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Epidemiological burden of meningococcal disease in Latin America: A systematic literature review

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ABSTRACT

Objective: To evaluate the epidemiological profile of invasive meningococcal disease (IMD), meningococcal meningitis, and *Neisseria meningitidis* carriers in Latin America.
Methods: A systematic review was conducted to identify and analyze studies published in 2008–2018. Incidence rates, case fatality rates (CFRs), and the relative distribution of cases per serogroup by country were assessed.
Results: Meningococcal surveillance in Latin America differs among countries, and most systems are based on passive sentinel surveillance. Thirty-nine studies were selected. In 2006, the incidence rate of IMD per 100 000 inhabitants was highest in Brazil (1.9), followed by Uruguay (1.3), Chile (0.8), Argentina (0.7), Colombia and Venezuela (0.3 each), and Mexico (0.06). Brazil reported the highest CFR (20%), followed by Uruguay (15%), Chile (11%), and Venezuela and Argentina (10% each). In 2012, the CFR in Chile increased to approximately 27%. The most frequent serogroups among IMD cases were C in Brazil (2007–2010) and Mexico (2005–2016), W in Chile (2012–2018), and B in Argentina (2012–2015). However, the true burden of IMD in Latin America is probably underestimated due to underreporting of cases.
Conclusions: Improvements in IMD notification, IMD registration, national surveillance programs (including active surveillance systems), diagnostic tools, and characterization of isolates may better elucidate the true epidemiological burden of IMD in Latin America.
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Introduction

Neisseria meningitidis is a common cause of invasive bacterial disease worldwide (Brehony and Jolley, 2007; Sáfadi et al., 2017). The disease can occur sporadically, with seasonal variations and outbreaks (Sáfadi et al., 2014a) and often occurs suddenly, rapidly progressing to death (Stephens, 2007). *N. meningitidis* is also frequently found in asymptomatic carriers (Schubert-Unkmeir, 2017). Invasive meningococcal disease (IMD) is caused by *N. meningitidis* invasion into the human bloodstream, which can result in meningococcemia and septic shock, purpura fulminans, meningococcal meningitis (MM), pneumonia, arthritis, and pericarditis (Gabutti et al., 2015; Pelton, 2016). Meningococcal infections can be lethal in at least 10% of cases, while up to 36% of survivors can develop permanent sequelae; they represent a significant cause of morbidity and mortality in infants and young children and are a serious public health problem (Gabutti et al., 2015; Pelton, 2016; Viner et al., 2012).

N. meningitidis can be classified into serogroups based on the antigenic differences in its capsular polysaccharides. Six of 12 distinct meningococcal serogroups (A, B, C, Y, X, W) are significant for humans from a pathogenic point of view (López and Debbag, 2012). Serogroups A, B, C, Y, and W are prevalent in regions of Latin America (Sáfadi et al., 2013), while X is more prevalent in other localities (Harrison et al., 2009). Serogroups B (29% in 2012) and C (44% in 2012) have been responsible for the majority of reported cases (Sáfadi et al., 2014a), with a virtual disappearance of serogroup A over the last decade and an increased frequency of serogroup W cases reported in

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Argentina, Chile, Uruguay, and Brazil (Sáfadi and McIntosh, 2011; Sáfadi et al., 2014a, 2015a). Brazil has experienced an increase in the frequency of serogroup C since 2002 followed by a decrease in this serogroup due to the implementation of routine vaccination for infants. There is also evidence of the emergence of serogroup W in the Southeast and South regions of Brazil (Sáfadi and McIntosh, 2011). The frequency of serogroup Y increased in Latin America from 2000 to 2006, ranging from 3.6% to 50% in Colombia, and was also the most detected serogroup in Costa Rica in 2001–2002. In 2006, serogroup Y was observed in values comparable to those of serogroups C and W in Argentina. However, its frequency did not increase in Brazil or Chile during this period (Abad et al., 2009).

A broad variation in the overall epidemiology of IMD in Latin America has been recorded across regions and time periods (Sáfadi et al., 2014a). IMD is a mandatory notifiable disease in all Latin American countries. However, restrictive case definitions may contribute to low reporting rates in some places. Countries with more advanced surveillance systems and laboratory services may present the highest rates of IMD (Sáfadi et al., 2015b).

There was a secular trend towards a reduction in the overall incidence of IMD in Chile starting in 2000 (Instituto de Salud Pública de Chile, 2015), with case fatality rates (CFR) remaining stable (Moreno et al., 2013). However, from 2011 to 2012, the incidence doubled, and there was a marked increase in the CFR (Instituto de Salud Pública de Chile, 2017a, 2017b, 2018), mainly due to the hypervirulent lineage W ST-11 reported in the country (Araya et al., 2015). Currently, this serogroup is the predominant one in Chile (Pelton, 2016), where a mass vaccination program was implemented in 2012 to control hypervirulent serogroup W (Sáfadi et al., 2017). This was followed by the introduction of the quadrivalent MenACWY conjugate vaccine in the national immunization program in 2014 (Borrow et al., 2017). After implementation of these vaccine programs, the incidence of IMD and related CFR decreased. According to Chilean national epidemiological databases, the incidence of IMD has continued to decrease in recent years (0.58 and 0.44 cases per 100 000 inhabitants in 2016 and 2017, respectively) (Instituto de Salud Pública de Chile, 2017a, 2017b, 2018).

In Colombia, the incidence of IMD increased from 0.13 to 0.21 cases per 100 000 inhabitants from 2013 to 2016 (Instituto Nacional de Salud, 2017). Additionally, the number of confirmed IMD cases also increased in Mexico from seven cases in 2015 to 37 cases in 2017, with seven confirmed cases reported in the first 8 weeks of 2018 (Secretaría de Salud de México, 2016a, 2016b, 2017, 2018).

