Epidemiologia da meningite em crianças de um estado do nordeste Brasileiro

Epidemiology of meningitis in children in a Brazilian northeastern state

Epidemiología de la meningitis en niños de un estado del noreste de Brasil

Mona Lisa Lopes dos Santos Caldas

ORCID: https://orcid.org/0000-0002-3701-2836

Centro Universitário de Patos, Brazil

E-mail: monalisalopes13@gmail.com

Eitan Naaman Berezin

ORCID: https://orcid.org/0000-0003-4575-0430

Faculdade de Ciências Médicas da Santa Casa de São Paulo, Brazil

E-mail: eberezin2003@yahoo.com

Resumo

Descrever o perfil epidemiológico da meningite em crianças menores de cinco anos residentes no estado da Paraíba entre 2007 a 2017. Estudo epidemiológico descritivo, de série temporal, cuja população foi composta por todos os casos confirmados fornecidos pela Gerência Executiva de Vigilância em Saúde do Estado da Paraíba. A amostra obtida foi analisada por meio de recursos estatísticos utilizando o software SPSS versão 18.0. A faixa etária apontou uma concentração acentuada em crianças menores de 1 ano, correspondendo a um coeficiente de incidência de 24,1/10.000 habitantes O critério de confirmação apontou 44,3% através do exame quimiocitológico, 77,6% evoluíram para alta e 9,8% para óbito. No tocante a distribuição temporal dos casos, o ano de 2012 surge com o maior número de casos confirmados 20,06% e 2015 apresentando a menor incidência dentre o período estudado 3,61%. O enfrentamento das meningites ainda se caracteriza como um importante agravo no Estado avaliado, apesar da tendência declinante dos casos confirmados, a incidência ainda pode ser considerada alta em virtude da proteção vacinal que é disponibilizada.

Palavras-chave: *Neisseria meningitidis*; Doença meningocócica; Crianças.

Abstract

To describe the epidemiological profile of meningitis in children under the age of five resident in the State of Paraiba between 2007 and 2017. A time series analysis in a descriptive

epidemiological study, whose population comprised all the cases confirmed by the Executive Management of Health Surveillance of Paraiba. The obtained sample was analyzed through statistical resources using the SPSS software version 18.0. The age group indicated an increased concentration in children under the age of 1year old, corresponding to a coefficient of incidence of 24.1/10.000 habitants. The criteria of confirmation indicated 44.3% by means of the chemical and cytological examination, 77.6% progressed to hospital discharge and 9.8% to death. Regarding the temporal distribution of the cases, the year 2012 appears with the highest number of confirmed cases 20.06% and 2015 presented the lowest incidence 3.61%, within the period studied. The combat of Meningitis is still characterized as a relevant issue in the State, despite the declining tendency of confirmed cases, the incidence may still be considered as being high due to the vaccine protection that is available.

Keywords: *Neisseria meningitides*; Meningococcal disease; Children.

Resumen

Describir el perfil epidemiológico de la meningitis en menores de cinco años residentes en el estado de Paraíba entre 2007 y 2017. Estudio epidemiológico descriptivo, de serie temporal, cuya población estuvo compuesta por todos los casos confirmados proporcionados por la Dirección Ejecutiva de Vigilancia de la Salud del Estado de Paraíba. La muestra obtenida se analizó mediante recursos estadísticos utilizando el software SPSS versión 18.0. El grupo de edad señaló una marcada concentración en menores de 1 año, correspondiente a un coeficiente de incidencia de 24,1 / 10.000 habitantes. El criterio de confirmación apuntó a 44,3% a través del examen quimiocitológico, 77,6% evolucionó al alta y 9, 8% por muerte. En cuanto a la distribución temporal de los casos, el año 2012 aparece con el mayor número de casos confirmados, 20.06% y 2015 presenta la menor incidencia entre el período estudiado 3.61%. Hacer frente a la meningitis sigue siendo un problema importante en el estado evaluado, a pesar de la tendencia a la baja en los casos confirmados, la incidencia aún puede considerarse alta debido a la protección de la vacuna disponible.

