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TERROR IN THE AIR: MENINGOCOCCAL DISEASE OUTBREAK IN THE PHILIPPINES

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KEYWORDS
Neisseria meningitidis, meningococcemia, meningococcus, meningococcal meningitis, meningococcal outbreak

ABSTRACT
Introduction: Meningococcal disease is caused by ***Neisseria meningitidis*** that can present as fever or respiratory infection developing into a fulminant course. In February 2005, WHO experts confirmed that the Cordillera Administrative Region of the Philippines experienced an outbreak of Serogroup A Meningococcal Disease where there was an unusually large proportion of meningococcemia cases.
Objectives: This study aims to describe the clinical profile of pediatric patients discharged from a tertiary hospital with a diagnosis of meningococcal disease and to identify the etiologic agent.
Methodology: This is a retrospective descriptive study involving chart review of patients 0-18 years of age discharged from October 2004 to October 2006 with a diagnosis of either meningococcemia, meningococcal meningitis or both.
Results: There were 217 discharges with this diagnosis. Of these, 100 (46.08%) belonged to the 0-18 years of age, 47% of who were male, 64% were Baguio residents, 28% were 0-1 year old, 19% were between 2-5 years old and 26% were 15-18 years old. 100% had a history of fever and 90% had rashes. 51% had a discharge diagnosis of Meningococcemia. 32% died due to septic shock, DIC. The etiologic agent was identified as ***Neisseria meningitidis.***
Conclusion: Of the study population, 53% were female. Children 0-5 years of age were most affected (47%). 100% had a history of fever. 32% died of septic shock. 62% were confirmed by laboratory. The culprit of this epidemic was a hypervirulent strain of ***Neisseria meningitidis Serogroup A Subtype A 1.9*** sensitive to Penicillin.

INTRODUCTION

John W. Boslego, et. al.[1] stated that the history of meningococcal disease is both fascinating and humbling. Fascinating when one reflects on what we have learned over the years about the epidemiology, pathogenesis, pathophysiology, and the principal determinant of host susceptibility, like lack of bactericidal antibody; but humbling from the standpoint of how little we understand about the virulence properties of the organism or the dynamics involved in epidemic disease. Perusing through the annals of microbiology will bring us to the year 1805 when Vieusseux first described meningococcal disease based on several patients seen presenting with a course having similar clinical signs and symptoms in Switzerland. But it was only in the year 1886 when Weichselbaum first identified the causative agent of this disease which caused several major outbreaks ravaging Napoleonic and Persian armies as well as epidemics in New England[1, 2, 3]. At first, high rates of this disease predominated over Europe and North America, but over time it spread all over the world, especially to sub-Saharan Africa and then to Asia. The next 150 to 200 years were marked by peculiar patterns of periodic outbreaks occurring every 8 to 15 years interspersed with sporadic cases[1, 2,3,12]. Today the largest epidemics affect mainly the sub-Saharan African countries within the meningitis belt. However, epidemics have become a global problem that can affect any country regardless of climate, race, age or any environmental or social factors[2, 3]. Studies have shown that in any outbreak, 80-90% are cases of meningococcal meningitis, while the rest (10-20%) have septicemia[2, 4].

The Regional Epidemiological Surveillance Unit (RESU) [5] of the Department of Health (DOH) of the Cordillera Administrative Region (CAR) of the Philippines did not receive any report of meningococcal disease cases from 1990 to 2003, except for the following years: 29 cases in 1993, one case in 1995, two cases in 1998. However, in the last quarter of 2004[6], the Baguio General Hospital and Medical Center of Baguio City, Philippines experienced an increasing number of patients admitted and clinically diagnosed as meningococcemia (Appendix A). Before the end of that same year, confirmatory laboratory examinations were made available to corroborate the diagnosis of meningococcal disease among the succeeding admissions. Therefore, in February 2005, the World Health Organization (WHO) [7] experts confirmed that the Cordillera Administrative Region (CAR) of the Philippines was experiencing an outbreak of Serogroup A Meningococcal Disease. This is the first documented epidemic of a meningococcal disease outbreak north of the National Capital Region of the country and the largest recorded outbreak in the history of the Philippines[8].

