Original Research Article

Post-vaccination alteration in meningococcal disease rate in the US from 1980-2019

ABSTRACT

Aim: To study the impact of vaccination on Meningococcal infection in the United States from 1980 to 2019.

Study Design: The study used deidentified publicly available data.

Place and duration of Study: Department of Anatomical & Developmental Sciences, and Pathological Processes, Microbiology & Immunology, Department of Preventive Medicine & Epidemiology, Department of Nutritional, Biochemical & Molecular Sciences American University, School of Medicine, Aruba, Between July 2023 to September 2023.

Methodology: All analyses for this study were conducted using The Health, United States Data Finder, Center for Disease Control, which provides detailed trend tables and charts for recent editions of Health, United States. All the data was collected and compared year-wise, age-wise, and new cases of meningococcal infection per 100,000 population. The data was also compared concerning the year of initiation of the vaccine.

Results: With time, it was observed that the cases of meningococcal infection declined. The rate was found to be higher with the initiation of vaccination.

Conclusion: Stringent vaccination, surveillance, and timely use of antibiotics in the United States contributed to the drop in instances of meningococcal infection. However, the recent outbreak in Florida could be due to negligence among the people.

Keywords: *Meningococcal disease, Vaccination, Neisseria meningitides, United States*

1. INTRODUCTION

Neisseria meningitides is the source of meningococcal disease and a prominent contributor to bacterial meningitis in the United States. In addition to pneumonia and localized diseases such as septic arthritis, it can also result in meningitis and sepsis. Weichselbaum made the initial discovery of *Neisseria* *meningitides* in 1887 while evaluating the cerebrospinal fluid (CSF) of a patient with meningitis (Rouphael and Stephens 2012). The gram-negative, aerobic diplococcus bacterium *Neisseria meningitides* is encased in a polysaccharide capsule that enhances its pathogenicity. Based on the polysaccharide capsule's structure Meningococci has different serogroups. So far twelve different polysaccharide capsules with unique antigens and chemical compositions have been identified. One of the six serogroups—A, B, C, W, X, and Y—have reported invasive infections that affect the entire world (Brandtzaeg and Deuren 2012; Mishra, 2023).

Humans are the only source of *Neisseria meningitides*; in around 25% of the population, it establishes as a commensal diplococcus in the nasopharynx (Pizza and Rappuoli 2015). Meningitis and bloodstream infection are the two most prevalent kinds of meningococcal infections, both of which can swiftly turn fatal. The infection through *Neisseria meningitides* can spread from person to person by respiratory droplets or secretions with asymptomatic colonization.

Bacteria adhere to the nasopharynx's and oropharynx's mucosal cells, multiply there, then break through the host's mucosal cells and enter the bloodstream. After crossing the blood-brain barrier and entering the cerebrospinal fluid, it can cause systemic illness and, lately, fulminating meningitis.

The incubation phase can last anywhere from 1 to 10 days, but it usually lasts 3 to 4 days. Meningococcal invasive illness is the primary cause of 50% of reported cases of meningitis in the United States (https://www.cdc.gov/vaccines/pubs/pinkbook/mening.html.). The patient displays the typical abrupt onset of fever, headache, and stiff neck. Additional symptoms, such as nausea, vomiting, photophobia (eye sensitivity to light), and altered mental status are frequently present as well.

Meningococcal septicemia without meningitis can occur in about 30% of invasive meningococcal infections (https://www.cdc.gov/vaccines/pubs/pinkbook/mening.html.). Meningococcal septicemia is characterized by an abrupt onset of fever, chills, cold hands, and feet, intense aches or pains in the chest or abdomen, vomiting, diarrhea, and a petechial or purpuric rash that is frequently accompanied by hypotension, shock, an acute adrenal hemorrhage, and multiorgan failure (Tsheten et al., 2016). Additionally, among the senior population in the United States, *Neisseria meningitides*-related bacteremia pneumonia accounts for 15% of cases.

Even with effective antibiotic therapy, the overall case-fatality ratio for meningococcal disease is 10% to 15%, and it may be higher in people with meningococcemia (https://www.cdc.gov/vaccines/pubs/pinkbook/mening.html.))

Meningococcal disease has a 10,000-fold greater risk in people with persistent deficiencies (e.g., genetic deficiencies) in the complement system (e.g., C3, properdin, Factor D, Factor H, or C5-C9), and these people can also have recurrent disease (Cohn et al., 2016). People with anatomic or functional asplenia, atypical hemolytic uremic syndrome, or paroxysmal nocturnal hemoglobinuria undergoing treatment with eculizumab are also at greater risk of meningococcal disease because the drug binds to C5 and suppresses the terminal complement pathway. The attack rate of laboratory-acquired meningococcal infection has been estimated at 13 per 100,000 people among microbiologists who frequently work with *Neisseria meningitides* isolates, which is significantly higher than the rate for adults in the general population (Sejvar et al., 2005).