Epidemiological studies are important to improve our understanding of *N. meningitidis* dynamics, contributing to the detection of strains that may change in different populations and over time. This study aimed to evaluate the epidemiological profile of IMD, MM, and *N. meningitidis* carriers in Latin America through a systematic literature review of incidence rates, CFRs, and the relative distribution of cases per serogroup.

Methods

A systematic literature review was conducted in January 2018 using the following databases: MEDLINE (via PubMed), Latin American and Caribbean Literature on Health Sciences, Centre for Reviews and Dissemination, and the Cochrane Library. Electronic searches were complemented by manual searches of the bibliographic references of selected publications. Searches were conducted using the following terms: "meningitis, meningococcal", "meningococcal infections", and "Latin America", through MeSH-controlled vocabulary for the PubMed database and adapted for other databases, according to the requirements of each one. In order to enhance the sensitivity, the names of all Latin American countries were included in the search.

Publications considered for inclusion were systematic reviews of cohort studies, as well as prospective or retrospective observational studies that provided epidemiological information (CFR, incidence, and/or serogroup) regarding IMD, MM, or *N. meningitidis* carriers in Latin America. Studies with any population group, including all ages, were considered. Studies in Portuguese, English, or Spanish were considered. Abstracts, case reports, case series, letters to the editor, studies with only immunological outcomes, and those reporting results associated with other types of meningitis were excluded. A time limit was set to evaluate only studies published from 2008 to 2018.

Two reviewers from the SENSE Company Brazil conducted the search in the databases, using the predefined strategy, and selected the studies. In cases without a consensus, a third reviewer was consulted about possible eligibility and was responsible for the final decision.

Results

Bibliographic research and characteristics of the included studies

The initial literature review resulted in 344 bibliographic references. After reviewing the titles and abstracts, 59 articles were selected for detailed analysis. Of these, 39 studies fulfilled the inclusion criteria and were considered for the review (Figure 1, Table 1), of which 25 were performed in Brazil, four in Chile, four in Mexico, two in Argentina, two in all of Latin America, and one each in Panama and Colombia. Studies evaluating other Latin American countries (Bolivia, Costa Rica, Cuba, Ecuador, El Salvador, Guatemala, Haiti, Honduras, Nicaragua, Paraguay, Peru, and Dominican Republic) were not found or were not considered eligible.

Twenty-nine studies included patients with IMD, two included patients with MM, and eight included *N. meningitidis* carriers. The follow-up period of the studies ranged from less than 1 year to 36 years. Among the 19 studies that reported sex distribution data, the majority of the populations were male, with the exception of three studies with a female predominance (Nieto-Guevara et al., 2011; Nunes et al., 2016; Weckx et al., 2017), one study with the same proportion of each sex (Chacon-Cruz et al., 2011), and one study with only male patients (Liphaus et al., 2013). Only nine studies reported median age data, and this ranged from 12.5 months to 21.5 years.

Epidemiological data

Incidence

Only 20 studies reported incidence data. Incidence rates varied throughout the Latin America countries (Table 2). The highest IMD incidence rate per 100 000 inhabitants among the Latin American countries was reported for Brazil in 2006 (1.9), in a systematic

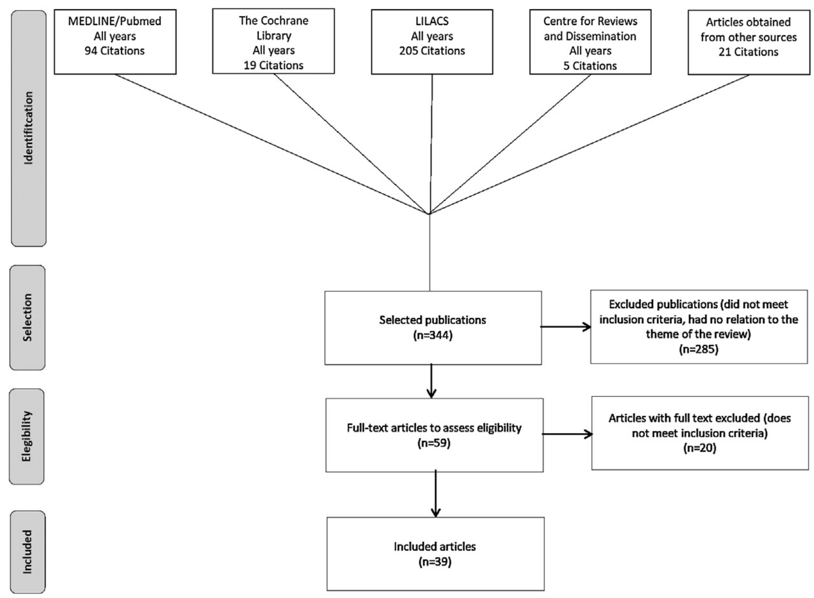

Figure 1. Flowchart of study selection.

review conducted by Sáfadi and Cintra (2010); this was followed by Uruguay (1.3), Chile (0.8), Argentina (0.7), and Colombia and Venezuela (0.3 each). Mexico reported the lowest incidence rate (0.06 cases per 100 000 inhabitants).

