Prognostic Factors in Meningococcal Disease

Development of a Bedside Predictive Model and Scoring System

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Context.—Meningococcal disease is associated with significant morbidity and mortality. Development of a prognostic model based on clinical findings may be useful for identification and management of patients with meningococcal infection.

Objectives.—To construct and validate a bedside model and scoring system for prognosis in meningococcal disease.

Design.—Prospective, population-based study.

Setting.—Twenty-four hospitals in the metropolitan area of Barcelona, Spain.

Patients.—A total of 907 patients with microbiologically proven meningococcal disease. Patients diagnosed with meningococcal disease from 1987 through 1990 were used to develop the prognostic model, and those diagnosed in 1991 and 1992 were used to validate it.

Outcome Measures.—Clinical independent prognostic factors for mortality in meningococcal disease. The association between outcome and independent prognostic factors was determined by logistic regression analysis. A scoring system was constructed and tested using receiver operating characteristic curves.

Results.—Among 624 patients in the derivation set, 287 (46%) were male, the mean age was 12.4 years, and 34 patients (5.4%) died. Among 283 patients in the validation set, 124 (43.8%) were male, the mean age was 12.7 years, and 17 patients (6.0%) died. In multivariate analysis, independent predictors of death were hemorrhagic diathesis (odds ratio [OR], 101; 95% confidence interval [CI], 30-333), focal neurologic signs (OR, 25; 95% CI, 7-83), and age 60 years or older (OR, 10; 95% CI, 3-34), whereas receipt of adequate antibiotic therapy prior to admission was associated with reduced likelihood of death (OR, 0.09; 95% CI, 0.02-0.4). Hemorrhagic diathesis was scored with 2 points, presence of focal neurologic signs with 1 point, age of 60 years or older with 1 point, and preadmission antibiotic therapy was scored as −1. The clinical scores of −1, 0, 1, 2, and 3 or more points were associated with a probability of death of 0%, 2.3%, 27.3%, 73.3%, and 100%, respectively.

Conclusions.—Hemorrhagic diathesis, focal neurologic signs, and age of 60 years or older were independent predictors of death in meningococcal disease, whereas receipt of adequate antibiotic therapy was associated with a more favorable prognosis. The scoring system presented is simple, is based on findings readily available at the bedside, and may be useful to help guide aggressive therapy.

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MENINGOCOCCAL disease has been feared for decades by physicians and the public, not only because of the speed with which it can spread through the community, but also because of its occasionally overwhelming nature. The knowledge that meningococcal disease can cause death within hours has conferred on it the reputation of a lethal illness, even though meningococcal disease was not invariably fatal even before serotherapy became available.[1] Forming a correct judgment of the probable outcome for patients with meningococcal disease is a complex process. Reports from the preantibiotic era mention hopeless clinical situations, such as those involving extensive cutaneous bleeding,[2] shock,[3] coma,[3] extreme ages of life, and delay in instituting serotherapy.[4]

A new approach to prognosis began in 1966 when Stiehm and Damrosch[5] developed a predictive model for meningococcal disease using the following features: petechiae, shock, meningitis, blood leukocyte count, and erythrocyte sedimentation rate. Since then, several scoring systems have been developed and usually have been based on a combination of clinical and laboratory parameters.[6-16] However, laboratory results are not available when the physician first sees the patient, and, to our knowledge, previous scoring systems have not been validated. Because a prognostic score based on exclusively clinical parameters would be desirable, we developed and validated a bedside model to predict outcome for patients with meningococcal disease.

METHODS

Study Setting

We performed a prospective, population-based study in the metropolitan area of Barcelona (Mancomunitat de Municipis de l' Area Metropolitana de Barcelona) from January 1, 1987, through December