Palabras clave: Neisseria meningitidis; Enfermedad meningocócica; Niños.

1. Introduction

The *Neisseria meningitidis* also called meningococcus, belong to the family *Neisseriaceae*, and qualifies as aerobic Gram-positive diplococci, presenting 12 serogroups which among them 6 present capsular specificity (A, B, C, Y, X and W-135) and constitutes

the etiological agent of greatest frequency among the bacterial meningitis (Sáfadi, Bezerin & Oselka, 2012).

The meningococcal vaccine serogoup C were first introduced in the immunization schedule of the United Kingdom, where in one year, around 15.000.000 children and adolescents under the age of 17 were vaccinated, reducing by 81% the incidence of due to meningococcus serogroup C and reducing the number of carriers of the agent. The success of the mass vaccine response was simultaneously associated to the high-level vaccine effectiveness (direct protection) as well as to the herd effect (indirect protection) (Sáfadi, Bezerin & Oselka, 2012). In Brazil the conjugate vaccine for meningococcal C was introduced in the year 2010 and the target population were infants under 24 months. More recently was included an additional dose after 9 years of age.

Bacterial meningitis is a disease of mandatory reporting in Brazil, since 1975. In recent years the incidence rate of meningitis in Brazil, is around 1.8 cases for each 100.000 individuals. According to data obtained from the SINAN (National Disease Notification System), the annual average occurrence of 2001 and 2010 in children under five years of age and one year of age was of 1.09 and 8.62 cases/100 thousand inhabitants and the average lethality was of 33.6% and 31.3%, respectively in all of Brazil (Grando et al., 2015).

However, there is a high proportion of notified meningitis without diagnosis of the causative agent, which could mean that the true incidence of the disease is higher than the reported. The incidence of the disease may be closely related to the host's immunity and its indices may be related to the vaccination coverage rate (Berezin, 2015).

The study is justified by the high impact in relation to the morbidity and mortality associated with meningitis, and the scarce number of studies conducted in the Northeast region of Brazil. So a more effective and organized Epidemiological Surveillance service is fundamental, in order to adequately monitor the incidence of the disease in a way that a reduction in the frequency of cases occurs, thus presenting a positive feedback in the face of the interventions recommended by the Health Ministry.

Therefore, the objective of this study was to outline the epidemiological profile of the meningococcal meningitis in children in the period from 2007 to 2017 in the State of Paraiba.

2. Methods

A descriptive epidemiological study, ecological time series analysis, with a quantitative approach, determined between the years of 2007 to 2017.

The place of choice was the State of Paraiba, which is located in the Northeast region, with an estimated population of four million inhabitants, corresponding to the 13th most populous State of Brazil. Its capital city João Pessoa is the most populous municipality, still existing other municipalities with a population higher than a hundred thousand inhabitants such as Campina Grande, Santa Rita and Patos. Currently it is divided into four mesoregions, 23 microregions and 223 municipalities (Instituto Brasileiro de Geografia, 2010).

The evaluated population information was composed by the database supplied by the Executive Management of Health Surveillance of the State of Paraiba. And the sample constituted by all the confirmed cases of Meningitis in children from 0 to 14 years of age in the state of Paraiba between 2007 and 2017 in the National Disease Notification System-Sinan.

For the data collection, was requested to the Executive Management of Health Surveillance of the State of Paraiba, by means of an authorization instrument, the liberation of the information contained in the meningitis notification forms recorded in the SINAN. After the liberation by the Ethics and Research Committee, the information was provided and the analysis of the data began. Subsequently, the relevant data was inserted and analyzed by means of statistical resources, using the software *Statistical Package for the Social Science* (SPSS) version 18.0. The data analysis was conducted using the techniques of descriptive statistics. With the purpose of comparing the existence of the correlation of the data, using Pearson's chi-square test, which considered as being significant the p value $\leq$ 0.05. These were revealed in tables and were discussed in the light of relevant literature at national and international level.

