Original article

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CLINICAL AND LABORATORY FINDINGS AS PROGNOSTIC FACTORS OF MENINGOCOCCEMIA (2006-2010)

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Objective - Through our study we sought to evaluate clinical and laboratory findings as prognostic factors for meningococcemia in our country, and the predictive value of the Stiehm and Damrosch criteria and the Glasgow Meningococcal Septicemia Prognostic score (GMSPS).

Material and methods - This is a retrospective study. We evaluated the clinical and laboratory findings for all patients: age, presence of meningitis, presence of shock, time of petechial presentation, white blood cell count, platelet count, erythrocyte sedimentation rate (ESR), base deficit, and their relation to the mortality of these patients. To assess the severity of meningococcal septicemia we used two scores: the Stiehm and Damrosch criteria and GMSPS.

Results - Twenty-five patients were admitted to the Pediatric Intensive Care Unit (PICU) with meningococcemia during the study period. Ten deaths were recorded, representing an overall mortality rate of 40%. Sixteen cases (64%) were associated with meningitis. All patients with thrombocytopenia <40000/mm^3 died within 24 hours. Leucopenia was found in 64% of patients, 63% of them with fatal outcome. All deceased patients had a base deficit >8mEq/l. The sensitivity was 100%, specificity was 100%, positive predictive value was 100% and negative predictive value was 100% for a score >5 of GMSPS. For Stiehm and Damrosch (>2 criteria) the sensitivity was 90%, specificity was 80%, positive predictive value was 75% and negative predictive value was 92.3%.

Conclusion - Leucopenia, thrombocytopenia, severe basis deficit, low ESR rate, absence of meningitis and shock were significant findings, predicting mortality in these patients. Both prognostic scores, Stiehm and Damrosch and GMSPS, were accurate in identifying patients with good outcome and predicting poor outcome, without statistical significance between them.

Key words: Meningococcemia ▪ Prognostic factors ▪ Laboratory findings

Introduction

Meningococcemia represents a relevant worldwide health problem. Despite the progress in patient management it remains a severe disease, associated with significant mortality (1-3), therefore it warrants special consideration for a clear understanding of the disease as well as the familiarity with the management strategies (3, 4).

Several investigators have identified unfavourable prognostic factors in patients with meningococcal septicemia using clinical and laboratory findings at the time of hospitalization, in order to validate a bedside model and scoring system for prognosis in meningococcal disease (1, 5-9). Older and new scores seem to be comparable. The determination of prognostic factors and the development of scoring systems has helped to identify those patients with meningococcal infection who require a higher level of intervention, resulting in improved survival in patients predicted to die (3, 4). This is likely to be due to improved quality of management (aggressive volume replacement, ventilation, inotropic support) and possibly some of the newer therapies that have been introduced in recent years.

The Stiehm and Damrosch criteria (10) and the Glasgow meningococcal septicemia prognostic score (GMSPS) (11) are clinically based scoring systems that can be calculated rapidly and repeated frequently if required and are used to predict mortality in the intensive care unit. Over the years reevaluation of the scoring systems has been undertaken for their predictive value (12-14).

Through our study we sought to evaluate clinical and laboratory findings as prognostic factors for meningococcemia in our country, and the predictive value of Stiehm and Damrosch and GMSPS.

Material and methods

This is a retrospective study. Collection of data was done from the medical records of patients with a definite diagnosis of meningococcal septicemia who were admitted to the Pediatric Intensive Care Unit (PICU) at the "Mother Theresa" University Hospital Centre in Tirana over the period 2006 - 2010. For all patients we evaluated the clinical and laboratory findings: age, presence of meningitis, presence of shock (BP <75 mmHg systolic, age ≤4 years; <85 mmHg systolic, age >4 years), time of petechial presentation, white blood cells count, platelets count, erythrocyte sedimentation rate (ESR), base deficit, and their relation to mortality. To assess the severity of meningococcal septicemia we used two scores: the Stiehm and Damrosch criteria (Table 1) and the Glasgow Meningococcal Septicemia Prognostic score (Table 2).