Table 1.—Characteristics of Patients With Meningococcal Disease

Clinical Parameter	No. (%) of Patients: Primary Series* (n=624)	Secondary Series* (n=283)	P Value
Age, y			
<15	465 (74.5)	210 (74.2)	
15-59	124 (19.9)	55 (19.4)	.90
≥60	35 (5.6)	18 (6.4)	
Female sex	337 (54.0)	159 (56.2)	.59
Comorbid condition present‡	20 (3.2)	9 (3.2)	.85
Upper respiratory tract infection	245 (39.3)	107 (37.8)	.73
Received preadmission antibiotics	223 (35.7)	96 (33.9)	.71
Meningeal signs	296 (47.4)	132 (46.6)	.88
Shock	84 (13.5)	38 (13.4)	.92
Hemorrhagic diathesis	22 (3.5)	11 (3.9)	.93
Focal neurologic signs	23 (3.7)	9 (3.2)	.85
Coma	32 (5.1)	14 (4.9)	.96
Clinical form of meningococcal disease			
Subacute	144 (23.1)	65 (23.0)	
Acute	448 (71.8)	202 (71.4)	.94
Fulminant	32 (5.1)	16 (5.7)	
In-hospital antibiotic treatment			
Penicillin	454 (72.8)	159 (56.2)	
Third-generation cephalosporins	160 (25.6)	124 (43.8)	<.001
Other§	10 (1.6)	0 (0)	
Interval between hospital admission and therapy, mean (SD), min	24.9 (17.8)	23.9 (20.1)	.87
Deaths	34 (5.4)	17 (6.0)	.85
Cause of death			
Multiorgan failure	26 (76.5)	13 (76.5)	
Cerebral edema	5 (14.7)	2 (11.8)	.92
Myocarditis	3 (8.8)	2 (11.8)	

*Data from the primary series of patients were used to derive the model, and data from the secondary series of patients were used to validate the scoring system.
†*P* values from χ^2 test with continuity correction.
‡Comorbid conditions were considered to be present when the patient had one of the following: liver cirrhosis (12 patients), cancer (7 patients), autoimmune disease (3 patients), acquired immunodeficiency syndrome (2 patients), complement deficit (2 patients), chronic renal failure (1 patient), neutropenia (1 patient), and previous splenectomy performed (1 patient).
§Other antibiotic treatments were chloramphenicol (for 8 patients) and imipenem (for 2 patients).

31, 1992. This area includes 23 municipalities with 24 hospitals in and around Barcelona in an area of 407.2 km^2 (157.22 square miles); the population of this area was 3 002 012 in 1986 and 2 948 311 in 1991.

Case Identification and Incidence

A case was considered as meningococcal disease when *Neisseria meningitidis* was isolated from blood culture, cerebrospinal fluid culture, or both. Meningococci were identified as previously described.[17] Cases detected from January 1, 1987, through December 31, 1990, were used to derive the scoring system, and those diagnosed from January 1, 1991, through December 31, 1992, were used to validate the new scoring system. The average annual incidence rate was calculated as (the number of cases × 100 000/population)/number of years studied.

Definitions

The interval from onset of the symptoms and signs until therapy (interval of symptoms to therapy, IST) was the elapsed time between the appearance of the first symptom or sign attributable to meningococcal disease and the institution of antibiotic therapy in the hospital. When the precise beginning of symptoms could not be determined, the onset of illness was assumed to be the mean interval between the last time the patient was seen asymptomatic by a household member or the primary physician and the first time he or she was seen ill.

Shock was defined as persistent hypoperfusion and an initial systolic blood pressure of less than 70 mm Hg in children younger than 12 years or an initial systolic blood pressure less than 85 mm Hg or a decrease of 60 mm Hg from the previous measured blood pressure in patients aged 12 years or older that required fluid therapy, vasoactive drugs, or both for at least 24 hours or until death.[18] On the basis of the IST and the presence of shock at the time of admission to the hospital, meningococcal disease was classified in 3 clinical forms: fulminant (IST <7 hours with shock), acute (IST <7 hours without shock, IST >24 hours with shock, or IST between 7 and 24 hours [with or without shock]), and subacute (IST >24 hours without shock).

Preadmission receipt of adequate antibiotic therapy was only considered when the patient had received at least 1 adequate dose of antibiotics active against *N meningitidis* at intervals considered adequate from a therapeutic point of view and without an interval of longer than 12 hours between the last dose administered and admission to the hospital.

Coma was defined by a Glasgow Coma Scale score of 6 or less in the absence of sedative treatment.[19] For children, a modified pediatric coma scale was used,[20] and coma was defined by a score less than 8. If sedative therapy had been administered, the data for coma were considered as missing.