The research project was registered and approved by the Brazil platform, and legal consent was obtained for the accomplishment of the research, in the light of the ethical principles, under the approval number 3.008.029 and CAAE 02491718.0.0000.5181.

3. Results

Table 1 shows predominance of confirmed meningitis cases between 2011 and 2012 (17,4 and 16,2% respectively), which can be justified by the low vaccination coverage in the years after the implementation of the vaccine. After 2013, there is a significant decrease in the number of cases that could be related to the intensification of the vaccination campaigns and to the progress in the coverage of both the PCV10 and meningococcal vaccines (93,34% and 96,81% respectively).

After comparing the percentage of cases that occurred before (2007 – 2009) and after (2011 – 2017) the implementation of the meningitis vaccine in the country, we notice a decrease in this last period, especially among the age group under 4 years of age. Therefore, routine vaccination must occur according to the NIP regulations aiming at supporting all promotion and prevention programs to this population group.

Table 1. Frequency of the confirmed cases of Meningitis in children by age group by year in the State of Paraiba: (2007 – 2017).

Age group	2007	2008	2009	2010	2011	2012	2013	2014	2015	2016	2017	Total
> 1 year	19	14	15	12	19	22	10	10	5	14	2	142
%	13,4	9,9	10,6	8,5	13,4	15,5	7,0	7,0	3,5	9,9	1,4	100
1 – 4 years	16	26	31	6	29	26	10	6	4	12	11	177
%	9,0	14,7	17,5	3,4	16,4	14,7	5,6	3,4	2,3	6,8	6,2	100
5 – 9 years	19	27	25	4	48	33	10	11	7	12	12	208
%	9,1	13,0	12,0	1,9	23,1	15,9	4,8	5,3	3,4	5,8	5,8	100
10 –14 years	11	23	15	8	19	25	10	6	9	2	3	131
%	8,4	17,6	11,5	6,1	14,5	19,1	7,6	4,6	6,9	1,5	2,3	100
Total	65	90	85	30	115	106	40	33	25	40	28	658
%	10	13,6	13,3	4,5	17,4	16,2	6,0	5,0	3,8	6,0	4,2	100

Source: Health Ministry/SVS - National Disease Notification System - Sinan Net (2018).

Table 2 presents a predominance of cases of male patients with a percentage of 62.2% over female patients. Regarding the *etiology*, meningococcal disease was present in 23,7 % of the patients; and in most of the cases (59%), the etiology was not specified. Such high rate indicates the need to carry out examinations to identify the etiological agents in order to employ the most appropriate pharmacotherapy. Another important factor which contributes to the detection of high levels of this type of meningitis regards the inexistence of a checkbox in the SINAN's form which informs whether the meningitis is bacterian or if it is of a non-specified etiology.

As for the *confirmation criteria*, it was found that 44.3% of the cases were confirmed by the Cerebrospinal Fluid (CSF) cell count and protein and glucose CSF level and 27.3% by clinical criteria. It should be reminded the existence of a financial limitation which involves the diagnostic criteria, since they are exams incur costs to the SUS, which leads to either late or mere clinical diagnosis as revealed in the data collect by this study.

Among the *evolution* criteria we emphasize the high death rate caused by the meningococcal disease reaching 9,8% of the cases. Considering the death predictors by that disease identified in this study, it is possible that such fact is partially related to the gravity of the condition, its fast evolution, as well as to the immune response of that age group (1 – 4 years). In addition, it is important to understand that those results may contain possible analysis bias regarding the information system, including the possibility of incomplete data and undernotifications, thus stressing the need for a thorough filling of the notification forms by the health professionals.