In Brazil, Azevedo et al. (2013) reported a decrease in the incidence rate of IMD from 2000 to 2010, as shown in Table 2. In Southern Brazil, from 1995 to 2003 and from 2003 to 2005, the incidence rates of IMD (cases per 100 000 inhabitants) were 2.5 and 1.54, respectively (Baethgen et al., 2008; Weidlich et al., 2008). In the Northeast region, the highest incidence occurred in 1998 (1.8 IMD cases per 100 000 inhabitants) and the lowest in 2007 (0.9 cases per 100 000 inhabitants) (Nunes et al., 2011). The only study reporting data from the Central-West region revealed that in 2005–2009, 2010, and 2011, the annual incidence rates of IMD were 2.0, 1.8, and 0.8 per 100 000 inhabitants, respectively (Tauil et al., 2014). In the Southeast region, annual incidence rates varied from 5.3 per 100 000 inhabitants for 1986–2004 (Masuda et al., 2015) to 0.88 cases for 2000–2009 (Nascimento et al., 2012). In the North region, the incidence rate ranged from 3.9 cases per 100 000 inhabitants in 2003 to 0.7 in 2011 (Saraiva et al., 2015). Considering outbreak data, Iser et al. (2012) reported an incidence of 46 cases per 100 000 inhabitants in 2008 in children aged <1 year, while Liphaus et al. (2013) reported an incidence of 34 cases per 100 000 inhabitants in adults in 2010. Among studies that classified the incidence rate by age, Andrade et al. (2017) reported a higher incidence rate among children aged <1 year (5.01 per 100 000 inhabitants) between 2008 and 2014.

Considering Chile, two studies reported incidence rates. For the period 2006–2012, incidence rates for IMD fluctuated over time, ranging from 0.47 to 0.59 cases per 100 000 inhabitants, according to data obtained from the Instituto de Salud Pública de Chile (Araya et al., 2014). During the 2012 outbreak of serogroup W in Chile, the incidence rate increased to 0.7 (Valenzuela et al., 2013). Argentina reported a higher annual IMD incidence (5.1 cases per 10 000 hospitalized children) from 2012 to 2015 (Gentile et al., 2017). Additionally, Nieto-Guevara et al. (2011) reported an incidence rate of 0.25 per 100 000 inhabitants in Panama in children with a mean age of 4.1 (standard deviation 4.6) years (Nieto-Guevara et al., 2011).

In Mexico, two studies reported IMD incidence (Chacon-Cruz et al., 2011, 2017). Chacon-Cruz et al. (2011) reported an annual incidence rate of 3.08 cases per 100 000 children for 2005–2008 in those aged <17 years. During 2005 and 2016, Chacon-Cruz et al. (2017) reported 7.61 and 2.69 cases per 100 000 inhabitants in children aged <2 years and <16 years, respectively. There were no reported incidence rates for Colombia, or reported MM or *N. meningitidis* incidence rates for Central American countries, except for Panama.

Case fatality rate

Twenty-two studies reported CFR data (Table 2). According to Sáfadi and Cintra (2010), Brazil reported the highest CFR among Latin American countries (20%), followed by Uruguay (15%), Chile (11%), Venezuela and Argentina (10% each) in 2006. In Brazil, the IMD-related CFR varied according to geographic region: Emmerick et al. (2014) reported higher CFR in the North (19.4%) and Central-West (17.7%) regions, and the lowest rate was reported for the Northeast region (11.9%). In Panama, the IMD-related CFR was 12.5% between 1998 and 2008 in a pediatric population (Nieto-Guevara et al., 2011). Only one study from Argentina reported CFR data; the rate was 9.6% in children with a mean age of 32.1 months (standard deviation 40.8) from

Table 1
Characteristics of studies included in the systematic review.

Study (country)	Number	Sex	Age group	Study period
Araya et al., 2014 (Chile)	486[a]	NR	NR	2006–2012
Barra et al., 2013 (Chile)	119[a]	NR	1 month to 90 years	2010–2011
Valenzuela et al., 2013 (Chile)	133[b]	NR	NR	2012
Espinosa de los Monteros et al., 2009 (Mexico)	37[c]	NR	Daycare centers: 2–71 months Social rehabilitation centers: 15–19 years	2004–2005
Rodriguez et al., 2014 (Chile)	20[c]	Male: 75%	Median: 21.5 years (range 18–24)	2012
Sorhouet-Pereira et al., 2013 (Argentina)	133[b]	NR	NR	2010
Nieto-Guevara et al., 2011 (Panama)	32[b]	Female: 66%	Mean: 4.1 (SD 4.6)	1998–2008
Moreno et al., 2015 (Colombia)	100[c]	Male: $n = 54$ Female: $n = 46$	15–21 years	2012
Ibarz-Pavón et al., 2012 (Latin America)	4735[a]	NR	NR	2006–2010
Nunes et al., 2011 (Brazil)	2070[b]	NR[d]	NR	1998–2007
Cardoso et al., 2012 (Brazil)	2000–2006: 281[b] 2007–2011: 437[b]	NR	NR	2000–2011
Nunes et al., 2016 (Brazil)	59[c]	Female: 61.8%	NR	2014
Tauil et al., 2014 (Brazil)	309[b]	Male: 52.1%	Median: 2005–2009: 3 years 2010: 5 years 2011: 4 years	2005–2011
Nascimento et al., 2012 (Brazil)	1690[b]	Male: 54.7%[e]	NR	2000–2009
Barroso et al., 2010 (Brazil)	2413[b]	Male: 55% Female: 45%	Median: 6 years	1990–1996
Baethgen et al., 2008 (Brazil)	2215[b]	NR	NR	1995–2003
Weidlich et al., 2008 (Brazil)	493[b]	NR	NR	2003–2005
Coch Gioia et al., 2015 (Brazil)	18[c]	Male: 55.5%	Mean for students: 23.6 years (range 18–38) Mean for staff workers: 41 years (range 20–63)	2011
Leme and Zanetta, 2012 (Brazil)	490[b]	NR	NR	1999–2008
Moraes et al., 2015 (Brazil)	120[c]	Male: 63% Female: 57%	11–19 years	2012
Masuda et al., 2015 (Brazil)	10 087[b]	Male: 53.8%	Median: 4 years	1986–2004
Weckx et al., 2017 (Brazil)	87[c]	Male: $n = 470$; 48.6% Female: $n = 497$; 51.4%	1–24 years	2011–2012
Gentile et al., 2017 (Argentina)	94[b]	Male: $n = 54$; 57.4%	Median: 12.5 months (range 6–46) Mean: 32.1 months (SD 40.8)	2012–2015
Strelow et al., 2016 (Brazil)	316[f]	Male: $n = 186$; 60%	Median: 16 years (range 7–27)	2006–2011
Saraiva et al., 2015 (Brazil)	2007[b]	NR	NR	1976–2012
Barroso et al., 2013 (Brazil)	46[b]	NR	Mean: 13 years (range 10 months to 51 years)	2003–2012
Azevedo et al., 2013 (Brazil)	34 997[b]	NR	NR	2000–2010
Liphaus et al., 2013 (Brazil)	18[b]	Male: 100%	20–43 years	2010
Chacon-Cruz et al., 2011 (Mexico)	16[b]	Male: 50%	<17 years	2005–2008
Iser et al., 2012 (Brazil)	16[g]	Male: 63%	Median: 6 years (range 2 months to 45 years)	2008
Andrade et al., 2017 (Brazil)	13 341[b]	NR	NR	2008–2014
Moraes et al., 2017 (Brazil)	19 997[b]	NR	NR	2001–2013
Emmerick et al., 2014 (Brazil)	3492[b,e]	NR	NR	2008–2009
Nunes et al., 2013 (Brazil)	488[b]	Male: 56% Female: 44%	Mean: 2005: 18.34 2006: 14.5 2007: 13.23 2008: 19.69 2009: 16.96 2011: 23.01 2012: 24.88	2005–2009 2011–2012
Vasconcelos et al., 2011 (Brazil)	3174[f]	NR	NR	2000–2006
Chacon-Cruz et al., 2017 (Mexico)	51[b]	Male: $n = 28$; 55% Female: $n = 23$; 45%	Median 36 months (range 3 days to 15 years)	2005–2016
Chacon-Cruz et al., 2014 (Mexico)	19[b]	Male: $n = 11$ Female: $n = 8$	Median: 16 years (range 2–47)	2013
Sáfadi et al., 2014b (Brazil)	104[c]	NR	18–39 years	2010
Sáfadi and Cintra, 2010 (Latin America)	NR[b]	NR	NR	1998–2008