OBJECTIVE

This paper is aimed to describe the clinical profile of pediatric patients zero to eighteen years of age discharged from a tertiary government training hospital given a diagnosis of meningococcemia, meningococcal meningitis or meningococcal disease, meaning the patient was diagnosed to have both meningitis and septicemia due to ***Neisseria meningitidis***. Specifically, we wanted to investigate the proportion of meningococcemia, the common signs and symptoms of this disease, the most common cause of death, and identify the specific serotype of the etiologic agent which caused the outbreak.

MATERIALS AND METHODS

This was a retrospective descriptive study involving a chart review of patients 0-18 years of age discharged from a tertiary government hospital (Baguio General Hospital and Medical Center) located in Baguio City, Philippines from October 1, 2004 to October 31, 2006. Included were patients who were given a final diagnosis of either: meningococcemia, meningococcal meningitis or meningococcal disease. These included cases diagnosed based on clinical signs and symptoms where laboratory work up were not done due to lack of resources.

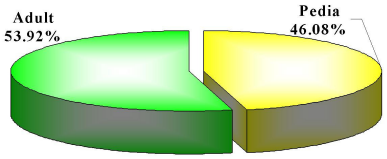
OPERATIONAL DEFINITIONS

1. Meningococcemia: an acute septicemia characterized with abrupt onset of fever, petechial rash and/or purpura, oftentimes presenting with shock; meningeal symptoms are usually absent. Blood cultures usually grow ***Neisseria meningitidis.***
2. Meningococcal meningitis: an acute purulent meningitis which is characterized by fever, sometimes associated with rash and presenting with neurological signs like headache vomiting, neck rigidity, lethargy, coma, changes in sensorium, convulsions, etc. which is often associated with abnormal cerebrospinal fluid studies[5,6,7]. Cerebrospinal fluid and/or blood cultures and/or rapid antigen tests usually are positive for ***Neisseria meningitidis.***
3. Meningococcal disease: an acute bacterial illness caused by a gram-negative intracellular diplococci characterized by fever, petechiae and/or purpuric rashes and meningeal signs like headache, vomiting, neck rigidity, seizures, etc. sometimes associated with shock. Blood and/or cerebrospinal fluid cultures or rapid antigen tests usually show *Neisseria meningitidis.*
4. Confirmed case: laboratory confirmation by one or more of the following methods: isolation of *Neisseria meningitidis* from a sterile site (cerebrospinal fluid, blood), positive test for *Neisseria meningitidis* DNA/antigen from a sterile site (cerebrospinal fluid, blood)[8,10]
5. Suspect case: a person or individual with fever of acute onset (within 7 days) with at least one of the following: hemorrhagic rash (e.g., petechiae or purpura), meningeal signs (e.g., nuchal rigidity or stiff neck)[8]
6. Primary case: a case that occurs in the absence of previous known close contact with another case-patient[8,10]
7. co-primary case: occurrence of two or more cases among a group of close contacts with onset of illness separated by < 24 hours[8,10]
8. Secondary case: a case that occurs among close contacts of a primary case-patient ≥ 24 hours after onset of illness in the primary case-patient[8,10]
9. Baguio City-resident: an individual who stayed in Baguio City continuously for six months; however, during the outbreak, if the individual stayed at a certain place within the City of Baguio continuously for more than two weeks this address was considered as the home address

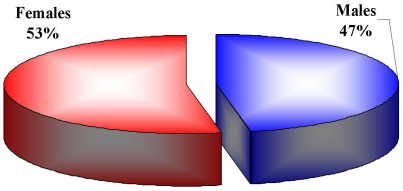
RESULTS

From the total number of suspect cases admitted in this institution which included the adult and pediatric populations, 217 were discharged with any of the following diagnosis: meningococcemia, meningococcal meningitis or meningococcal disease (meningococcemia with meningococcal meningitis). Of these 217 patients, 46.08% (100) belonged to the pediatric population consisting of children 0-18 years of age. Of this study population (100), 47% were males and 53% were females. 64% were identified to be Baguio City residents and 36% were non-Baguio residents leaving in areas surrounding the city like La Trinidad, Tuba, Itogon, etc. Twenty-eight per cent were between 0 to one year of age, 19% were 2-5 years old, 8% were 6-9 years old, 19% were aged 10-14 years and 26% were 15-18 years of age. Ninety seven per cent were considered as primary cases, 1% as a co-primary case and 2% as secondary cases. Twenty six per cent of this pediatric study population were students while 5% were working as waitresses in local bars within the vicinity of the city, 2% were identified as gardeners and 1% each as a gold panner, a saleslady, a porter, a food vendor, a manager in a billiard area and a helper. The rest of the charts of the study population failed to indicate the status of the patient with regards to work or education (61%).