Table 2. Percentage distribution of the confirmed cases of Meningitis in children by gender, etiology, confirmation criteria and evolution in the State of Paraiba: 2007 – 2017.

VARIABLES		N	%
GENDER	Masculine	431	62.2
	Feminine	262	37.8
ETIOLOGY	Meningococcal Disease	93	23.7
	Tuberculous Meningitis	3	0.7
	Unspecified Meningitis	231	59.0
	Aseptic Meningitis	60	15.3
	Meningitis by Haemophilus	6	1.5
	Meningitis by Pneumococcus	26	6.6
CONFIRMATION CRITERIA	Absent	89	12.9
	Culture	62	8.9
	Clinical	189	27.3
	Bacterioscopy	25	3.6
	Chemocytological	307	44.3
	Clinical epidemiological	8	1.2
	Other technique	12	1.7
EVOLUTION	Absent in the medical record	78	11.3
	Hospital discharge	538	77.6
	Death by Meningitis	68	9.8
	Death by other causes	9	1.3

Source: Health Ministry/SVS - National Disease Notification System - Sinan Net (2018).

Table 3 shows the distribution of the total number of cases of meningitis per year compared to Meningococcal disease. It is highlighted that in the confirmed cases of meningitis in children, variations occurred over the years of the evaluation period. In 2010 a significant decrease to 30 of the cases occurred, however, between 2011 and 2012 there was an expressive increase, indicating 2012 as the year with the highest number of confirmed cases corresponding to 139 of the cases.

After analyzing the total percentage of confirmed meningitis cases within the period before (2007 – 2009) and after (2011 – 2017) the implementation of the vaccine, we see a positive impact, as the cases noticeably declined - where 2015 was the year with the lowest amount of cases with 25 occurrences. Such fact attests the importance immunization during

childhood in addition to adequate monitoring with the primary purpose of reducing the number of cases.

Related to the cases by Meningococcal disease in the temporal distribution, were observed oscillations over the years, obtaining its greatest frequency in 2011 with 18 cases, and similar to the total number of cases by meningitis, there was a significant decrease in subsequent years, registering in the year of 2017 its lowest frequency, corresponding to 01 of the case.

Furthermore, it is worth mentioning that the inclusion of the meningococcal and the PCV10 vaccines in the National Immunization Program (NIP) had a great impact in the State, observed by the significant drop in the number of cases in the investigated age group. Therefore, adoption of precautionary strategies, such as vaccination, has been shown to be highly effective. Even when restricted to a few age groups, it becomes an important tool in reducing the cases of the disease.

Finally, it is possible to observe that even in cases in which the etiology is not well defined, the immunization prompted a decrease in the number of cases, reinforcing the need for epidemiological studies to support different public health strategies in the studied population.

Table 3. Temporal distribution of the total number of confirmed cases of Meningitis in children from 0 to 14 years of age and of the Meningococcal disease in Paraiba, 2007-2017.

CONFIRMED CASES OF MENINGITIS			MENINGOCOCCAL DISEASE	
Year	N	%	n	%
2007	67	9.67	14	14.74
2008	90	12.99	14	14.74
2009	86	12.41	18	18.95
2010	30	4.33	07	7.37
2011	115	16.59	18	18.95
2012	139	20.06	07	7.37
2013	40	5.77	04	4.21
2014	33	4.76	04	4.21
2015	25	3.61	02	2.11
2016	40	5.77	06	6.32
2017	28	4.04	01	1.05
TOTAL	693	100	95	100

Source: Health Ministry/SVS - National Disease Notification System- Sinan Net (2018).

4. Discussion

Our results indicate an important decline in the incidence of the meningitis over the years in the state of Paraiba, demonstrating similarity to other studies carried out in other states of Brazil that show this declining tendency.