NR, not reported; SD, standard deviation; NIG, not identified by sex.
[a] *Neisseria meningitidis* strains isolated from patients with invasive disease.
[b] Meningococcal disease cases.
[c] Colonized by *Neisseria meningitidis*.
[d] Meningococcal meningitis suspected cases, 415 in 2008–2009 and 259 in 2011–2012.
[e] Notifiable Diseases Information System (SINAN) data after 32.9% correction.
[f] Meningococcal meningitis cases.
[g] Included 14 meningococcal disease cases, one possible case defined as a patient who presented clinical purpura fulminans without specific laboratory results, and five probable cases defined as a reported case with an epidemiological link to a laboratory-confirmed case but without positive laboratory results.

Table 2
Epidemiological data from included studies.

Study (country)	Incidence/100 000 inhabitants or population	Case fatality rate, %
Araya et al., 2014 (Chile)	2006: 0.47 2007: 0.51 2008: 0.36 2009: 0.36 2010: 0.33 2011: 0.37 2012: 0.59	NR
Barra et al., 2013 (Chile)	NR	NR
Valenzuela et al., 2013 (Chile)	0.7	26.7[a]
Espinosa de los Monteros et al., 2009 (Mexico)	NR	NR
Rodriguez et al., 2014 (Chile)	NR	NR
Sorhouet-Pereira et al., 2013 (Argentina)	NR	NR
Nieto-Guevara et al., 2011 (Panama)	0.25	12.5
Moreno et al., 2015 (Colombia)	NR	NR
Ibarz-Pavón et al., 2012 (Latin America)	NR	NR
Nunes et al., 2011 (Brazil)	1998: 1.8 2007: 0.9	19–31
Cardoso et al., 2012 (Brazil)	NR[b]	NR[b]
Nunes et al., 2016 (Brazil)	NR	NR
Tauil et al., 2014 (Brazil)	2005–2009: 2.0/year 2010: 1.8 2011: 0.8	2005–2011: 20.7
Nascimento et al., 2012 (Brazil)	0.88/year	26.8
Barroso et al., 2010 (Brazil)	NR[c]	1990–1992: 45 1993–1995: 28 1996: 30
Baethgen et al., 2008 (Brazil)	2.5 ± 0.6 (range 3.5 in 1995 to 1.8 in 2003)	22.2[d]
Weidlich et al., 2008 (Brazil)	1.54	NR
Coch Gioia et al., 2015 (Brazil)	NR	NR
Leme and Zanetta, 2012 (Brazil)	1999 and 2000: >3 (Sorocaba and other cities) 2001: 2 (Sorocaba and other cities) 2008: 5.5 (Sorocaba city); 0.9 (other cities)	21.8 (range 8.1–34.8)
Moraes et al., 2015 (Brazil)	NR	NR
Masuda et al., 2015 (Brazil)	1986 to 2004: 5.3/year 1995 (peak): 8.1 1986 (minimum): 1.2	Mean: 20.5 (range 15–24.6)
Weckx et al., 2017 (Brazil)	NR	NR
Gentile et al., 2017 (Argentina)	5.1/10 000 hospitalized children per year (95% CI 4–6)	9.6
Strelow et al., 2016 (Brazil)	NR	Total: 5.4 ≤5 years: 2.8 >5–15 years: 1.2 >15–50 years: 6.6 >50 years: 22.7
Saraiva et al., 2015 (Brazil)	2003: 3.9[e] 2004: 3.2 2005: 2.0 2006: 1.7 2007: 1.9 2008: 1.6 2009: 1.7 2010: 0.9 2011: 0.7 2012: 0.8	NR[f]
Barroso et al., 2013 (Brazil)	NR	18
Azevedo et al., 2013 (Brazil)	2000–2002: 2.21 2003–2005: 1.81 2006–2008: 1.48 2009–2010: 1.51	NR
Liphaus et al., 2013 (Brazil)	34.1	33[g]
Chacon-Cruz et al., 2011 (Mexico)	3.08	18.8
Iser et al., 2012 (Brazil)	<1 year: 46 1–4 years: 77 5–9 years: 9 10–19 years: 12 20–29 years: 4 30–39 years: 0 ≥40 years: 8 Total: 12	<1 year: 100 1–4 years: 43 5–39 years: 0 ≥40 years: 33 Total: 31