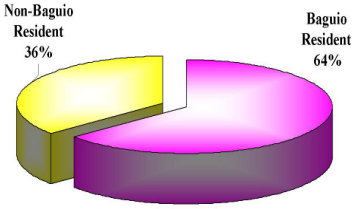
MENINGOCOCCAL CASES
Baguio General Hospital and Medical Center
October 2004 - October 2006 (n = 217)



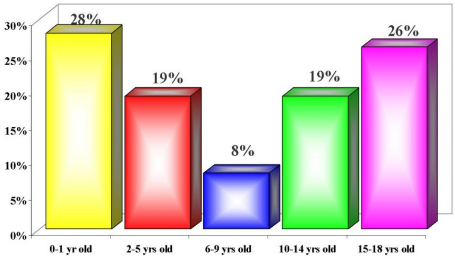
MENINGOCOCCAL CASES
Department of Pediatrics
Baguio General Hospital and Medical Center
October 2004 - October 2006, As to Gender (n = 100)



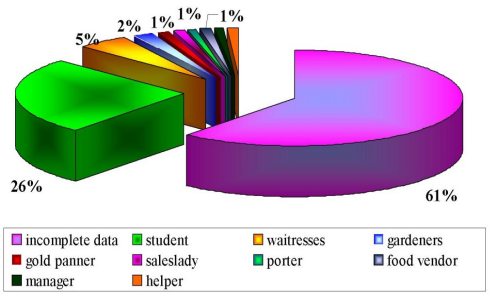
MENINGOCOCCAL CASES
Department of Pediatrics
Baguio General Hospital and Medical Center
October 2004 - October 2006, Place of Origin (n = 100)



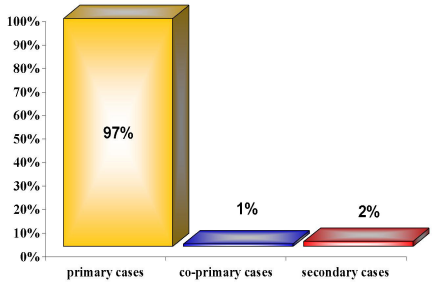
MENINGOCOCCAL CASES
Department of Pediatrics
Baguio General Hospital and Medical Center
October 2004 - October 2006, According to Age (n = 100)



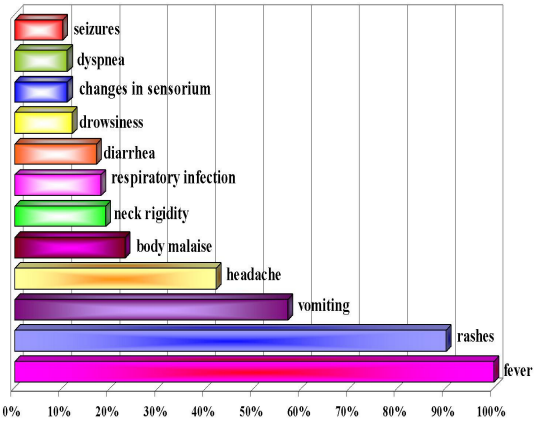
MENINGOCOCCAL CASES
Department of Pediatrics
Baguio General Hospital and Medical Center
October 2004 - October 2006, According to Occupation (n = 100)



MENINGOCOCCAL CASES
Department of Pediatrics
Baguio General Hospital and Medical Center
October 2004 - October 2006, According to Exposure (n = 100)