To fight back against Meningococcal disease threetypes of meningococcal vaccines are available in the United States. Meningococcal vaccines also vary by the number of serogroups they provide protection against.Three conjugate vaccines are quadrivalent (4 serogroups: A, C, W, and Y).Two recombinant protein vaccines are monovalent (1 serogroup: B).ne conjugate and the recombinant protein vaccine is pentavalent (5 serogroups: A, B, C, W, and Y). MenACWY is against serogroups A, C, W, and Y and was introduced in 2005. Later after the outbreakby Serogroup B, Men B was also introduced. Meningococcal illness is sporadic, but outbreaks continue to occur. Despite of meningococcal vaccination schedule recently CDC observed an outbreak of meningococcal disease in Florida (https://www.cdc.gov/meningococcal/outbreaks/FL2022-sp.html). In the present study, we studied the impact of vaccination on meningococcal diseases from 1980 to 2019.

2. MATERIALS AND METHODS

The National Notifiable Disease Surveillance system (NNDSS) is used in the United States to monitor for meningococcal disease. If data lacks some information, data from complementary meningococcal surveillance systemis used to complete the information that involves. These complementary system involves, Active Bacterial core surveillance (ABC) and enhanced meningococcal disease surveillance activities. The nationwide serogroup distribution of cases with unknown serogroup was estimated using these complimentary systems.

Analysis of data collected through these surveillance systems were determined by human participants, review at Center for Disease Control (CDC)and the information given to CDCby state health departments. Patient consent and Institutional review board review was not required, as data was collectedusing The Health, United States Data Finder, Center for Disease Control, which provides detailed trend tables and charts for recent editions of Health, United States. These trend tables and charts cover a number of subjects and population groups.

For the cases of Meningococcal disease reported from 1980 to 2019 serogroup data from ABC was used to estimate number of cases due to serogroup A, C, W and Y.

After the introduction of a new strain, later recognized as Serogroup B, the data was collected from the same source. The complete data was grouped and analysed under four decades; 1980-1990, 1990-2000, 2000-2010 and 2010-2019. Due to Pandemic the data was not available for 2020.

All the data was subjected to one way ANOVA to identify the significant difference in different decades and to assess the impact of vaccination on the Meningococcal disease rate and on number of new cases.

The estimated incidence by case year, patient age group and serogroup is calculated using population denominator produced by US Census Bureau in collaboration with national center for health statistics by CDC.

Two Men ACWY vaccine were licensed for use during evaluation period: Menactra in 2005 and Menveo in 2010.

We also calculated the percentage change in Meningococcal incidence before MenACWY vaccine introduction (2005) after Primary dose recommendation (2006-2010) and booster dose recommendation (2011-2017). Along with one way ANOVA, the t-Test was also performed between consecutive decades to determine if there is significant difference in Meningococcal disease. The statistical analysis was done using Statistic Kingdom.

The data summarize the new cases per 100,000 population and the Number of new cases of Meningococcal diseases all through the years. The collective data is from 1980 to 2019. The study used deidentified publicly available data.

3. RESULTS AND DISCUSSION

The study includes cases of Meningococcal infection from the year 1980 to 2019. The data was collected for all age groups and all the serogroups from CDC.

From the year 1980 to 2019, a total number 61,085 cases of Meningococcal disease were reported in the United States: 49227 cases (18.92 cases/100000 population) during the Pre-vaccine Period from 1980 to 2005, 5256 cases (1.74/100000 population) during post primary dose, period from 2006 to 2010, and reduced cases to 4097 (1.3/100000 population) during the post booster dose period from 2011 to 2019. The data shows that with the inclusion of vaccine there was a complete decline of number of cases as compared to the Pre vaccination period.

The percentage number of cases during the period from 1980 to 2000 was found to be 72% of the total number of cases. It was that period where public health officials and CDC tried to spread public awareness through their various programs. As the first vaccination was introduced in 2005, so during the period of Primary dose recommendation this percentage reduced to 26.2% and after the booster dose percentage decline to 8.07%.

The data expressed in Figure 1 shows that there is no significant decline in the number of new cases or Meningococcal disease rate,On comparing the decades from 1980-1990 to 1990-2000, the value of P was found to be greater than 0.01. While comparing the data for decade 1990-2000 with that of 2000-2010 there is a significant difference with value of $P<0.01$. this was the post Primary vaccination period.

The results are more compelling on comparing the data of Post booster dose with Primary dose periodand with Pre vaccination Period. The data shows significant differences among the different periods.

Figure 2 shows the number of new cases in these four decades, that also shows a similar pattern.

