

Trends in Mortality in Children Hospitalized with Meningococcal Infections in Albania from 2006 to 2014



Healthcare

Keywords: Meningococcal disease, meningococemia, meningitis, children, scoring system.

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Abstract

Background: Lack of vaccination and modern health care facilities in many countries including Albania let meningococemia to remain as a serious challenging disorder especially among children and in spite of improved diagnosis and earlier treatment its prognosis is still dismal. Patients expected to develop life-threatening complications in acute meningococcal infections require early recognition and appropriate monitoring. Different prognostic scoring systems have been developed. **Aim:** The aim of this study was to evaluate mortality in children hospitalized with meningococcal infections in Albania, including scoring systems in prognosticating mortality rate. **Materials and Methods:** This was a retrospective descriptive study, performed on 40 patients with definite diagnosis of meningococcal infection admitted to PICU in UHC "Mother Teresa", Tirana, Albania, between 2006 and 2014. There were 40 patients, 22(55%) males and 18(45%) females, from 2 months to 10 years old. We evaluated all the patients based on Stiehm and Damrosch and Glasgow meningococcal septicemia prognostic score. Data were collected by filling checklists. SSPS software was applied to analyze the data using chi-square test. **Results:** Overall mortality was 42%. According to the GMSPS(3) prognostic score of meningococemia: 28 (70%) patients had a score <8 points and was recorded four deaths representing a mortality rate of 14.2%; the mortality rate among 12(45%) patients with a score ≥8 points resulted in 100% mortality. The sensitivity was 100%, specificity was 100%, the positive predictive value was 100% and the negative predictive value was 100% for a GMSPS score ≥8. According to the Stiehm and Damrosch criteria (2): 22(55%) patients had two or less factors present and was recorded three deaths representing a mortality rate of 13.6%; the mortality rate among 18(45%) patients with three or more factors present the mortality rate was 72.2%. The sensitivity was 90%, specificity was 80%, the positive predictive value was 75% and negative predictive value was 92.3% for the criterion ≥3 of the Stiehm and Damrosch criteria. **Conclusions:** Meningococci are still killers, they affect men more than women. The Stiehm and Damrosch and Glasgow meningococcal septicemia prognostic score can rapidly identify children with fulminant meningococcal disease and poor prognosis and help us starting prompt administration of suitable antibiotics, critical care and special therapeutic measures.

Introduction

Meningococcal disease (MCD) is caused by a bacterial microorganism called *Neisseria meningitidis*, a member of the genus *Neisseria*, which is an obligate human-specific pathogen that preferentially colonizes the mucous membrane of the nasopharynx^[1]. Rates of meningococcal disease in the US have remained relatively stable, at approximately 0.9 to 1.5 cases per 100, 000 persons per year, or 2500 to 3000 cases per year. Meningococemia is a medical emergency, early recognition is essential so that appropriate antibiotic therapy and supportive care can be promptly instituted^[1,2]. Childhood Meningitis continues to be an important cause of mortality in many countries. Lack of vaccination and modern health care facilities in many countries including Albania let meningococemia to remain as a serious challenging disorder especially among children and in spite of improved diagnosis and earlier treatment its prognosis is still dismal^[3,4].

Meningococcal infection is a communicable disease, which is spread via pharyngeal secretion through respiratory route. Acute meningococemia generally follows an upper respiratory infection, whereby rapid clinical deterioration may occur^[5]. Meningococcal Septicemia (Meningococemia) results from the systemic