With relation to the age group, there was a higher concentration of cases among under 1 year-olds with an incidence coefficient of 24.1/10.000 in habitants, followed by the age group of 1-4 years with an incidence of 7.52/10.000 in habitants. This data corroborates with several studies in different states of Brazil in which the age group from 0 to 4 years still is the most affected by this disease (Leme & Zanetta, 2012; Andrade et al., 2014; Ferreira, Gomes & Oliveira, 2015).

The results from Table 1 indicate a decline in the number of confirmed meningitis cases after the implementation of the 10-valent Pneumococcal conjugate (PCV10) and Monovalent C meningococcal vaccines in 2010, with greater impact in the age group of children between the ages of 1 and 4. Thus, it is possible to infer that the vaccination coverage

has been effective in the state of Paraiba as the hereby presented data reveals a reduction in children's morbidities caused by meningitis.

A similar study carried out in the region of Sorocaba – SP pointed to predominance of the age group to 0-4 years in a period of 10 years with an incidence coefficient of 50.2/100.000 inhabitants. Such data reinforces the importance of immunization in children of this age group (Leme & Zanetta, 2012). Meningitis basically affects all the age groups, particularly the pediatric age range, and as it is a disease with a high morbidity-mortality, not always with specific signs and symptoms, the understanding of the epidemiological profile of the cases attended to in each service is required (Andrade et al., 2014).

The male gender was the most affected with 62.2%. This pattern was observed by several authors (Leme & Zanetta, 2012; Andrade et al., 2014; Souza, Costa & Paim, 2012). Coinciding with the data found in literature, a study which analyzed the etiological profile of meningitis in children in the state of Pernambuco, identified a concentration of 57.26% in the male gender (Ferreira, Gomes & Oliveira, 2015). Therefore, despite the literature showing that there is a variation of age, of the occurrence peak in the dependence of the agent involved and the local epidemiological conditions, the male gender presents itself as predominant (Mantese et al., 2002). This reinforces the similarity between these researches which were carried out in the region.

Unspecified meningitis was responsible for the highest number of cases 59.0%, indicating that this may happen due to the lack of confirmation of the type of infection which is not accomplished effectively in the health service, however it can be noted that the disease of viral etiology is prevalent, as the viruses can spread more easily by respiratory route and contact, and have a higher contagion factor than the bacteria.

To the contrary, the study which evaluated the epidemiological situation of meningitis in the North of Brazil, demonstrated that in the etiology criteria, that the unspecified bacterial meningitis point to a predominance corresponding to 46.37% of confirmed cases (Dias, Rodrigues & Cardoso, 2017).

Researches inform that the bacterial meningitis are characterized as the ones of highest incidence regarding the morbidity-mortality, however, they tend to present a lower incidence when compared to viral meningitis which are responsible for 90% of the cases. It is still shown in literature that the 3 most frequent bacterial meningitis are caused by *Neisseria meningitidis, Streptococcus pneumoniae* and *Haemophilus influenzae,* representing almost 90% of the cases (Dias, Rodrigues & Cardoso, 2017; Heckenberg, Brouwer & Van, 2014).

The most frequent confirmation criteria was the chemocytological 44.3% corroborating with another study in the same region (Ferreira, Gomes & Oliveira, 2015) and 27.3% by clinical criteria. A research conducted about the incidence of meningitis in Rio de Janeiro identified that in the majority of cases the lumbar puncture and the cytochemistry were predominant (Vasconcelos; Thuler; Girianelli, 2011).

The chemocytological method is one of the main tests preconized by the Health Ministry, for the diagnosis of a suspect case of meningitis, however the culture test is still considered gold standard, for the epidemiological surveillance sector, as it enables the characterization of the infectious agent (Ministério da Saúde, 2005).

The majority of cases evolved to hospital discharge corresponding to 77.6%; However, the number of deaths with a percentage of 9.8% by meningitis is considered as being high. The importance of the evaluation of the deaths is highlighted, seen as it is an immune predictable disease in its great majority, which reflects on assistential issues and in the profile of the service network of the local health.