Table 2 (*Continued*)

Study (country)	Incidence/100 000 inhabitants or population	Case fatality rate, %
Andrade et al., 2017[h] (Brazil)	<12 months: 5.01 12–23 months: 0.63 2–4 years: 2.04 5–9 years: 2.65 10–19 years: 1.96 20–24 years: 1.14 25–29 years: 0.86 30–39 years: 0.74 ≥40 years: 0.79	NR
Moraes et al., 2017[g] (Brazil)	2001: 0.53 2002: 0.50 2003: 0.54 2004: 0.76 2005: 0.75 2006: 0.81 2007: 0.81 2008: 0.95 2009: 1.09 2010: 1.15 2011: 1.01[i] 2012: 0.91[i] 2013: 0.70[i]	NR
Emmerick et al., 2014 (Brazil)	NR	Brazil: 14.4 North Region: 19.4 Northeast Region: 11.9 Southeast Region: 14.6 South Region: 13.9 Central-West Region: 17.7
Nunes et al., 2013 (Brazil)	NR	All period: 12.3 2005: 15.1 2006: 9.7 2007: 15.7 2008: 13.2 2009: 12.5 2011: 11.1 2012: 19.6
Vasconcelos et al., 2011 (Brazil)	NR	20.9
Chacon-Cruz et al., 2017 (Mexico)	<2 years: 7.61 <16 years: 2.69	25.49
Chacon-Cruz et al., 2014 (Mexico)	NR	36.8
Sáfadi et al., 2014b (Brazil)	NR	NR
Sáfadi and Cintra, 2010[j] (Latin America)	Argentina: 0.7 Brazil: 1.9 Chile: 0.8 Colombia: 0.3 Mexico: 0.06 Uruguay: 1.3 Venezuela: 0.3	Argentina: 10 Brazil: 20 Chile: 11 Colombia: N/A Mexico: N/A Uruguay: 15 Venezuela: 10

NR, not reported; CI, confidence interval; CFR, case fatality rate.
[a] Data regarding serogroup W.
[b] Reported only for serogroup C. Cumulative incidence of serogroup C meningococcal disease in the city of Salvador was 0.1 cases per 100 000 inhabitants per year from 2000 through 2006, with one death (CFR, 5%). In 2007, 13 cases (0.45 cases/100 000 inhabitants) of serogroup C meningococcal disease were identified, with two deaths (CFR, 15%); in 2008, 53 cases (1.8 cases/100 000 inhabitants) were identified, with four deaths (8%); in 2009, there were 69 cases (2.3 cases/100 000 inhabitants) with 10 deaths (14.5%).
[c] Not possible to obtain data from the graphic.
[d] Information about outcome was not available for 515 cases; thus, the CFR was 22.2% for cases with known information.
[e] The study reports data for the years 1976 to 2012; data for the last 10 years only are presented here.
[f] The study only reported data for the years 1976–2012.
[g] Reported only for serogroup C.
[h] Brazil data except for Salvador city.
[i] Indicates period post-vaccine implementation.
[j] Data from 2006.

2012 to 2015 (Gentile et al., 2017). Two studies from Mexico documented that, in children aged <17 years, the CFR increased from 18.8% for 2005–2008 (Chacon-Cruz et al., 2011) to 25.49% for 2005–2016 (Chacon-Cruz et al., 2017).

During a 2008 outbreak in Brazil, the CFR was highest among children ≤4 years of age and decreased in adults aged <40 years (Iser et al., 2012). In contrast, during a 2010 IMD outbreak in Brazil, the CFR was reported to be 33% among adults aged 20–43 years (Liphaus et al., 2013). Regarding subjects with MM, a 20.9% CFR was found in Brazil for 2000–2006 (Vasconcelos et al., 2011) and 5.4% for 2006–2011 (Strelow et al., 2016). Stratifying by age, the MM-related CFR was lower in children aged ≤5 years and 5–15 years

Table 3
Serogroup distribution.