release of various mediators in response to bacteria endotoxins leading to generalized increase in capillary permeability. Meningococemia is characterized by shock and disseminated intravascular coagulation (DIC). Meningococcal septicemia is a fulminant infection (sometimes < 24 hours) with initial symptoms that are nonspecific (fever, muscle aches) and is difficult to diagnose before the onset of a maculopapular, petechial, or purpuric rash. Septicemia can result in rapid onset of hypotension, multiorgan dysfunction shock, peripheral ischemia, limb loss, and death. Meningococcal Meningitis is the invasion of the meninges and crossing of the blood-brain barrier with the sequential liberation of endotoxins and activation of pro- and anti-inflammatory cytokines are the underlying pathophysiological processes of the clinical picture from meningococcal meningitis. Overall mortality for invasive meningococcal disease is approximately 10% of infected individuals but is up to 40% in cases of septicemia^[6,7,8]. In clinical practice, meningitis and sepsis, or more often a combination of both, are the most commonly encountered conditions. The main purpose of the paediatric intensive care unit (PICU) is to prevent mortality by intensively monitoring and treating critically ill children who are considered at high risk of mortality. Since 1966, 25 specific scoring systems have been proposed to identify the degree of severity of meningococcal diseases. More than 12 prognostic scores have been developed to predict mortality^[9,10,11]. Physicians are in general poor prognosticators^[12,13]. To meet the need for a rapid clinically based assessment, several prognostic scoring systems have been devised, the most popular of which are Stiehm and Damrosch and Glasgow meningococcal septicemia prognostic score (GMSPS)^[3,4]. The importance of early recognition of meningococemia through clinical, laboratory findings and prognostic score continues to be a major concern for clinicians and especially for us.

Materials and Methods

Design: Retrospective case-note study.

Setting: Pediatric Intensive Care Unit in UHC “Mother Teresa”, Tirana, Albania.

Patients: Forty children with proven meningococcal septicemia (some with concurrent meningitis) from January 1, 2006 to December 31, 2014. We evaluated all the patients based on Stiehm and Damrosch criteria (Table.2) and Glasgow meningococcal septicemia prognostic spore (Table.3).

Table 2. Stiehm and Damrosch criteria[2]

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|--|
| 1. Petechiae present for less than 12 hours before admission |
| 2. Hypotension (systolic blood pressure< 70mm Hg) |
| 3. Absence of meningitis (<20 WBCs in CSF) |
| 4. Peripheral white blood cell count<10,000/mm3 |
| 5. ESR < 10 mm/hour |

Table 3. (GMSPS) Glasgow Meningococcal Septicemia Prognostic Score[3]

| Criteria | Score |
|---|-------|
| Hypotension* | 3 |
| Skin/rectal temperature differences>3°C | 3 |
| Base deficit (capillary sample) <8mmol/l | 1 |
| Coma score**<8 at any time or deterioration of 3 ≥ in an hour | 3 |
| Lack of meningitis | 2 |
| Parental opinion that child’s condition has become worse over the past hour | 2 |
| Widespread ecchymoses or extending lesions on review | 1 |

*Systolic BP<75mm if below4 years of age, <85 if older

** Modified pediatric coma scale. (Simpson and Reilly)

We presumed a score over 8 out of 15(GMSPS) and three or more factors out of Stiehm and Damrosch systems as fatal outcome. All patients received the same therapy on admission.

Statistical Analysis

Data analysis was conducted using SPSS 18 statistical software (SPSS Inc., Chicago, IL, USA). We compared clinical characteristics on admission between patients with meningococemia who died and those who survived. We used ROC curves to analyze sensitivity and the specificity and to highlight the positive and predictive value of our variables. Statistical significance was set at a =0.05. All statistical tests were two tailed.

Results

The age distribution of patients was as follows: 7(17.5%) < 1 year old, 27 (67.5%), 1-5 years, 6(15%), 6-10 years old (Tab.1 and Fig. 1).

Figure 1. Frequency of age.

| Age | N | % |
|-----------------|----|-------|
| <1 year old | 7 | 17.5% |
| 1-5 years old | 27 | 67.5% |
| >5-10 years old | 6 | 15% |

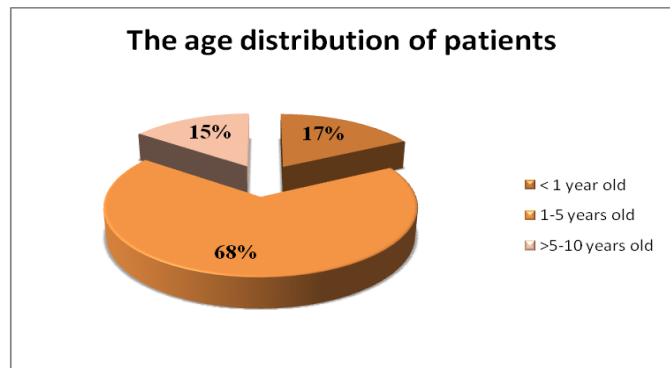


Table 1. Frequency of age

The season prevalence declined in the order of winter 5(12.5%), spring 13(32.5%), summer 7(17.5%) and fall 15(37.5%), (Tab.2 and Fig. 2).