Hemorrhagic diathesis was defined as spontaneous clinically apparent bleeding, including bleeding from wounds, hematoma, hematuria, spontaneous gingival bleeding, epistaxis, or gastrointestinal or gynecological bleeding together with perivenipuncture bruises or venipuncture bleeding at the time of establishing venous access. The diagnosis of hemorrhagic diathesis was made irrespective of the presence of petechiae and once prior coagulation disorders or anticoagulant therapy had been ruled out by assessing patient's medical history.

Focal neurologic signs were defined as motor, sensory, or cranial nerve disturbances of central origin that were not present before the episode of meningococcal disease.

Deaths were attributed to meningococcal disease if the patient died within 7 days of receiving in-hospital antimicrobial therapy and had a clinical course that suggested persistent infection or if death occurred during the phase of acute infection.

Data Collection

The following data were collected at the time of admission to the hospital for use in the prognostic analysis: age, sex, comorbid conditions, upper respiratory tract infection on admission or during the 5 days prior to admission, preadmission antibiotic therapy, clinical form of meningococcal disease, meningeal signs, hemorrhagic diathesis, coma, and focal neurologic signs. All data were collected daily and were entered into a computerized database. Each patient, the person(s) living with him or her, and the hospital physician were contacted personally to obtain and confirm clinical data, including information on outcome.

Data Analysis

All dichotomous variables (including converted ones), without problems of collinearity, were entered in a logistic regression model to identify independent predictors of outcome. The risk was quantified using odds ratios (ORs) with 95% confidence intervals (95% CIs). Reference categories were those with the patients hav-

ing the lowest case-fatality rate. For preadmission adequate antibiotic therapy, the reference category was the one with the highest case-fatality rate to determine any beneficial effect. After identifying independent predictors, points were assigned to each prognostic factor by dividing the coefficient of each predictor (from the logistic regression analysis) by the smallest coefficient, then rounding each quotient to the nearest integer. Finally, we calculated a prediction score for each patient by summing the total number of points. Sensitivity, specificity, positive and negative predictive values, and overall accuracy of each score were calculated.

Receiver operator characteristic (ROC) curves[21] were constructed by a series of cut points from both the derivation and validation sets. Both curves were analyzed by calculating the area under ROC curves and their 95% CIs to establish if model prediction was better than chance prediction.[22] Discrimination, the ability to separate patients with and without the outcome of interest, was compared using the distribution of predictions for patients with and without the outcome of intent (dead vs alive). Reliability, the concordance between predicted and observed outcomes, was analyzed by grouping the patients into quintiles of predicted risk and comparing the observed prevalence of the outcome in each quintile with the expected value.

Statistical analyses were performed with the SPSS-PC+ statistical package.[23] The χ^2 test, with Yates correction when indicated, and the Fisher exact test were used to compare categorical qualitative variables. The Student t test was used for comparison of continuous qualitative and quantitative variables. Logistic regression analysis was performed with the EGRET statistical package, using the backwards elimination procedure.[24] The goodness of fit of the logistic regression model was tested with the Hosmer-Lemeshow test[25] and with appropriate indications when some columns had no observed values.[26,27]

RESULTS

Primary Series of Patients: Derivation Set

A total of 651 cases of meningococcal disease were diagnosed in the Barcelona metropolitan area from 1987 through 1990 (average annual incidence rate, 5.47/100 000 inhabitants). Twenty-six cases (4.0%) identified by surveillance were excluded because of incomplete data; also excluded was 1 patient who died because of anaphylaxis to penicillin. Of 624 cases available for analysis, there were 287 male (46.0%) and 337 female cases (54.0%) with a mean (SD) age of 12.4 (18.7) years (median, 4.9 years; range, 31 days to 89 years). Two hundred twenty-three patients (35.7%) had received antibiotics before admission, mainly because of upper respiratory tract infection. Preadmission adequate antimicrobial agents included β-lactams (mostly amoxicillin alone or combined with clavulanic acid [98 patients]), oral second-generation and third-generation cephalosporins (59 patients), macrolides (49), trimethoprim-sulfamethoxazole (9), quinolones (6), and others (2). Four hundred thirty-seven patients (70.0%) had petechiae. Thirty-four patients (5.4%) died, and the average annual mortality rate was 0.28 per 100 000.