Study (country)	Serogroup						
	B, *n* (%)	C, *n* (%)	W, *n* (%)	Y, *n* (%)	A, *n* (%)	E, *n* (%)	Other (%)
Araya et al., 2014 (Chile)	NR[a]	NR[a]	NR[a]	NR[a]	NR[a]	NR	NR
Barra et al., 2013 (Chile)	2010: NR (63.6) 2011: NR (51.6)	2010/2011: average of 11.5	2010: NR (7.8) 2011: NR (33.9)	NR	NR	NR	NR
Valenzuela et al., 2013 (Chile)	36.9%	NR	58.2%	NR	NR	NR	NR
Espinosa de los Monteros et al., 2009 (Mexico)	NR (10.8)	NR (24.3)	NR	NR (29.7)	NR	NR	NR
Rodriguez et al., 2014 (Chile)	NR (20.0)	NR	NR (15.0)	NR	NR	NR	NR
Sorhouet-Pereira et al., 2013 (Argentina)	56 (42.1)	7 (5.2)	65 (48.9)	4 (3)	NR	NR	1 (NR)[b]
Nieto-Guevara et al., 2011 (Panama)	NR[a]	NR[a]	NR	NR	NR[a]	NR	NR
Moreno et al., 2015 (Colombia)	15 (NR[a])	3 (NR[a])	3 (NR[a])	22 (NR[a])	NR[a]	NR	NR[b,g]
Ibarz-Pavón et al., 2012 (Latin America)	NR[a]	NR[a]	NR[a]	NR[a]	NR[a]	NR	NR
Nunes et al., 2011 (Brazil)	327 (71.9)	121 (26.6)	NR[a]	NR[a]	NR[a]	NR[a]	NR
Cardoso et al., 2012 (Brazil)	2000–2006: 105 (83) 2007–2011: NR	2000–2006: 20 (16) 2007–2011: NR	2000–2006: 1 (<1) 2007–2011: NR	NR	2000–2006: 1 (<1) 2007–2011: NR	NR	NR
Nunes et al., 2016 (Brazil)	7 (11.9)	2 (3.4)	2 (3.4)	5 (8.5)	NR	6.8	5.1%[c]
Tauil et al., 2014 (Brazil)	2005–2009: 25 (20.7) 2010: 2 (11.1) 2011: 2 (20.0)	2005–2009: 85 (70.2) 2010:14 (77.8) 2011: 6 (60.0)	2005–2009: 7 (5.8) 2010: 1 (5.6) 2011: 1 (10.0)	2005–2009: 4 (3.3) 2010:1 (5.6) 2011: 1 (10.0)	NR	NR	NR
Nascimento et al., 2012 (Brazil)	189 (37.8)	285 (57)	14 (2.8)	3 (0.6)	9 (1.8)	NR	NR
Barroso et al., 2010 (Brazil)	1990–1992: NR (89) 1993–1996: NR	1990–1992: NR (9) 1993–1996: NR (43)	NR	NR	NR	NR	NR
Baethgen et al., 2008 (Brazil)	229 (79)	41 (14.1)	18 (6.2)	2 (0.7)	NR	NR	NR
Weidlich et al., 2008 (Brazil)	NR (64)	NR (18)	NR (17)	NR (1)	Not detected	Not detected	Not detected[d]
Coch Gioia et al., 2015 (Brazil)	3 (NR)	NR	NR[b]	NR[b]	NR[b]	1 (NR)	14 (NR)[b]
Leme and Zanetta, 2012 (Brazil)	NR (45.7)	NR (47.3)	NR (3.7)	NR (1.5)	NR	NR	NR
Moraes et al., 2015 (Brazil)	12 (10.0)[e]	16 (13.4)[e]	3 (2.5)[e]	6 (5.0)[e]	NR	9 (7.5)	73 (60.8)[c]
Masuda et al., 2015 (Brazil)	260 (51.5)[f]	132 (26.1)[f]	24 (4.8)[f]	1 (0.2)[f]	NR	NR	88 (17.4)[g]
Weckx et al., 2017 (Brazil)	1–4 years: 3 (NR) 5–9 years: 2 (NR) 10–14 years: 1 (NR) 15–19 years: 2 (NR) 20–24 years: 3 (NR)	1–4 years: 2 (NR) 5–9 years: 1 (NR) 10–14 years: 5 (NR) 15–19 years: 6 (NR) 20–24 years: 2 (NR)	1–4 years: 1 (NR)	5–9 years: 2 (NR) 10–14 years: 2 (NR)	NR	NR	1–4 years: 14[h] (NR) 5–9 years: 13[h] (NR) 10–14 years: 12[h] (NR) 15–19 years: 8[h] (NR) 20–24 years: 8[h] (NR)
Gentile et al., 2017 (Argentina)	44 (52)	2 (2)	36 (43)	1 (1)	NR	NR	1 (1%)[b]
Strelow et al., 2016 (Brazil)	22 (10.7)	184 (84.5)	8 (3.9)	NR	1 (0.5)	NR	NR
Saraiva et al., 2015 (Brazil)	NR[i]	NR[i]	NR	NR	NR	NR	NR
Barroso et al., 2013 (Brazil)	NR	NR	NR	NR	NR	NR	NR
Azevedo et al., 2013[j] (Brazil)	2007: 232 (19.4) 2008: 217 (16.4) 2009: 183 (13.5) 2010: 178 (10.8) Total: 810 (14.7)	2007: 491 (41) 2008: 665 (50.2) 2009: 736 (54.1) 2010: 1018 (61.7) Total: 2910 (52.6)	2007: 32 (2.7) 2008: 66 (5) 2009: 53 (3.9) 2010: 70 (4.2) Total: 221 (4)	2007: 8 (0.7) 2008: 9 (0.7) 2009: 15 (1.1) 2010: 11 (0.7) Total: 43 (0.8)	2007: 1 (0.1) 2008: 5 (0.4) 2009: 8 (0.6) 2010: 4 (0.2) Total: 18 (0.3)	2007: 0 (0) 2008: 1 (0.1) 2009: 0 (0) 2010: 3 (0.2) Total: 4 (0.1)	2007: 433[k] (36.1) 2008: 356[k] (27.0) 2009: 365[k] (26.8) 2010: 366[k] (22.2) Total: 1520[k] (27.5)
Liphaus et al., 2013 (Brazil)	NR	100%	NR	NR	NR	NR	NR

Table 3 (*Continued*)