Figure 3 gave a clear picture of continuous decline of the number of cases from 2001 to 2019. Although in 2008 there is a little rise in the number of cases, which is due to higher rate of meningococcal disease in infants during that period (Judelsohn and Marshall 2012). According to ABCs statistics, serogroup B accounted for 25% of cases in the US in 2007, followed by serogroup C for 30%, serogroup Y for 37%, and serogroup W-135 for 9% of cases (www.cdc.gov/ncidod/DBMD/abcs/survreports/mening07.pdf). The National Immunization Survey found that just 33% of 13-year-olds had gotten MCV4 in 2007 (Vaccination coverage 2008), Which could also be one of the reasons for the rise in infection in 2008, our results are in corroboration with Burman et al., 2023 stating that the infants and young adults are at higher risk.The t-tests between consecutive decades reveal that there is no significant difference in Meningococcal disease rates between the 1980s and 1990s. However, there are significant differences between the 1990s and 2000s, and between the 2000s and 2010s.

The active bacterial core surveillance (ABC's) network, a population-based surveillance system for bacterial pathogens, has consistently supplied a wealth of information about the different infectious diseases, their rate of rise and decline, and their distribution across the population. (https://www.cdc.gov/abcs/bact-facts-interactivedashboard.html.).

Other parts of the world, including China, Russia, Niger, Togo, and Western Kenya, as well as the United States, are affected by meningococcal illness.

In many countries, including the United States, serogroup B strains are the main culprits behind endemic meningococcal illness and protracted outbreaks [Diermayer et al., 1999; Baker et al., 2001;Purmohamadet al., 2019]. In the US and other countries in the Americas, serogroup Y strains account for a significant fraction of infections (Rosenstein et al., 1999; Harrison et al., 2006). Although the causes of the diverse serogroup distribution around the world are unknown, probable processes include population immunity variations and environmental influences.

Age has a significant impact on the incidence of meningococcal infection, with infants being at the greatest risk [Hedari et al., 2013]. One of the most significant host factors influencing the likelihood of infection is low blood bactericidal antibody (SBA) levels. Minority ethnicity and low socioeconomic level have also been linked to higher risk. Meningococcal illness has been linked to immune system-compromising conditions like functional or anatomic asplenia, HIV infection, genetic polymorphisms, and deficits in innate immune system components. The risk of meningococcal illness has long been linked to population crowding. Behavioral risk factors have also been linked to the likelihood of meningococcal carriage and disease. Other risk factors include passive and active smoking, drinking in pubs and bars, kissing, and living in a university dorm (Harrison, 2010).

After introducing the MenB vaccine against serotype B in 2015, there has been a continuous fall in meningococcal infection, our study is also supported by Mbaeyi et al.,2020.

Additionally, prompt antibiotic use for postexposure prophylaxis and treatment aids in limiting the spread of illness (Bröker, et al 2011). The vaccination strategies used by Italy (Neri et al, 2008;) Canada (Siu et al 2008), and Germany (Hellenbrand, et al., 2013; Cardoso, et al., 2022) demonstrated that vaccination in children decreased the rate of Paediatric meningococcal infection, which is consistent with our observation. The tight and effective monitoring system of the Enhanced Meningococcal Diseases Monitoring (EMDS), centers for Diseases Control & Prevention, is another significant element contributing to the decrease in meningococcal cases. The EMDS gathers, isolates from the health departments of all the states and major jurisdictions, evaluates them, and maintains track of the infection rate. 98–99% of the population of the United States is still being monitored, and quick action is being taken to halt the spread of illness.

4. CONCLUSION

The present study was conducted to assess the association between Meningococcal vaccination and disease rate in the period of 40 years. The data was compared between Pre vaccination and post vaccination diseases rate. This analysis shows that meningococcal vaccination is linked to a decrease in the incidence of meningococcal disease in the United States population,even if these reductions are probably multifactorial.In environments where the incidence of meningococcal disease is higher, adolescents may benefit even more from meningococcal immunization. In order to fully benefit from the vaccination program and to further evaluate the potential for herd protection of persons in different age groups, more work is required to raise the coverage of meningococcal booster doses among adolescents. Stringent vaccination, surveillance, and timely use of antibiotics in the settings where disease rate is higher can contribute to the drop in instances of meningococcal infection.

ETHICAL Approval

This study does not involve any ethical issues as data was collected from the Centers for Disease Control & Prevention.

Disclaimer (Artificial intelligence)

Author(s) hereby declare that NO generative AI technologies such as Large Language Models (ChatGPT, COPILOT, etc.) and text-to-image generators have been used during the writing or editing of this manuscript.