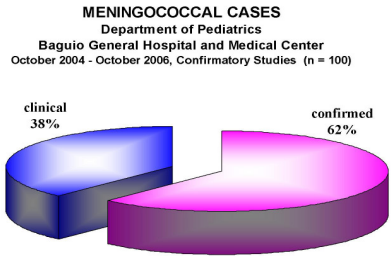


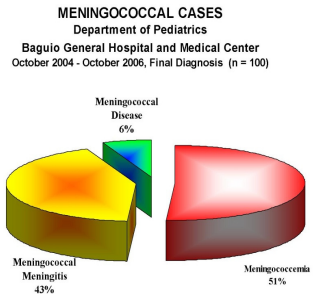
MENINGOCOCCAL CASES
Department of Pediatrics
Baguio General Hospital and Medical Center
October 2004 - October 2006, Clinical Manifestation (n = 100)

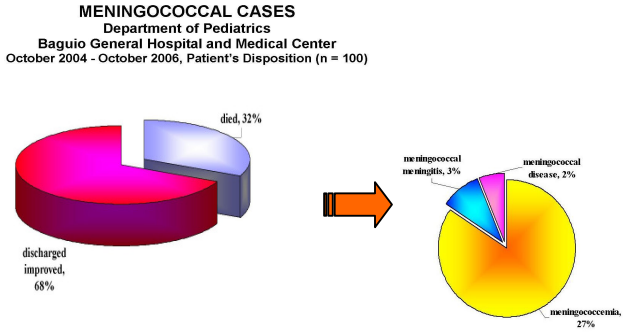


All patients (100%) had a history of fever during the course of their illness. 90% had rashes, wherein 39% were identified to be purpuric in character. 57% complained of vomiting while 42% had a history of headache. 23% had body malaise while 19% were observed to have neck rigidity. Among the study population, 18% had a complaint of some form or respiratory infection like cough, sore throat or colds while 17% had diarrhea. 12% had a history of drowsiness but 11% were observed to have changes in sensorium. 11% presented with either dyspnea, hypotension and/or cyanosis. On the other hand, 10% had seizures.

Of the total number of the study population, 62% were given a diagnosis based on confirmatory laboratory results; while 38% were given a diagnosis based on clinical signs and symptoms and/or the clinical course of their illness. Laboratory confirmatory tests included any one of the following: growth of ***Neisseria meningitidis*** in the blood or cerebrospinal fluid cultures or positive for rapid antigen detection using latex agglutination tests. Among those discharged improved, the final diagnosis of 46% were confirmed while 22% were based on clinical assessment. And, among those who died, 16% of those who were diagnosed were based on laboratory results; while, also 16% were based on history, signs and symptoms and the clinical course of the patients. 51% had a discharge diagnosis of Meningococcemia, 43% Meningococcal Meningitis while 6% were discharged as Meningococcal Disease or Meningococcemia with Meningococcal Meningitis. 68% were discharged improved while 32% died. 27% died with a diagnosis of meningococcemia while 3% had a diagnosis of meningococcal meningitis and 2% with meningococcal disease. 14% died among the children 0-1 year of age followed by 6% among the 2-5 and 15-18 years age range of the study population; giving us a 20% case fatality rate among children 0-5 years old. Data showed 3% died among children between the 6-9 and 10-14 years old age range. The cause of death of these patients was septic shock, disseminated intravascular coagulopathy. The etiologic agent was identified as a hypervirulent strain of ***Neisseria meningitidis Serogroup A Subtype A1.9*** which was reported to be sensitive to Penicillin[11].







DISCUSSION

Meningococcal disease is caused by gram negative intracellular diplococci called ***Neisseria meningitidis.*** This organism was believed to have been first reported in the early 16th century[2]. Throughout time, it has created havoc across the globe from Europe to the Americas, to Africa and then to Asia. This fulminant disease built a name in the history of science by creating major epidemics all over the world which occur every 8-15 years[1,2,3,12]. Several literature will show that the largest

epidemic occurred in 1996-1997 in sub-Saharan Africa where more than 300,000 were affected with Serogroup A meningococcal disease and 30,000 reportedly died[13]. In the year 2000, a serogroup W-135 epidemic occurred in Mecca, Saudi Arabia in association with the Hajj pilgrimage[9,12,13]. In 2005, outbreaks were reported in Asia particularly in the Philippines and India.