Study (country)	Serogroup					
	B, *n* (%)	C, *n* (%)	W, *n* (%)	Y, *n* (%)	A, *n* (%)	E, *n* (%)	Other (%)
Chacon-Cruz et al., 2011 (Mexico)	2 (12.5)	10 (62.5)	0	2 (12.5)	0	NR	Not typeable: 0 Not typed: 2 (12.5)
Iser et al., 2012 (Brazil)	NR	8 (NR)	NR	NR	NR	NR	NR
Andrade et al., 2017 (Brazil)	NR	7,217 (54.1)	NR	NR	NR	NR	NR
Moraes et al., 2017 (Brazil)	NR	19,997 (100)	NR	NR	NR	NR	NR
Emmerick et al., 2014 (Brazil)	NR	NR	NR	NR	NR	NR	NR
Nunes et al., 2013 (Brazil)	NR	NR	NR	NR	NR	NR	NR
Vasconcelos et al., 2011 (Brazil)	NR (61.5)[l]	NR (32.2)[l]	NR	NR	NR	NR	NR
Chacon-Cruz et al., 2017[d] (Mexico)	5 (9.8)	32 (62.74)	NR	12 (23.53)	NR	NR	2 (3.92)
Chacon-Cruz et al., 2014 (Mexico)	NR	19 (100)	NR	NR	NR	NR	NR
Sáfadi et al., 2014b[f] (Brazil)	9 (16.1)	27 (48.2)	5 (8.9)	7 (12.5)	NR	8 (14.3)	NR
Sáfadi and Cintra, 2010[m] (Latin America)	Brazil 2006: NR (38.2)	Brazil 2006: NR (55.2)	Brazil 2006: NR (5)	Brazil 2006: NR (1.6)	NR	NR	NR
	Chile 2006: NR (78)	Chile 2006: NR (12)	Argentina 2007: NR (13)	Venezuela 2006: NR (50)			
	Venezuela 2006: NR (36)	Venezuela 2006: NR (14)		Dominican Republic 2006: NR (10)			
	Costa Rica 2006: NR (85)	Dominican Republic 2006: NR (35)		Argentina 2007: NR (6.8)			
	Dominican Republic 2006: NR (44)	Argentina 2007: NR (11.4)		Mexico 2000–2005: NR (8)			
	Argentina 2007: NR (68.8)	Mexico 2000–2005: NR (71)					
	Mexico 2000–2005: NR (12)	Mexico 2006: NR (100)					
	Ecuador 2000–2006: NR (16)	Ecuador 2000–2006: NR (69)					

NR, not reported.
[a] Unable to obtain information from the graphic.
[b] Non-groupable.
[c] Serogroup Z.
[d] Serogroup X.
[e] Data of serogroups B-5, C-32, and Y-12.
[f] Serogroup could not be determined for 46.1% isolates. The serogroup was determined for 56 of 104 meningococcus-positive samples.
[g] Could not be determined.
[h] Non-groupable and serogroups E and X, which had one subject each in the 5–9 years and 20–24 years age groups, respectively.
[i] The study only reported data from 1990 to 2012.
[j] *Neisseria* meningitis cases.
[k] No information.
[l] Only 25.9% of 3174 meningococcal meningitis cases had serogroup evaluation.
[m] In 2006, Chile reported 6% for serogroups W and Y together. From 2000 to 2006, Ecuador reported 15% for serogroups W and Y together. In 2006, Costa Rica reported 15% for serogroups C and Y together.

(2.8% and 6.6%, respectively), and increased in subjects aged >50 years (22.7%) (Strelow et al., 2016). During a 2012 outbreak of serogroup W in Chile, the CFR was approximately 27% (Valenzuela et al., 2013). The study conducted in Colombia did not provide CFR data.

Serogroup distribution

Thirty-five studies reported data on serogroup distribution. For four of these, it was not possible to extract data from the graphics; these included both studies with general Latin America serogroup data (Sáfadi and Cintra, 2010; Ibarz-Pavón et al., 2012) and studies conducted in Panama (Nieto-Guevara et al., 2011) and Chile (Araya et al., 2014). In general, serogroup frequency and distribution varied among the Latin American countries (Table 3).

In Brazil, for 2007–2010, serogroup C was the most important capsular type among IMD cases (Azevedo et al., 2013). In the Northeast region during 1998–2007, the most prevalent serogroup was B (71.9%), followed by serogroup C (26.6%) in subjects with IMD (Nunes et al., 2011). In the South region, the proportion of meningococcal cases attributable to serogroup B remained predominant over time: from 79% during 1995 and 2003 to 64% during 2003 and 2005. Serogroup C was the second most prevalent (Baethgen et al., 2008; Weidlich et al., 2008). In the Central-West region, from 2005 to 2011, there was a predominance of serogroup C, followed by serogroup B, and serogroups W and Y to a lesser extent (Tauil et al., 2014). Similarly, in the Southeast region, serogroup C (57%) was the most frequent in IMD cases, followed by serogroup B (37.8%), and serogroups A (1.8%), W (2.8%), and Y (0.6%) (Nascimento et al., 2012). No data were reported for serogroup type in the North region.

Regarding serogroup data in *N. meningitidis* carriers, according to Nunes et al. (2016), serogroup B was the most frequently reported (11.9%) among adolescents (11–19 years) in the Northeast region in Brazil in 2014. In these subjects, serogroup Y (8.5%) was reported more frequently than serogroups C and W (3.4% each) (Nunes et al., 2016). In general, carriage of serogroup C dominated in the Southeast region, followed by serogroups B, E, Y, and W (Sáfadi et al., 2014b; Moraes et al., 2015). For MM cases, from 2000 to 2006, serogroup B was more prevalent in Brazil, followed by serogroup C (Vasconcelos et al., 2011). From 2006 to 2011, serogroup C became the most prevalent (Strelow et al., 2016).

In Mexico, during 2005–2008, serogroup C was most commonly identified in children with IMD (62.5%) (Chacon-Cruz et al., 2011). Similarly, serogroup C was most frequently reported during 2005–2016 (62.74%), followed by serogroup Y (23.53%) and B (9.8%) in children with IMD aged <17 years (Chacon-Cruz et al., 2017). Additionally, serogroup C was the only serogroup identified in samples collected from an outbreak in 2013 (Chacon-Cruz et al., 2014). Regarding *N. meningitidis* carriers, serogroup Y was the most prevalent (29.7%) during 2004–2005, followed by 24.3% for serogroup C and 10.8% for serogroup B (Espinosa de los Monteros et al., 2009).

