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Impact of the introduction of pneumococcal conjugate vaccine on rates of community acquired pneumonia in children in northeast Brazil

Impacto da vacina pneumocócica conjugada 10-valente (pcv10) na hospitalização de crianças por pneumonia no sertão da Paraíba

Impacto de la vacuna neumococcica conjugada 10-valente (pcv10) en hospitalización infantil para neumonía en el sertão da Paraíba

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Abstract

Evaluating the impact of the 10-valent pneumococcal conjugate vaccine on the hospitalization of children under five years of age before and after its implementation in the city of Patos, PB – Brazil. The first part of this paper comprises a descriptive study with a transversal approach; the data were collected through scrutiny of the patients' hospital records. For that effect, every medical record found from 2005 until 2015 (periods before and after the introduction of the PVC10 to the Brazilian vaccination schedule) were examined, the ones diagnosed with pneumonia were selected and those that belonged to children from Patos were analysed. The second part includes an ecological time series, whose data were collected from the Paraiba State 6thRegional Health Section database to access information from the National Immunization Program Information System (NIP-IS). It has been found that there were 1,094 hospitalizations for pneumonia on children under 5 years of age within the ten-year-period investigated. The data confirm a declining tendency of hospital admissions for pneumonia in the city of Patos-PB in the analyzed time series, and the PVC10 vaccination coverage has

been effective in the analyzed municipality. Despite the declining tendency, the number of cases is still considerably high. Being aware that in the health-disease process children's hospitalizations are caused by multiple variables including social, economic and cultural issues, it is fundamental the establishment of public policies as well as active surveillance that continuously evaluates the profiles and occurrences of pneumonia cases in Brazil.

Keywords: Pneumonia; Pneumococcal Vaccines; Hospitalized Children.

Resumo

Avaliar o impacto da vacina pneumocócica conjugada 10-valente (PCV10) nas hospitalizações em crianças <5 anos no período pré e pós-vacinal residentes do município de Patos – PB, Brasil. Trata-se de um estudo descritivo de abordagem transversal, na sua primeira parte, através de coleta em prontuários hospitalar. Para isso, realizou-se a consulta a todos os prontuários de 2005 a 2015 (período anterior e posterior à introdução da PCV10 no calendário brasileiro), em seguida foram separados apenas os prontuários com diagnóstico de pneumonia e por fim analisados aqueles cujas crianças residiam no município de Patos. Em um segundo momento, realizou-se um estudo ecológico de série temporal, cuja coleta se deu através de consulta ao banco de dados da 6ª Gerência Regional de Saúde do Estado da Paraíba para coleta das informações contidas no Sistema de Informação do Programa Nacional de Imunizações (SI-PNI). Observou-se um total de 1.094 hospitalizações por pneumonia em crianças menores de 5 anos ao longo de 10 anos. Os dados coletados confirmaram uma tendência declinante de hospitalização no município de Patos-PB por pneumonia na série temporal analisada, efetiva cobertura vacinal contra o PCV10 no município analisado. Apesar da tendência declinante, os níveis atuais ainda são altos. Ciente de que no processo saúde-doença a hospitalização infantil sofre interferência de múltiplas variáveis, dentre elas sociais, econômicas e culturais, torna-se essencial o desenvolvimento de políticas públicas e vigilância ativa com avaliação contínua do perfil e distribuição dos casos no Brasil.

Palavras-chave: Pneumonia; Vacinas Pneumocócicas; Crianças Hospitalizadas.

Resumen

Evaluar el impacto de la vacuna conjugada antineumocócica 10-valente en la hospitalización de niños menores de cinco años antes y después de su implementación en la ciudad de Patos, PB - Brasil. La primera parte de este trabajo comprende un estudio descriptivo con enfoque transversal; los datos se recopilaron mediante el escrutinio de los registros hospitalarios de los pacientes. Para tal efecto, todos los registros médicos encontrados desde 2005 hasta 2015

