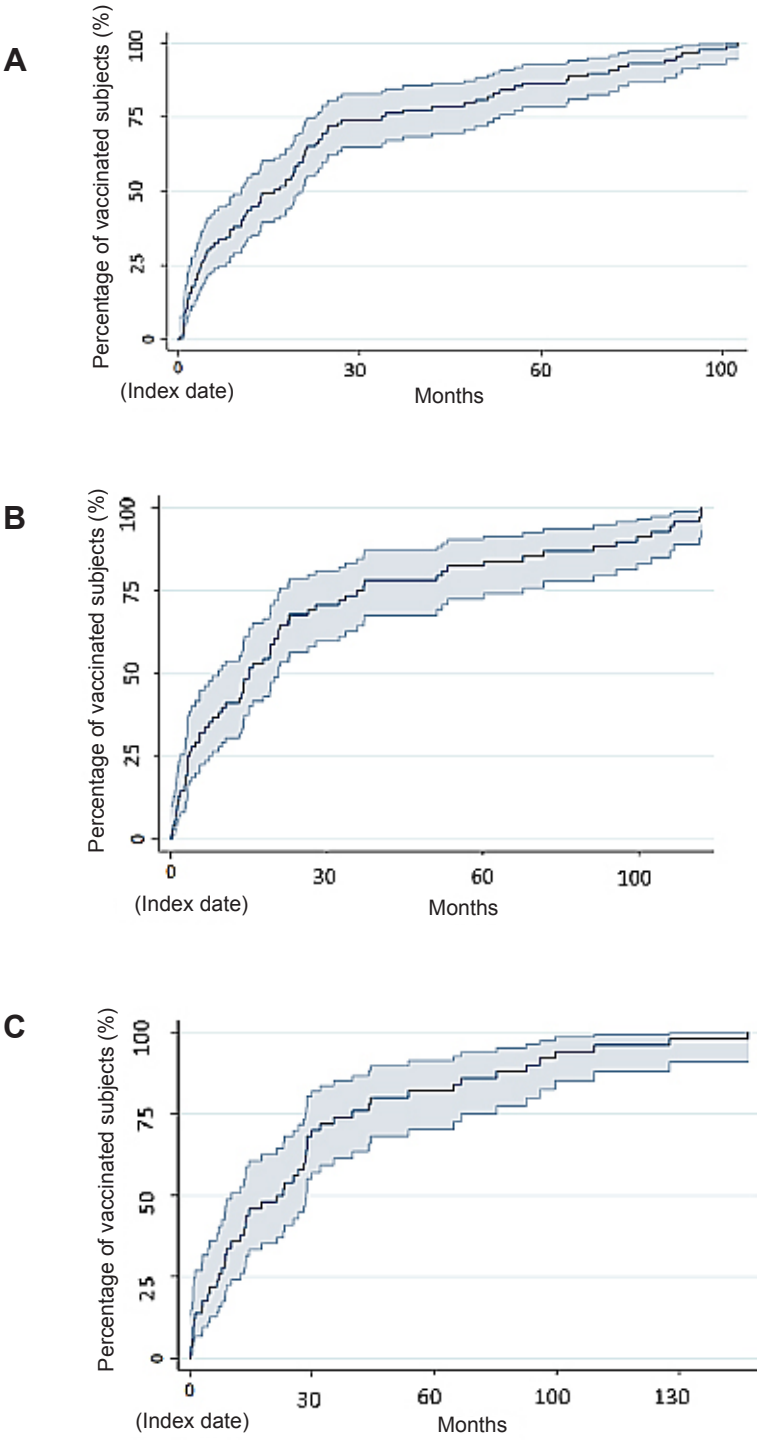
No associations were observed between sociodemographic variables, vaccination variables

Table 2. EB vaccination status (N = 104)

Vaccine	Meningococcal ACWY conjugate vaccine	13-valent pneumococcal conjugate vaccine	PPSV23	Hib
Complete % (95% CI)	45.2 (35.8–54.8)	42.3 (33.1–5)	42.3 (33.1–5)	97.1 (92.4–99.3)
Time* until vaccination (months)				
Mean (SD)	22.5 (27.6)	19.4 (31)	27.7 (35)	1.3 (8.04)
Median (IQR)	12 (1.7–26.9)	3.5 (0–22.6)	14.7 (0.7–33.2)	0
Delay* due to the pandemic				
Mean (SD)	5.7 (6.7)	4.7 (6.3)	3.8 (5.6)	0.3 (2.2)
Median (IQR)	1 (0–13)	0 (0–12)	0 (0–8)	0
Delay* adjusted for the pandemic				
Mean (SD)	16.8 (20.9)	14.7 (24.6)	23.9 (29.4)	0.97 (5.8)
Median (IQR)	11 (1.7–13.9)	3.5 (0–10.6)	14.7 (0–25.2)	0
Timely % (95%CI)	20 (13.3–28.7)	36.5 (27.7–46.1)	26.7 (19–36)	91.3 (84.7–95)