Table 1 Stiehm and Damrosch criteria* (10)

Criterion	Feature
1	Petechiae present for less than 12 hours before admission
2	Hypotension
3	Absence of meningitis (<20 WBC[1] in CSF[2])
4	Peripheral white blood cell count <10,000/mm^3
5	ESR[3] <10 mm/hour

*The presence of three or more features indicates a >85% chance of dying, while patients with two or less features have a fatality rate of <10%; [1]WBC – White Blood Count; [2]CSF – Cerebrospinal Fluid; [3]ESR – Erythrocyte sedimentation rate.

Table 2 Glasgow Meningococcal Septicemia Prognostic score*(11)

Feature	Points
BP** < 75 mm Hg systolic, age ≤ 4 y; <85 mm Hg systolic, age > 4 y	3
Skin/rectal temperature difference > 30 °C	3
Modified coma scale score < 8 or deterioration of ≥ 3 points in 1 hour	3
Absence of meningism	2
Extending purpuric rash or widespread ecchymoses	1
Base deficit (capillary or arterial) > 8.0	1
Maximum score	15

*A score > 7 points had a specificity of 100% and a positive predictive value of 100%; **BP – Blood pressure.

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 meningococcemia 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. The risk of death was analyzed by means of Binary logistic regression analysis and chi-squared test. Statistical significance was set at $\alpha \leq 0.05$. All statistical tests were two tailed.

Results

Twenty-five patients were admitted to the PICU with meningococcemia during the study period, with an average incidence (according to the Public Health Department) of 0.24/100000 inhabitants. Most patients were older than 1 year old (92%), range 0 – 10 and the most frequent age group was 2-5 years old. (OR = 0.53, 95% CI 0.28 to 0.96; p =0.0079). The ratio male/female was 1.8. Ten deaths were recorded, representing an overall mortality rate of 40%. None of the patients had received meningococcal vaccination. The mortality rate among patients less than 1 year old was higher compared to patients older than 1 year old (OR=6.3, 95%CI 0.9 – 43.6, p =0.06)

Sixteen cases, or 64% of them, were associated with meningitis. The odds ratio for death in patients with meningococcemia with meningitis compared to patients with meningococcemia without meningitis, was 0.01 (OR =0.01, 95% CI: 0 to 0.2; p <0.001). Thirteen cases (52%) presented with shock and severe acidosis, in 11 (44%) cases it was necessary to use inotropic agents and in 10 (40%) cases even hydrocortison. ($\chi 2$=12.3; p <0.01).

The appearance of petechial and ecchymotic elements <12 hours was found in 17 cases, 41% (7 cases) of whom with fatal outcome. The odds ratio for the time of petechial presentation <12 hours in comparison to the time of petechial presentation >12 hours was 1.2 (OR=1.2, 95% CI 0.2 to 16.5; p =0.8).

Thrombocytopenia with <40000 platelet/mm3 was found in 5 cases. Fatal outcome occurred within 24 hours for all cases ($\chi 2$=6.5; p =0.01). Leucopenia was found in 64% (16 cases) of patients, 63% of them with fatal outcome ($\chi 2$=6.9; p <0.01), but all deceased patients had leukopenia. Fourteen cases (56%) presented with base deficit >8 mEq/l and 71% of them with fatal outcome. All deceased patients (100%) had the base deficit >8 mEq/l. ($\chi 2$= 10.2; p<0.01). Six patients presented with low ESR (<10 mm/hour), 5 of them died ($\chi 2$=4.03; p =0.04) (Table 3).