(periodos antes y después de la introducción de la PVC10 al calendario de vacunación brasileño) se examinaron los diagnosticados de neumonía y se analizaron los que pertenecían a niños de Patos. La segunda parte incluye una serie de tiempo ecológico, cuyos datos fueron recolectados de la base de datos de la Sexta Sección Regional de Salud del Estado de Paraíba para acceder a la información del Sistema de Información del Programa Nacional de Inmunización (NIP-IS). Se encontró que hubo 1.094 hospitalizaciones por neumonía en niños menores de 5 años dentro del período de diez años investigado. Los datos confirman una tendencia decreciente de los ingresos hospitalarios por neumonía en la ciudad de Patos-PB en la serie temporal analizada, y la cobertura de vacunación con PVC10 ha sido efectiva en el municipio analizado. A pesar de la tendencia a la baja, el número de casos sigue siendo considerablemente alto. Conscientes de que en el proceso salud-enfermedad las hospitalizaciones infantiles son causadas por múltiple variables que incluyen aspectos sociales, económicos y culturales, es fundamental el establecimiento de políticas públicas así como una vigilancia activa que evalúe continuamente los perfiles y ocurrencias de los casos de neumonía en Brasil.

Palabras clave: Neumonía; Vacunas antineumocócicas; Niños hospitalizados.

1. Introduction

In our country, several achievements have been conquered in the area of public health since the consolidation of the *SUS* (Brazilian acronym for Unified Health System) by the Federal Constitution of 1988 as a national policy (Constituição Federal Brasileira, 1988). This event validated the right of all citizens to social and economic policies with the objective of reducing health risks as well as granting them universal and egalitarian access to all actions of health promotion, protection and recovery in every level.

In the history of public health, child assistance has always been a matter of relevance, where attempts to improve the quality of the services provided are a continuous challenge. In Brazil, the *NIP* (National Immunization Program) allowed the expansion of available public health actions, emphasizing the need for control of community respiratory-infections, considered a top priority in developing countries, due to their high morbimortality in children under five years of age (Brasil, 2013).

Pneumonia is globally seen as a major concern in the health sector. In 2010, 120 million cases were registered worldwide. Among them, 14 million evolved from milder to severe conditions, especially in children under the age of 5 (Walker, et al., 2013).

In 2014, 562.402 children under 1 year of age were hospitalized from a total population of 2.713.244 (IBGE, 2010), which accounts for 20,7% of the total; and pneumonia was, once again, the number one cause of the admittances (Brasil, 2014).

Aiming at lowering pneumonia-caused child mortality in Brazil, in 1997, Brazil incorporated the *AIDPI* (Brazilian acronym from Integrated Management of Childhood Illness – IMCI) from the World Health Organization, that accounted for the diverse epidemiological realities in the Brazilian municipalities (Brasil, 2017). In 2005, the Ministry of Health published an agenda of compromises with the Integrated Child Health and Reduction in Child Mortality programs, by regulating the policies to be followed by every state and municipal units. In 2006, the Reduction in Child Mortality as a government policy was confirmed as it was incorporated among the operational priorities of the Life Pact program. For that matter, actions to reduce the number of pneumonia-caused deaths by 20% were implemented along with the establishment of death-surveillance committees and interventional measures to child prevalent illnesses (Brasil, 2018).

Consequently, even with the great advances in child health in our country, several regional limitations should still be considered. The latest prevention and promotion procedures should be put into practice in every municipality in Brazil. However, such measures are not yet equally conducted among the children in need for medical services.

Due to the epidemiological importance of the pneumonias, we find necessary the execution of studies on the knowledge of the social/demographical characteristics and the peculiarities of every region so that public health action plans, that comprise the principle of integrality to SUS patients, may be implemented as well as efficient and effective targeting of investments and public policies.

Therefore, this paper aims at evaluating the impact of the 10-valent pneumococcal conjugate vaccine on children under five years of age hospitalized for pneumonia admitted to a public hospital in a northeastern Brazilian state and aimed to analyze the groups most affected and the main clinical manifestations of the disease; hence seeking to contribute with further information to aid surveillance actions and strengthen the public health policies in our country.

2. Metodologia

The first part of this article comprises a descriptive study with a time series transversal approach conducted by means of an examination of every single medical record found from

2005 until 2015 (periods before and after the introduction of the PVC10 to the Brazilian vaccination schedule). So, to avoid a statistical bias caused either by the low vaccination coverage on that year or by the seroconversion period lapse, the cases from 2010 were excluded. The data were collected from the medical records from the File Store Sector of the Noaldo Leite Hospital, located in Patos, PB, which happens to be the only pediatric hospital in that state area, serving 40 surrounding towns with an average of 300 daily attendances. The data collection instrument used was a semi-structured script previously prepared by the authors, containing questions related to the hospitalization date, discharge date, sex, clinical manifestations and treatment.