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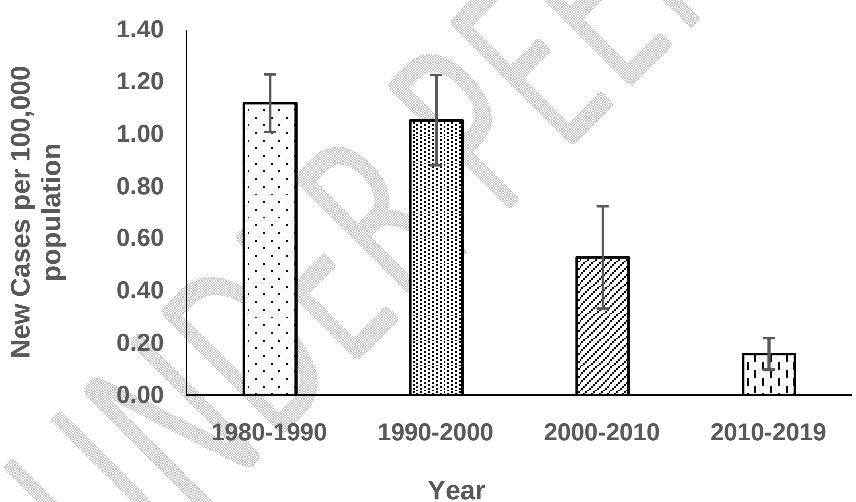

Figure 1: New cases of Meningococcal infection per 100,000 population from 1980 to 2019 in the United States

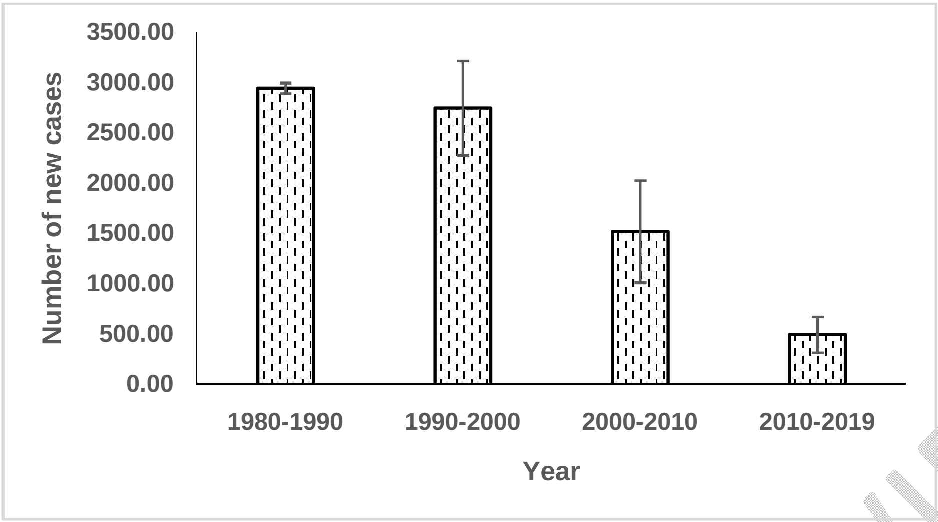

Figure 2: Overall new cases of Meningococcal infection in Pre vaccination, and Post vaccination Period in the United States

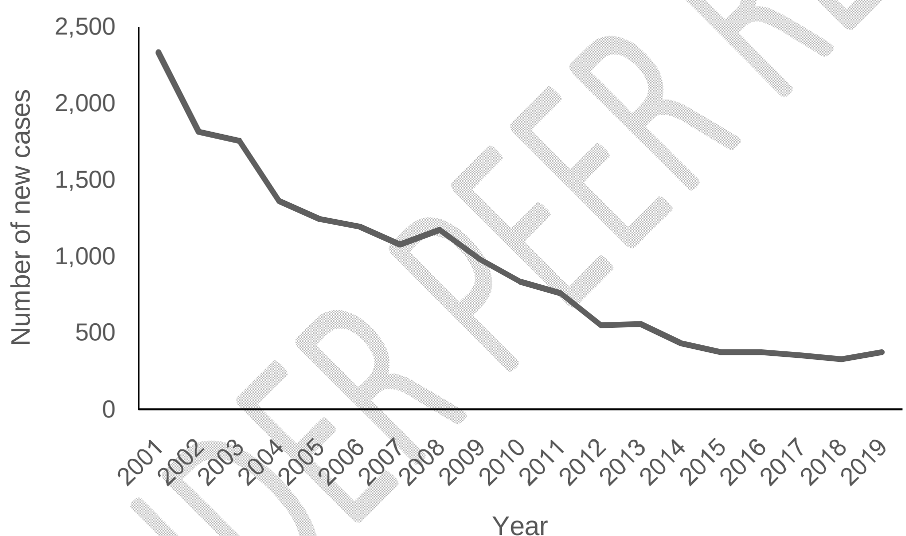

Figure 3: Overall new cases of Meningococcal infection from 2001 to 2019 in the United States