Table 3 Clinical and laboratory findings and their relation to mortality

Clinical and laboratory findings	Patients n (%)	Mortality rate n[1]/n (%)	χ^2 p
Presence of meningitis	16 (64)	2/16 (13)	11.0; <0.01
Without meningitis	9 (36)	8/9 (89)	
Without shock	12 (48)	0/12 (0)	12.3; <0.01
Presence of shock	13 (52)	10/13 (77)	
Time of petechial presentation			
< 12 hours	17 (6)	7/17 (41)	0.06; 0.7
≥ 12 hours	8 (32)	3/8 (37)	
Glasgow Coma Scale			
< 8 points	20 (80)	5/15 (0)	6.5; 0.01
≥ 8 points	5 (20)	5/5 (100)	
White blood count < 10000/mm^3	16 (64)	10/16 (63)	6.9; <0.01
≥ 10000/mm^3	9 (36)	0/9 (0)	
Platelets count < 40000/mm^3	5 (20)	5/5 (100)	6.5; 0.01
≥ 40000/mm^3	20 (80)	5/20 (20)	
Base deficit ≥ 8 mEq/l	14 (56)	10/14 (71)	10.2; <0.01
< 8 mEq/l	11 (44)	0/11 (0)	
Erythrocyte sedimentation rate			
< 10 mm/hour	6 (24)	5/6 (83)	4.03; 0.04
≥ 10 mm/hour	19 (76)	5/19(26)	
Stiehm and Damrosch			
≥ 3 criterion	12 (48)	9/12 (75)	9.1; <0.01
< 3 criterion	13 (52)	1/13 (8)	
GMSPS[2]			
< 8 points	16 (64)	1/16 (6)	
≥ 8 points	9 (36)	9/9 (100)	17.3; <0.01
Complications			
Renal failure	7 (28)	7/7 (100)	11.3; <0.01
DIC[3]	11 (44)	6/11 (54)	0.81; 0.36
Profound tissues necrosis	3 (12)	0/3 (0)	0.77; 0.37
Leg amputation	1 (4)	0/1 (0)	0.04; 0.83

[1]Number of deaths; [2]Glasgow Meningococcal Septicemia Prognostic score; [3]Disseminated intravascular coagulation.

Disseminated intravascular coagulation (DIC) was a complication in 11 cases, 54% of them with fatal outcome (OR=1.2, 95%CI: 0.4 to 11.5; p =0.3). According to the Stiehm and Damrosch criteria (13), when three or more factors were present, the mortality rate was 75%. When two or less factors were present, the mortality rate was 8%. The sensitivity was 90%, specificity was 80%, the positive predictive value was 75% and negative predictive value was 92.3% for the criterion >2 of the Stiehm and Damrosch criteria (Fig. 2).

According to the GMSPS prognostic score of meningococcemia: 16 (64%) patients had a score <8 points and only one death was recorded representing a mortality rate of 6%; the

mortality rate among 9 (36%) 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 >5. Pairwise comparison of ROC curves for both scoring system results had no statistical difference (p =0.17) (Fig. 3).