Therefore, all patients' medical records from 2005 until 2015 were examined. From all of them, a total of 2,707 cases of diagnosis of pneumonia were selected; and 1,094 cases that fulfilled the inclusion criteria of belonging to residents of Patos under the age of five were scrutinized. 5 records that had their diagnosis altered within the hospitalization period were excluded along with other 3 with illegible data. A few records from the samples did not contain all information they were supposed to have, thus hindering the fulfillment of some of the variables of the study. The diagnostic confirmation criteria used by the hospital were the clinical data and chest radiographs.

The research project was submitted to the Faculdades Integradas de Patos's Committee for Ethics in Research on Human Beings and approved for execution under the Certificate of Presentation for Ethical Consideration number 1.800.583.

The data analysis was conducted through descriptive statistics techniques. As for the data matching, the Pearson's chi-squared testwas employed which considered significant the p value <0.05. In addition, the *Student* ***t*** test was carried out to check the differences among the averages. The statistical analysis were performed with the use of the program *Statistical Package for the Social Sciences* for Windows (SPSS*)* version 22.2.

3. Results

Table 1 shows a decline in the number of hospital admittances after the implementation of the PVC10, with the highest amount of cases in the year of 2005 (19,5%) and lowest in 2012 and 2015 respectively (4.8% and 5.03%). 740 admittances (67.6%) were catalogued between 2005 and 2009; and 354 (32,4%) between 2011 and 2015, thus confirming a declining tendency on cases within the time series analyzed throughout this work.

The number of hospitalizations for pneumonia among children under five years of age who reside in Patos, PB that occurred within the analyzed period (1.094 cases) accounted for 40,41% of the total amount of admittances to that same hospital by children in the same age bracket, in the same period, and with the same clinical diagnosis from other surrounding towns (2.707 cases).

As for the monthly distribution of the cases, a seasonal tendency was perceived with a higher incidence of hospitalizations in April (14,6%), May (13,5%), June (11,2%) and July (9,4%). On the other hand, the months of January and February showed the lowest sums – 4,8% and 4,3% respectively.

Table 1. Frequency of hospitalizations for pneumonia in children under the age of 5, residents in the municipality of Patos, Paraíba within the periods before (2005 – 2009) and after (2011 – 2015) the implementation of the 10-valent pneumococcal conjugate vaccine. Patos, PB – 2018.

Períod	n	%
2005	213	19,5
2006	139	12,7
2007	134	12,2
2008	120	11,0
2009	134	12,2
2011	62	5,7
2012	52	4,8
2013	86	7,9
2014	99	9,0
2015	55	5,0
2005-2009	740	67,6
2011-2015	354	32,4
Total	1094	100

Source: Prepared by the authors.

Table 2 shows predominance of hospitalizations of male patients, representing 56.7% of cases, of infants between 0 and 24 months (67.5%), and who remained in hospital between 2 to 4 days (65.8%). The most common clinical manifestation was cough found in 90,4% of

the cases. A few other clinical manifestations were mentioned, such as dehydration, lack of appetite, anorexia, chest pain, moaning, prostration, post-cough vomiting, cyanosis, among others.

Table 2. Frequency of variables: age group, sex, time in hospital, presented clinical manifestations in cases of hospitalization of children under 5 years of age for pneumonia. Patos, PB – 2018.

Variable	n	%
Sex		
Feminine	473	43,2
Masculine	620	56,7
Age group		
0-24 months	738	67,5
25-48 months	264	24,1
49-59 months	85	7,8
Time in hospital		
<2 days	214	19,6
2 a 4 days	720	65,8
>5 days	157	14,4
Clinical manifestations		
Coughing	989	90,4
Fever	961	87,8
Dyspnea	854	78,1
Pleural Effusion	14	1,3
Other manifestations	243	22,2

Source: Prepared by the authors.

Based on the analysis of the *age group* variable between the periods before and after the implementation of the vaccine, the first period (2005 – 2009) shows the mean age of the hospitalized children was 25 months and the median was 14 months. As for the second period (2011 – 2015), the scenario shifts and the children's mean age children is 37,56 months and the median was then 18 months. Therefore, there was no significant statistical difference between the means of the analyzed periods (p=0,360).