Figure 2. The season prevalence of meningococemia

| Seasons | N | % |
|---------|----|-------|
| Winter | 5 | 12.5% |
| Spring | 13 | 32.5% |
| Summer | 7 | 17.5% |
| Fall | 15 | 37.5% |

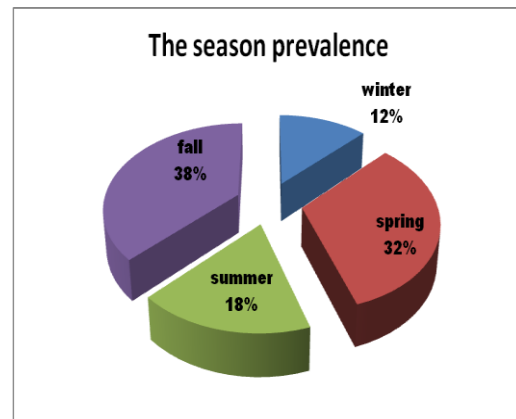


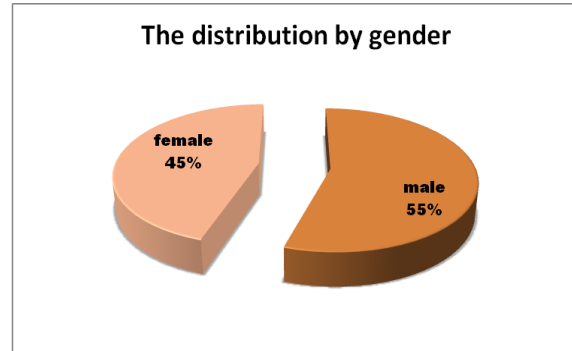
Table 2. The season prevalence of meningococemia

We found a distribution of the disease by gender in the following report: Female 18 (45 %) and male 22 (55 %), there is a preponderance of men who are more risked (Tab. 3 and Fig. 3).

| Gender | N | % |
|--------|----|-----|
| Male | 22 | 55% |
| Female | 18 | 45% |

Table 3. The distribution by gender

Figure 3. The distribution by gender



| Stiehm and Damrosch criteria | Number of patients (n,%) | Deaths (n,%) |
|--|-----------------------------|-----------------|
| Petechiae present for less than 12 hours before admission | 27 67.5% | 12 44.4% |
| Hypotension (systolic blood pressure < 70mm Hg) | 18 45% | 16 88.8% |
| Absence of meningitis (<20 WBCs in CSF) | 18 45% | 13 72.2% |
| Peripheral white blood cell count < 10,000/mm ³ | 24 60% | 15 62.5% |
| ESR < 10 mm/hour | 11 27.5% | 8 72.7% |

Table 4. Distribution of patients according to Stiehm and Damrosch criteria

| Glasgow Meningococcal Septicemia Prognostic Score | Number of patients (n,%) | Deaths (n,%) |
|---|-----------------------------|-----------------|
| Hypotension | 18 45% | 16 88.8% |
| Skin/rectal temperature differences > 3°C | 16 40% | 16 100% |
| Base deficit (capillary sample) < 8mmol/l | 16 40% | 16 100% |
| Coma score < 8 at any time or deterioration of 3 ≥ in an hour | 16 40% | 16 100% |
| Lack of meningitis | 18 45% | 13 72.2% |
| Parental opinion that child's condition has become worse over the past hour | 24 60% | 16 66.6% |
| Widespread ecchymoses or extending lesions on review | 27 67.5% | 12 44.4% |

Table 5. Distribution of patients according to Glasgow Meningococcal Septicemia Prognostic Score

Sixteen deaths were recorded, representing an overall mortality rate of 42%. None of the patients had received meningococcal vaccination. According to the GMSPS(4) prognostic score of meningococemia: 28 (70%) patients had a score <8 points and was recorded four deaths representing a mortality rate of 14.2%; the mortality rate among 12(45%) patients with a score ≥ 8 points resulted in 100% mortality. The sensitivity was 100%, specificity was 100%, the positive predictive value was 100% and the negative predictive value was 100% for a GMSPS score ≥ 8 .