In another research the notified cases in the Brazilian regions were evaluated, which concerning the evolution of the cases, 80% evolved to hospital discharge, corroborating with the findings in this research. Regarding the deaths, the authors identified that the North region evolved with more deaths by meningitis, 13.6%, whilst the South region obtained the lowest number pointing to 8.2%, being three percentage points below the overall average (11.4%) (Silva & Mezarobba, 2018).

When evaluation the temporal distribution of the cases, many fluctuations were observed throughout 2007 to 2017. An outbreak was noticed in 2011 – 2012 with 16.59% and 20.06% respectively registering the greatest incidence among the years studied. Compared to the cases of meningococcal disease in the same temporal distribution in the year of 2009 and 2011 corresponded to the highest incidence of the disease, a disturbing fact seen as a defined immunization for the etiological agent *Neisseria meningitidis* already exists.

In 2012, in the municipality of Balsas in the state of Maranhão, was registered an outbreak of meningitis with an increase of approximately 60%, compared to the previous year.[15] Aiming to identify the most common diseases of compulsory notification, between the period of 2008 to 2012, in a university training hospital of the state of Paraiba, was observed in the results that meningitis was the fourth-largest cause of morbidity, and was responsible for 6.58% of the notifications in the evaluated sector (Andrade et al., 2014).

The National Health Service (SUS) invests substantially in the expansion of the networks of basic healthcare by the Family Health Strategies (ESF), these, promote health and

prevention of diseases, in addition to promoting equity in the access to the to the healthcare services which promotes the universality of the healthcare, respecting the principles of the SUS. There still are some fragilities related to the ESF, however, it can be stated that these services are allies in the reduction of infant mortality, and in the control of infectious and immune predictable diseases, contributing to the child by means of the child healthcare, in which is included the monitoring of the immunization schedules (Facchini et al., 2006).

It should be highlighted that in order to strengthen the surveillance and control procedures in Latin America, must be emphasized the need for improvement of the indicators, the laboratorial capacity in relation to the diagnostic tests; the communication about the epidemiological and laboratorial analysis and the long-term monitoring of the consequences of the disease, as well as the improvement of the surveillance procedures for the delineation of prevention and control strategies (Sáfadi et al., 2017).

The great importance from the epidemiological point of view is estimated, if the immunization programs were more comprehensive, granting immunity to the various subtypes of the disease and a greater agility and efficiency in the diagnostic criteria contributing to a decline of this disease in its totality.

5. Final Considerations

Based on the results, it was possible to trace the epidemiological profile of the meningitis in the studied population, in addition to verify the temporal distribution of this disease. It was identified that children under five years of age obtained a higher incidence coefficient corresponding to the largest risk group for this disease; the male gender was the most affected and the unspecified meningitis the one that appeared most among the etiologies, this factor suggesting a certain difficulty in relation to the diagnosis of the disease. As a confirmation criteria the chemocytological predominated and in spite of the fact that the majority of cases evolve to hospital discharge, the mortality percentage in the State of choice is still concerning. Therefore, we highlight here that, epidemiological information of this type are relevant to initiate public health measures and to ensure an adequate care to the population.

We stress that children's immunization represents an important progress in terms of public health accomplishments. Therefore, it is possible to infer that the inclusion of the 10-valent Pneumococcal conjugate (PCV10) and Monovalent C meningococcal vaccines in the

schedule of the NIP has shown to be effective in the currently investigated context, as the meningitis cases declined.

As limitations of this study are highlighted the presence of faults in the register and cases of meningitis in addition to the incompleteness of the notification forms in a correct way, and, consequently compromise the quality of the acquired information, as well as the analysis and future hypothesis which can be suggested. It is suggested, however, implementation of constant strategies and monitoring, so as to ensure better results.

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Percentage of contribution of each author in the manuscript

Mona Lisa Lopes dos Santos Caldas – 50%

Eitan Naaman Berezin – 50%