In Chile, serogroup B was predominant in 2010 and 2011, and serogroup C was also identified, with a mean frequency of 11.5% of IMD cases in this period (Barra et al., 2013). However, IMD cases with serogroup W experienced a notable increase in 2011 compared to 2010 in Chile (Barra et al., 2013), with an outbreak of this serogroup reported in 2012 (Valenzuela et al., 2013). In 2012, serogroup B was the most prevalent among *N. meningitidis* carriers (20%), followed by serogroup W (15%) (Rodriguez et al., 2014).

In Argentina, serogroup W was the most prevalent related to IMD cases in 2010 (48.9%), followed by serogroups B (42.1%) and C (5.2%) (Sorhouet-Pereira et al., 2013). Between 2012 and 2015, the most prevalent serogroup among Argentine children with IMD was B (52%), followed by W (43%) and C (2%) (Gentile et al., 2017). However, there were no published serogroup data for *N. meningitidis* carriers in this country.

Discussion

This systematic literature review provides an insight into the epidemiological profile of meningococcal strains in Latin America. To date, a limited number of studies describing the epidemiological data for IMD, MM, or *N. meningitidis* carriers, in terms of incidence rate, CFR, and serogroup distribution, have been published for Latin America, although disease notification is compulsory in many countries (López and Debbag, 2012). It was found that only eight of the 20 Latin American countries had reported data. Furthermore, there was limited information on MM and *N. meningitidis* carriers; IMD data were more frequently reported.

Most of these studies were from Brazil, followed by Mexico and Chile. Brazil and Chile have experienced an improvement in their surveillance systems; however, the lack of infrastructure and trained professionals still hinders other Latin American countries and contributes to underreporting and a lack of monitoring of IMD, MM, and *N. meningitidis* cases (Sáfadi et al., 2015b). The true burden of IMD in Latin America is likely underestimated due to underreporting of cases, which is a consequence of several factors, such as inconsistencies in case definitions used for notifications and data input, difficulties in *N. meningitidis* isolation and serogroup identification (mainly in patients with prior antibiotic therapy), and delays in sample characterization (López and Debbag, 2012; Borrow et al., 2017). In addition, there is a lack of efficient diagnostic technology in laboratories (López and Debbag, 2012), although the increase in PCR technology has improved the identification of strains by up to 30% (Sáfadi and McIntosh, 2011).

According to literature data, the incidence of IMD in Latin American countries has ranged from <0.1 to 1.8 cases per 100 000 inhabitants in the last 5 years, based on country and year analyzed, representing low endemicity (<2 cases per 100 000 inhabitants) (PAHO, 2012; Sáfadi et al., 2017). These incidence rate results are similar to those reported in the current review, in which the overall incidence data ranged from 0.06 to 1.9 cases per 100 000 inhabitants in 2006 (Sáfadi and Cintra, 2010). However, the limitations of reporting IMD data across Latin American countries should be considered, and the interpretation of available data and related decision-making must be performed with caution (Sáfadi et al., 2017).

From 2008 to 2011 (Araya et al., 2014), a decrease in IMD incidence rate was observed in Chile, which was also reported by a national epidemiology database from 2016 to 2017 (Instituto de Salud Pública de Chile, 2017a). In 2006, the IMD incidence rate in Colombia was 0.3 cases per 100 000 inhabitants (Sáfadi and Cintra, 2010) and on comparison with the national epidemiology database, the IMD incidence has been stable since 2013, reaching 0.21 cases per 100 000 inhabitants in 2017 (Instituto Nacional de Salud, 2017).

Although Mexico reported the lowest incidence rate among Latin American countries (Sáfadi and Cintra, 2010), the number of reported IMD cases started to increase in 2015, according to a national database (Secretaría de Salud de México, 2016a, 2016b, 2017, 2018). In addition, according to active surveillance studies performed in the Tijuana area (Chacon-Cruz et al., 2011, 2017), IMD incidence rates were substantially higher than those described by Sáfadi and Cintra (2010), whose low incidence rate could be explained by the restrictive case definition used for reporting IMD cases in the country (Sáfadi et al., 2015b). However, the true burden of IMD is unknown in Mexico, since not all isolates are sent to the national reference laboratory, meaning a limited number of isolates are properly characterized (Borrow et al., 2017).

The epidemiological analysis of *N. meningitidis* carriage is also important, as these subjects are commonly asymptomatic but can still transmit the bacteria. Literature data reported 5% to 10% of carrier subjects in a non-epidemic Latin American scenario (Sáfadi et al., 2017). However, studies included in the present analysis regarding carriers focused on serogroup distribution, thereby preventing us from being able to confirm these data.

CFRs among Latin American countries are still high even though management of *N. meningitidis* has improved (Sáfadi and Cintra, 2010). The CFR in Latin America is approximately 20% (Sáfadi et al., 2017), similar to that reported in Brazil in 2006 (Sáfadi and Cintra, 2010). In Chile, the CFR of serogroup W during the 2012 outbreak was approximately 27%, which was the highest observed in the last 20 years in the country (Valenzuela et al., 2013). Literature data showed that serogroups B and C are the most prevalent in Latin American countries, although reports of serogroups W and Y have increased (Sáfadi and McIntosh, 2011), primarily among infants and children.

In conclusion, differences in epidemiological data notification and registration protocols across Latin American countries have likely contributed to the wide variability in information presented in the literature. Data interpretation should be done with caution in each region facing these inherent limitations (Sáfadi et al., 2015b). Enhancements in IMD notification and registration in epidemiological databases, as well as the improvement of national surveillance programs, diagnostic capabilities, and isolate characterization, may lead to the elucidation of the true epidemiological burden of IMD in Latin American countries.

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Ethical approval

Concerning ethical aspects, this study was conducted through a literature review, without subject identification, ensuring individual confidentiality and anonymity.

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All authors are employees of Pfizer Inc. and may hold stock in the company.

Conflict of interest

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