According to the Stiehm and Damrosch criteria (2): 22(55%) patients had two or less factors present and was recorded three deaths representing a mortality rate of 13.6%; the mortality rate among 18(45%) patients with three or more factors present the mortality rate was 72.2%. The sensitivity was 90%, specificity was 80%, the positive predictive value was 75% and negative predictive value was 92.3% for the criterion ≥ 3 of the Stiehm and Damrosch criteria.

Discussion

Numerous studies have looked at factors predictive of poor outcome in meningococcal disease, since the seminal study of Stiehm and Damrosch in 1966, which identified petechiae, hypotension, absence of meningitis, peripheral leukopenia and low erythrocyte sedimentation rate (ESR) as markers of a poor prognosis^[15].

During the study period 2006-2014 there were 40 patients from 2 months to 10 years old. The most frequent age group was 1-5 years (67.5%), differently from other countries, where the incidence of invasive meningococcal disease in pediatric patients has two peaks: the first peak with the highest incidence in infants younger than 12 months, the second peak in adolescents^[16]. The ratio male/female was 1.3 similar to data in the literature^[17, 18].

The incidence, according to the Public Health Department, has been low, with an average of 0.24/100000 inhabitants, as it is in countries of low incidence, while the majority of meningococcal disease in European countries range in incidence from 0.2-14 cases per 100000 inhabitants^[19]. Even though the incidence was low, the mortality rate in our country remained high $\sim 42\%$, with most deaths occurring within 48 hours of admission. Many academic medical centers report overall mortality rates of 5-10%^[20].

In our study we found that, the absence of meningitis, shock and Glasgow Coma Scale ≥ 8 points as significant predictors for death. According Algreen et al.^[21] the absence of meningeal involvement was not a good predictor of mortality, and that a low white count, the presence of a rash and altered mental status, particularly coma, were sensitivity indicators of mortality. Even in our study, significant laboratory findings to predict mortality were total white blood count $< 10000\text{mm}^3$ in 62.5% of cases, skin/rectal temperature differences $>3^\circ\text{C}$ in 100% of cases, severe basis deficit in 100% of cases and low ESR. Similar data are reported in the literature^[22].

GMSPS and the Stiehm and Damrosch criteria which combine clinical and laboratory markers continue to have clinical utility^[20].

In our study, the sensitivity was 100%, specificity was 100%, the positive predictive value was 100% and negative predictive value was 100% for GMSPS score >5 , thus confirming the positive predictive value, the negative predictive value and the high sensitivity of this scoring system. For the Stiehm and Damrosch criteria >2 we found that the sensitivity was 90%, specificity was 80%, positive predictive value was 75% and negative

predictive value was 92.3%, meaning that this scoring system is accurate in identifying patients with good outcome, as good as predicting poor outcome.

Regarding this severe presentation in our country, we lack data about the serotype of meningococcal. Given that from our results, none of the patients had a history of meningococcal vaccination, we believe that identifying the unfavorable prognostic factors helps to decrease the mortality rate, but the best way is preventing infection through meningococcal vaccination, which raises the need for meningococcal vaccination in our country.

Conclusions

The GMSPS is a rapid clinical score that performs well in identifying children with poor prognosis and is an easily performed, repeatable, clinical score that can rapidly identify children with fulminant meningococcal disease. We recommend that every physician who treats patients with meningococemia must consider the prognostic alarms, GMSPS score system.

Conflict of Interest Statement

No conflict of interest was declared. This article was not sponsored by any external organization.

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