*: time is described in months, SD: standard deviation, IQR: interquartile range, CI: confidence interval, PPSV23: 23-valent pneumococcal polysaccharide vaccine, Hib: *Haemophilus influenzae* type b.

Figure 1. ***Kaplan-Meier curves, proportion of subjects with delayed vaccination for Nm and Sp based on time. The X axis indicates the time in months, starting at the index date (date on which the subject should have received the vaccine). The Y axis shows the proportion of vaccinated subjects. The shaded area corresponds to the 95% CI. A: meningococcal ACWY conjugate vaccine; B: 13-valent pneumococcal conjugate vaccine; C: 23-valent pneumococcal polysaccharide vaccine.***



(status of regular and flu vaccination schedules) and score of vaccine confidence and having received all EB vaccines.

DISCUSSION

Our study assessed the vaccination status of children and adolescents at risk for invasive diseases with EB in a specialized vaccination center at a tertiary care children's hospital. Most were patients with asplenia.

The vaccination program for special hosts is a public health strategy developed by the Division for the Control of Vaccine-Preventable Diseases to promote an adequate protection against diseases of high morbidity and mortality in this group.[19]

This population has been increasing year after year, in part due to new therapies and the increase in patient survival.[20] The quality of life has also improved; chronically ill children are able to attend school, travel, and be active in their community. Vaccination should be a priority; however, immunocompromised patients are often not properly vaccinated.[21–23]

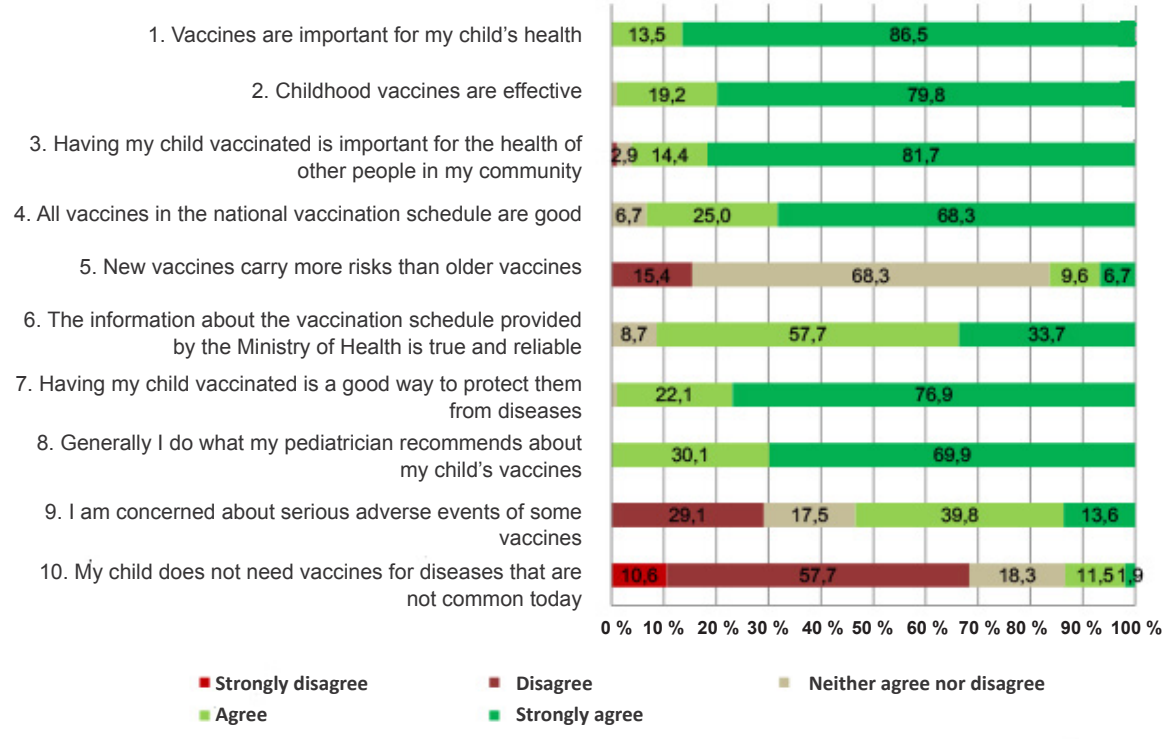
Our study found a high percentage of incomplete EB vaccination schedules. As it was performed during the COVID-19 pandemic, this situation was taken into account when assessing the results. It is worth noting that the study sample showed delays and non-compliance with the vaccination schedules before the pandemic, with a higher impact on the Nm and Sp vaccination schedules. A study in another country about the meningococcal conjugate vaccine showed similar results, and even a longer delay.[24]