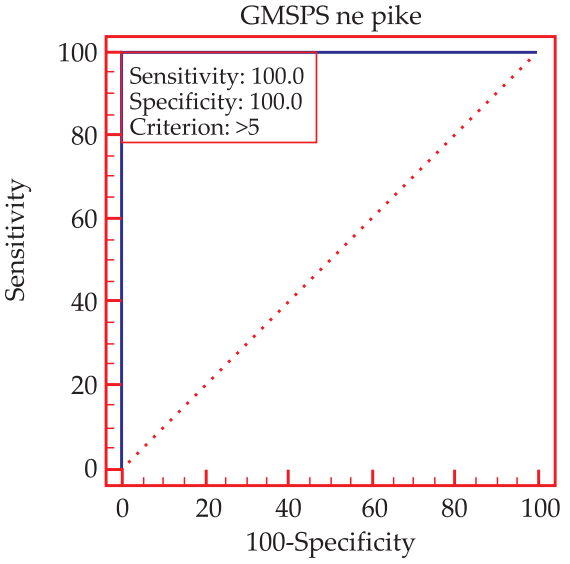

Fig. 1 *Roc curve for GMSPS scoring*

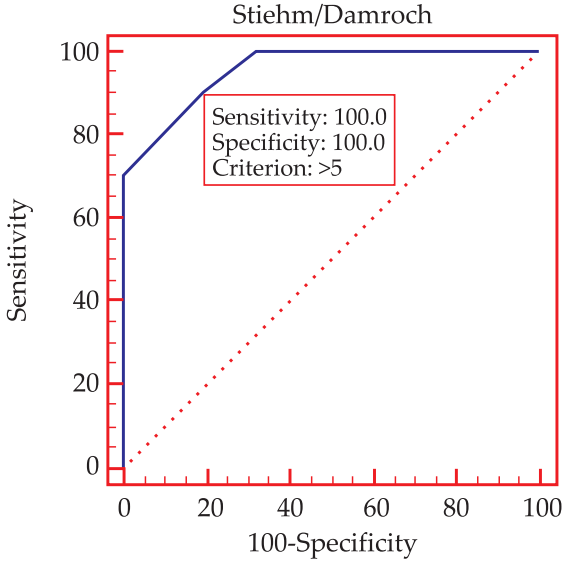

Fig. 2 *Roc curve for Stiehm Damrosch scoring*

Discussion

During the study period 2006–2010 at our PICU 25 cases presented with meningococcemia. The incidence during the last five years has been low, with an average of 0.24/100000 inhabitants (according to the Public Health Department), as it is in countries of low incidence, while the majority of meningococcal diseases in European countries range in incidence from 0.2 to 14 cases per 100000 inhabitants (15).

The most frequent age group was 2-5 years (60%), differently from other countries, where the incidence of invasive meningococcal disease in pediatric patients has 2 peaks: the 1st peak with the highest incidence in infants younger than 12 months, the 2nd peak in adolescents (3). The ratio male/female was 1.8 similar to data in the literature (16, 17).

Even though the incidence was low, the mortality rate in our country remained high - 40%, with most deaths occurring within 48 hours of admission. Many academic medical centers report overall mortality rates of 5-10% (8). In the USA it ranges from 10% in adolescents to 20% in infants (6). But even in industrialized countries the mortality rate can exceed 40% and can approach 70% in developing countries, depending on the clinical presentation (2, 18).

In our study, 64% of cases were associated with meningitis. Analyzing the clinical findings with binary logistic regression analysis we found the absence of meningitis, shock and Glasgow Coma Scale ≥8 points as significant predictors for death. The time of petechial presentation <12 hours did not result in a significant predictor for mortality.

According Algreen et al. (14) 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 sensitive indicators of mortality.

Even in our study, significant laboratory findings to predict mortality were total white blood count <10000mm3 in 100% of cases, thrombocytopenia in 50%, severe basis deficit in 100% of cases and low ESR. Similar data are reported in the literature (5, 6).

Over the years, re-evaluation of GMSPS showed that its positive predictive value has changed (12-14). Shah and Mathew (12) found that while the sensitivity of GMSPS remained 100%, the positive predictive value has fallen to 38% if the threshold value is >7, or 45.5% if the threshold value is >9. In our study, the sensitivity was 100%, specificity was 100%, the positive predictive value was 100% and negative predictive value was 100% for a GMSPS score >5, thus confirming the positive predictive value, the negative predictive value and the high sensitivity of this scoring system.

Re-evaluation (13) of the other scoring system, the Stiehm and Damrosch criteria, found that this scoring system was accurate in identifying patients with good outcome, but less good at predicting poor outcome. According to our study for this scoring we found that the sensitivity was 90%, specificity was 80%, positive predictive value was 75% and negative predictive value was 92.3% for Stiehm and Damrosch criteria >2, 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. As we discussed before, the mortality rate still remains very high, which is why vaccines are currently used in many countries, as an important form of prevention. 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.

Conclusion

Leucopenia, thrombocytopenia, severe basis deficit, low ESR rate, absence of meningitis and shock were significant findings, predicting mortality in these patients. Both prognostic scores, Stiehm and Damrosch and GMSPS, were accurate in identifying patients with good outcome and predicting poor outcome, without a statistical significance between them.

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