According to the National Epidemic Sentinel Surveillance System of the Department of Health of the Philippines, an average of 100 meningococcemia cases is reported every year, without seasonal variation[8]. In October 2004, the Baguio General Hospital and Medical Center reported an increase in the number of meningococcal disease cases. This caused unnecessary public anxiety bringing serious socio-economic effects in the area specially , since the area is a popular tourist destination. The country was not prepared socially and emotionally; health authorities though were prepared in dealing with the management of the disease. At this time, the health sector was having several trainings and workshops on how to deal with Severe Acute Respiratory Syndrome (SARS), the present crisis the world was dealing with then. The preparations being done at that time were applied in dealing with the meningococcal disease dilemma the city was faced with.

Because there was an occurrence of at least three confirmed cases in three months[3,8,10], by February 2005, the WHO declared that the Cordillera Administrative Region of the Philippines indeed had an outbreak[7]. It is worthwhile to note that in any outbreak, 80%-90% of cases are due to meningitis and 10%-20% are identified to be due to meningococcemia[2,4]. What was unusual in this outbreak was that most of the reported cases were due to meningococcemia; this study reports that 51% were diagnosed to have meningococcemia, a large proportion as compared to that which is stated by previous experiences globally.

In the United States[2], approximately 2,000 to 3,000 cases of meningococcal disease are reported: 0.8-1.3 cases per 100,000 population. Infants younger than 12 months of age have the highest rates of disease[2,16]; this study shows that 28% of the children affected were below one year of age. Incidence of disease in the United States[2] declines in early childhood, increases during adolescence and early adulthood, then declines among older adults. This investigation likewise reports a similar trend where 19% were 2-5 years old and 8% were 6-9 years old, increasing to 19% among children aged 10-14 years and still increasing to 26% among 15-18 years old adolescents. A retrospective review by Aswat, et. al.[14] on meningococcal disease among adult patients admitted in the same institution this research was done, showed that 54.54% of the study population was aged 19-28 years of age. In countries within the meningitis belt, literature[3] reports that maximum incidence is usually found among children aged 5-10 years of age; young people living in closed communities, such as boarding schools and military housing, are affected more than other individuals. The National Notifiable Disease Surveillance System (NNDSS) in Australia[9], on the other hand, reports that there has been a bimodal age distribution during the 1990's, with the highest rates in the 0-4 year age group and a second peak in the 15-25 year age group. This study in correlation with the study done by Aswat, et.al.[14] showed a similar trend.

Reports show that males and females are equally affected. Studies done in Australia[9] show that male to female ratio has consistently shown a slight male preponderance. Aswat, et.al.[14] in his review among adults show a male prevalence at 61.61%. In another study by Dacuycuy, et. al.[15] involving discharged pediatric patients with meningococcal disease in the same institution this research was done showed that 51.11% of his study population were males. This study, however, reveals that slightly more females (53%) were affected.

Meningococcal disease occurs throughout the year regardless of climate; however, there are more cases in the late winter and early spring[2,3,16]. In sub-Saharan Africa[3], the spread of infection may be enhanced by drought and dust storm; meningococcal epidemics generally stop with the onset of the rains. This study shows that there was an increasing number of cases during the cooler months of this region. Unfavorable climatic conditions may lead to overcrowding of people in poorly ventilated dwellings, where spread of the virulent meningococci is optimal[2,3,9]. Although the reasons for this seasonality are not clear, there is evidence[9] that influenza virus or *Mycoplasma pneumoniae* infections may predispose to invasive disease and transmission of meningococci. The association between acute respiratory infections and meningococcal disease has been found both in temperate and tropical climates[1,3,13]. In an epidemic in Chad in 1988[3], patients with meningococcal disease were noted to be more likely to have nasopharyngeal shedding of respiratory pathogens like *Mycoplasma hominis* and viruses like adenovirus, respiratory syncitial virus, etc. In this study, 18% had a complaint of some form or respiratory infection like cough, sore throat or colds while 17% had diarrhea. Low absolute humidity and dust may enhance meningococcal invasion by damaging the mucosal barrier directly or by inhibiting mucosal immune defenses[3].