Regarding the time in hospital, the mean remained 3 days of hospitalization and the median 3 and 2 days respectively. Thus, there was a significant statistical difference between the of the analyzed periods (p<0,001).

Table 3. Analysis of the *age group in months*, *length of hospitalization in days* within the periods before (2005 – 2009) and after (2011 – 2015) the implementation of the 10-valent pneumococcal conjugate vaccine. Patos, PB – 2018.

Variable	Period	Mean	Median	SD**	Min	Max	p*
Age group	2005-2009	25,76	14,00	186,75	0	50,81	
	2011-2015	37,56	18,00	274,40	0	51,75	0,360
Time in	2005-2009	3,11	3,0	2,43	0	33	
Hospital	2011-2015	3,21	2,0	3,30	0	30	<0,001

Source: Prepared by the authors. * Student t test. ** Standard Deviation.

Table 4 depicts the crossing of the variable *period* with the other variables of the study. Regarding the *sex*, on both periods, male patients were more frequent. The value p=0,034 from this variable shows statistical significance between the groups. As for the *age group*, infants between 0 and 24 months were the most affected on both periods and we notice a considerable decrease in hospitalizations by this group after the implementation of the vaccine. The value p=0,002 from this variable shows statistical significance, which indicates an influence of the period upon the *sex* variable.

With reference to *Time in hospital*, both periods showed a higher incidence of hospitalizations in the period between 2 and 4 days with significant statistical difference where p=<0,001. About *clinical manifestations*, the study presented a decline in them on both periods analyzed with significant statistical difference in coughing and other manifestations. Pearson's Chi-square p value was entered only for variables that showed significance.

Table 4. Analysis of the periods before (2005 – 2009) and after (2011 – 2015) the implementation of the 10-valent pneumococcal conjugate vaccine regarding sex, age group, time in hospital, clinical manifestations. Patos, PB – Brazil.

Category	Period		p*
	2005-2009	2011-2015	
Sex			
Masculine	436	184	0,034
Feminine	304	169	
Age group			
0-24 months	518	220	
25-48 months	174	90	0,002
49-59 months	44	41	
Time in hospital			
<2 days	124	91	
2 a 4 days	516	205	
>5 days	99	58	<0,001
Clinical Manifestations			
Cough	668	321	
Fever	637	324	
Dyspnea	578	276	
Pleural Effusion	8	6	
Other manifestations	196	47	<0,001

Source: Prepared by the authors. *Pearson's chi-squared test.

4. Discussion

Pneumococcal disease is a relevant health condition in Brazil and studies have demonstrated that hospitalization rates can be considered for the monitoring of the impact of the immunization program, thus contributing for a continuously evaluated active surveillance of the profile and distribution of cases within our country (Silva, et al., 2016; Kupek & Vieira, 2016; Kupek & Vieira, 2018).

We emphasize that, in this study, it was not possible to specify the etiology that caused the registered illnesses. The focus was to characterize the cases, associating the vaccine coverage to the decrease of hospitalizations in children under five years of age. We are also

aware that the use of patients' medical records may incur limitations, which may lead to inaccuracies, from the data search stage up until the insertion of information in a system. However, the results represent evidence that point to the impact of the PVC10 vaccine on the reduction of hospitalizations for pneumonia in Brazil.

The results presented through a metanalysis kind of systematic revision highlight a diminuition caused by the use of PCV10 and PCV13 on the reduction of hospital admittances for pneumonia by children under five years of age, particularly on infants under 2, thus validating the implementation of those vaccines in the National Immunization Program (Alicino, et al., 2017). A study conducted in the Negev district, south of Israel, with children under the age of five, reveals a drop by 47% in hospitalizations after the introduction of the PCV13 (Greenberg, et al., 2015).

At another research, which aimed at verifying the effect of the PVC10 on children in Brazil, it was identified that through the routine immunization program there was a considerable reduction (17,4% –26,5%; p <0,01) in the pneumonia-caused hospitalization rates among children in 3 out of the 5 investigated cities (Belo Horizonte, Curitiba e Recife). In the other two metropolises (São Paulo e Porto Alegre), there was no significant decline in the amount of cases, possibly because the vaccine coverage in those cities in 2011 was lower (80%) than in the other three (< 90%) (Andrade, et al., 2017).