Special hosts should receive additional doses to those established in the national schedule for Nm and Sp,[5] which may have influenced the results of incomplete schedules.[25] In addition, as of 2 years of age, children should complete the pneumococcal polysaccharide vaccine (PPSV23) schedule, a stage during which children usually do not attend vaccination centers, except for the flu vaccine.

In contrast, the Hib vaccination schedule was complete in most cases. The Hib vaccine has been part of the regular vaccination schedule for more than 20 years and does not require boosters in immunocompromised patients, except in the case of hematopoietic stem cell transplantation.

An assessment on timely vaccination has also been conducted, and our results showed

Figure 2. Percentage of response to the World Health Organization's vaccine hesitancy scale



a low percentage of vaccination within the ideal timeframe, turning it into a missed critical window of opportunity.

In our setting, the vaccination services offered at tertiary care hospitals have immunization specialists who act as advisors and provide support to the treating team. During the study, one third of patients attended the vaccination center only to request for advice; future studies should assess the reasons related to the lack of specific medical indication regarding necessary vaccines.

Studies have shown that a positive factor associated with vaccination is the recommendation by the health care provider.[26–28] The international literature suggests that the responsibility for vaccine indication in special hosts should be shared between the general practitioner and the subspecialist.[1] In our study, a minority of patients were referred by the pediatrician. A study carried out in a population at risk found similar results[23] and raised the need to define the role of health care providers working in different areas according to the institutional organization.

It is worth noting that, among the reasons for non-vaccination, most caregivers reported that they had not received any medical indication. However, this study did not inquire into the time at which the consultation was made.

Regular and flu vaccination schedules were incomplete in one quarter and one third of the patients, respectively. Most likely, the lack of vaccination is due to multiple associated factors, and it is also consistent with national coverage rates: by 2020, no vaccine in the national schedule exceeded 80% in the general population.[29] An additional factor that may have influenced flu vaccination is that it is a seasonal vaccine.

Parents' confidence in vaccines is an aspect to be taken into consideration for vaccination adherence. Hesitancy has been considered a global public health problem, responsible for the drop in vaccination coverage and the emergence of outbreaks.[30] In our study, the administration of the VHS showed high scores for confidence in vaccines and in the indication by the primary care pediatrician. However, half of the survey respondents reported that they were concerned about adverse events, information that should be taken into account in the medical consultation in case of caregiver´s doubts on the part of caregivers.

This study has weaknesses. The sample was selected by convenience; it is possible that risk associations could not be established due to the small sample size; however, previously published studies observed associations between a delay in vaccination and a low parental education level, the fact that it was not their first child, a lack of health insurance or a low socioeconomic level.[31–33]

In addition, only the parents who attended the selected health facility and the vaccination center were included; therefore, the target population is not represented in its entirety. To reduce such selection bias related to our accessible population, we included those children who attended to receive any vaccine.

The strength of this study lies in the information collected on the current situation of a group of hosts at a higher risk for invasive disease with EB, which may serve to expose the need for further improvement of vaccination strategies in this population.

CONCLUSIONS

A high percentage of the subjects who attended the vaccination center had not completed neither their EB vaccination nor their regular or flu vaccination schedules.

Most of them had not been vaccinated in a timely manner, and vaccination schedules were already delayed before the pandemic.

One of the main reasons of non-vaccination reported by caregivers was lack of medical indication. The level of confidence in vaccination was high. ■

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Supplementary material available at:
https://www.sap.org.ar/docs/publicaciones/archivosarg/2023/2648_AO_DelPino_Anexo.pdf

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