The communicability of *Neisseria meningitidis* is generally limited. In studies[2] among households in which a case of meningococcal disease occurred, 3%-4% of these households had secondary cases but most households had only one secondary case. In adolescents and young adults[2,9], social gatherings in crowded conditions, smoking and other close personal contact may be risk factors for acquisition of the bacteria. Data in this study shows that 97% were reported as primary cases, and 2% were secondary cases. These identified secondary cases were from different households with different primary cases. 26% of the study population was identified to be students and available data identified that 13% were undergraduates working as waitresses, sales lady, manager, etc. During outbreaks, overcrowding, bar or nightclub patronage and alcohol use have also been associated with higher risk for disease[2].

Numerous sources[2,3,9,13,16] indicate that the most common clinical manifestations in meningococcemia are abrupt onset of fever, muscle and joint pains, petechial or purpuric rash, hypotension or shock, multiorgan failure. Meningococcal meningitis would present clinically as acute fever associated with meningeal or neurologic findings like headache, vomiting, nausea, changes in sensorium, drowsiness, stiff neck or even coma. This review showed that all patients (100%) had fever, 90% had rashes, wherein 39% were identified to be purpuric in character. Vomitting and headache were common symptoms. Less common were body malaise, neck rigidity and changes in sensorium.

The early diagnosis of meningococcal disease depends largely on a high index of suspicion with the help of an overall view of the epidemiology of diseases in that certain area. A growth of *Neisseria meningitidis* in the blood, CSF or skin biopsy cultures indicates infection of this virulent organism. Blood cultures are often positive in 30-75% of cases[1,9,16]; while CSF cultures are positive in 70-95%[1,9,16] of cases. Skin biopsy cultures are positive in 60-75%[1,9,16] of cases. These rates however decrease if antibiotics have already been given before specimens are taken for culture studies. This investigation showed that of the study population, 62% were confirmed by any of the following: growth of *N. meningitidis* in the blood and/or CSF or a positive rapid antigen test using latex agglutination.

The case fatality rate of invasive meningococcal disease is 9%-12% in some literature[2] but 5%-15% in others[1], even with appropriate antibiotic therapy. The fatality rate of meningococcemia is usually about 40%[2], but may increase to 50%-60% during outbreaks.

More deaths have been observed among those diagnosed with meningococcemia. The Morbidity/Mortality Weekly Review (MMWR) of the RESU of the DOH Community Health Development (CHD-CAR) reported a 25.2% case fatality rate[5]. Studies done by Padilla, et. al.[17] and Dacuycuy, et. al.[15] show a case fatality rate of 32.5% and 33.33% respectively. This review shows a case fatality rate of 32%. 27% died with a diagnosis of meningococcemia while 3% died among those who had meningococcal meningitis. 2% died among those diagnosed with meningococcal meningitis with meningococcemia. This study also showed that there were 14% deaths among those aged less than one year old increasing to 20% when the 0-5 year age range is considered. The most common cause of death of this illness, is septic shock, disseminated intravascular coagulopathy; which was the cause of death noted in this study.

CONCLUSIONS

This review showed that out of 217 patients discharged with meningococcal disease, 46.08% were pediatric patients (0 to 18 years of age). 53% were female while 64% were Baguio City residents. 28% were 0-1 year old, 19% were 2-5 years old, 26% were between the age range of 15-18 years. More than 95%were identified to be primary cases. The most common clinical manifestations of this study population were: fever (100%), rashes (90%), vomiting (57%), headache (42%), body malaise (23%), and 19% were observed to have neck rigidity. 51% were diagnosed to have meningococcemia. 62% were diagnosed with the guidance of confirmatory laboratory studies. 68% were discharged improved while 32% died. 27% died with a diagnosis of meningococcemia. The case fatality rate of this study is 32%. The most common cause of death was septic shock. The "criminal" of the largest outbreak reported in the Philippines was identified to be a very potent strain of meningococci, the ***Neisseria meningitidis Serogroup A Subtype A1.9*** sensitive to Penicillin[11].

It is recommended that any area or country should always be prepared in any event that an epidemic or even a pandemic occurs. Terror and panic can be controlled through wisdom and serenity in the implementation of emergency measures, proper dissemination of correct information, immediate and proper response of health authorities in coordination with other government and non-government agencies through proper and respectful networking. Most of all, with the commencement of emerging and re-emerging infections worldwide, our best defense has always been protection. Protection through appropriate infection control practices particularly vaccination against these perilous diseases.

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