Apropos the months of hospitalization peak, it has been noted that April, May and June were the ones with higher incidence and, by the way, compose the Brazilian autumn. Similar results were found on a study that analyzed the hospitalization of children and adolescents for respiratory sicknesses in the city of Anápolis, GO, from which the greater median was during the fall (Silva, et al., 2016). An international study carried out with the objective of evaluating the pneumococcus's seasonal tendency suggested that those bacteria are less infectious when the weather conditions are hot and rainy, and their transmissibility is enhanced in colder and drier months (Numminen, et al., 2015).

In the municipality of Patos, a greater predominance of male patients was identified, with a similar predominance observed in another study. However, the gender of the child as being a predisposing factor for triggering pneumonia is not fully clarified and there is no consensus in the literature (Berezin, 2012).

A study conducted in Santa Catarina (Brasil) which aimed at evaluating the impact of PCV10 on reducing hospitalization rates due to pneumonia in children under 5 years of age, identified a decrease by 23.3% in children under 1 year and of 8.4% in children from 1 to 4 years (Vieira & Kupek, 2018). The results indicated by these decreases corroborate the

findings of this study, thus, one can affirm the effectiveness of PCV10 at the Brazilian level, when the results are compared with other studies in the country.

In addition, other academics demonstrated that after the introduction of the PCV10 in 2010 there was a reduction by 25,5% in hospital admittances for pneumonia among children under 12 months of age, 22% among nurslings under 3 months, and by 23% in infants between 3 and 11 months old (Warren, et al., 2017).

The classic clinical manifestations caused by pneumococcal infection include nasal obstruction, irritability, fever above 39 ° C, respiratory distress, nose wing beat, intercostal and subcostal retraction, tachycardia along with tachypnea (Poltronieri, 2017). There is a major drawback regarding both the diagnosis of pneumonia and the standard treatment, which is mostly empirical. The antimicrobial scheme should be chosen according to the gravity of the case; for instance, for the more severe cases, the treatment should be initiated by crystalline penicillin or ampicillin, and for most severe cases, it is necessary to use oxacillin combined with chloramphenicol or ceftriaxone (Machado, Oliveira & Vianna, 2017).

The vaccination coverage is defined by the NIP as the percentage of the target population covered by the complete vaccination schedule. Within the analyzed period, the NIP recommendation for children under 2 years of age corresponded to scheme 2, 4, 6 and 15 months, which means, 3 doses plus a reinforcement (Brasil, 2013).

Regarding coverage of the PCV10 vaccine that was implemented in Brazil in 2010, the data revealed that in 2011 (89.45%) and in 2012 (84.64%) the municipality of Patos did not reach the minimum coverage of 95% recommended by the Ministry of Health; But the percentage managed to be raised in the following year - 2013 (99.47%). The years 2014 (107.65%) and 2015 (104.90%) had a vaccine coverage that reached over 100%, justified by the vaccination of children from other towns (Programa Nacional de Imunização, 2018).

It is possible to infer that the vaccination coverage of the PCV10 has been effective in Patos. The presented data actively reflect the reduction of the morbidity caused by pneumonia in this population and demonstrate that, despite the progresses achieved through the pacts and policies created with the objective of providing a better quality of life in childhood, efforts are still necessary to prevent the disease more successfully.

Variations in the vaccine coverage, which sometimes come close to the sanctioned goals, but are constantly insufficient to guarantee the control or eradication of the disease, predisposes the occurrence of localized outbreaks with different potential for dissemination. Such fact points to the need for defining further strategies that (through the surveillance) are capable of directing the correct intervention to the problem areas. These strategies should

understand the variations that occur in those locations and the possible reasons that hindered the achievement of a homogenous coverage (≥ 95%). They should also be able to contribute effectively to the control, elimination or eradication of immune preventable diseases under surveillance (Teixeira & Rocha, 2010).

5. Conclusion

Thus, after five years of vaccination in Patos, PB with PCV10, a significant decline in hospitalizations for pneumonia among children targeted by the NIP was registered. It should be stressed that the results of this study should be interpreted considering some limitations. Descriptive studies that work with medical records generates limitations regarding clarification of the existing data and may, therefore, compromise the quality of the acquired information, the analysis and the hypotheses raised. On the other hand, the volume of attained data was quite representative considering the place of study.

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