Table 2.—Prognostic Factors in Meningococcal Disease: Summary of Univariate Analysis for Patients in the Derivation Set

Clinical Parameter	No. (%) of Patients: Survivors (n=590)	Nonsurvivors (n=34)	OR (95% CI)*	P Value†
Age, y				
<15‡	450 (96.8)	15 (3.2)	. . .	. . .
15-59	113 (91.1)	11 (8.9)	2.92 (1.18-7.00)	.007
≥60	27 (77.1)	8 (22.9)	8.89 (2.97-24.55)	<.001
Sex				
Male‡	272 (94.8)	15 (5.2)	. . .	. . .
Female	318 (94.4)	19 (5.6)	1.08 (0.51-2.34)	.82
Comorbid condition				
Absent‡	579 (95.9)	25 (4.1)	. . .	. . .
Present	11 (55.0)	9 (45.0)	18.95 (6.24-54.96)	<.001
Upper respiratory tract infection				
Present‡	240 (98.0)	5 (2.0)	. . .	. . .
Absent	350 (92.3)	29 (7.7)	3.98 (1.49-13.32)	.003
Preadmission antibiotic				
Not taken‡	369 (92.0)	32 (8.0)	. . .	. . .
Taken	221 (99.1)	2 (0.9)	0.10 (0.01-0.42)	<.001
Meningeal signs				
Present‡	285 (96.3)	11 (3.7)	. . .	. . .
Absent	305 (93.0)	23 (7.0)	1.95 (0.89-4.52)	.07
Shock				
Absent‡	529 (98.0)	11 (2.0)	. . .	. . .
Present	61 (72.6)	23 (27.4)	18.13 (7.97-42.95)	<.001
Hemorrhagic diathesis				
Absent‡	582 (96.7)	20 (3.3)	. . .	. . .
Present	8 (36.4)	14 (63.6)	50.92 (17.26-154.02)	<.001
Focal neurologic signs				
Absent‡	575 (95.7)	26 (4.3)	. . .	. . .
Present	15 (65.2)	8 (34.8)	11.79 (3.92-32.65)	<.001
Coma				
Absent‡	571 (96.5)	21 (3.5)	. . .	. . .
Present	19 (59.4)	13 (40.6)	18.60 (7.33-45.62)	<.001
Clinical form of meningococcal disease				
Subacute‡	140 (97.2)	4 (2.8)	. . .	. . .
Acute	432 (96.4)	16 (3.6)	1.30 (0.41-5.41)	.44
Fulminant	18 (56.3)	14 (43.8)	27.22 (7.28-121.83)	<.001

*OR indicates odds ratio; CI, confidence interval; and ellipses, data not applicable.
†P values from χ^2 test with continuity correction.
‡Reference category.

Table 3.—Prognostic Factors in Meningococcal Disease: Results of Multivariate Analysis

Variable	Coefficient	Standard Error	OR (95% CI)*	P Value	Points†
Preadmission antibiotic	−2.42	0.81	0.09 (0.02-0.43)	.003	−1
Age, y‡					
15-59	0.81	0.55	2.24 (0.77-6.56)	.14	0
≥60	2.31	0.63	10.08 (2.95-34.48)	<.001	1
Focal neurologic signs	3.20	0.62	24.60 (7.25-83.49)	<.001	1
Hemorrhagic diathesis	4.61	0.61	100.70 (30.44-332.8)	<.001	2

*OR indicates odds ratio; and CI, confidence interval.
†Each coefficient was divided by 2.42 and the quotient rounded to the nearest integer to determine the number of points assigned to that independent predictor.
‡The age group of 0 to 14 years (reference category) had a score of 0 points.

Baseline clinical characteristics of the patients at the time of admission to the hospital, the interval between admission and therapy, the in-hospital antibiotic treatment, and the ultimate cause of death are shown in Table 1. Results of univariate analysis for the clinical parameters are shown in Table 2. The presence of comorbid conditions, shock, hemorrhagic diathesis, focal neurologic signs, coma, the fulminant form of meningococcal disease, and age greater than 15 years were associated with a poor outcome at the univariate level, whereas the presence of upper

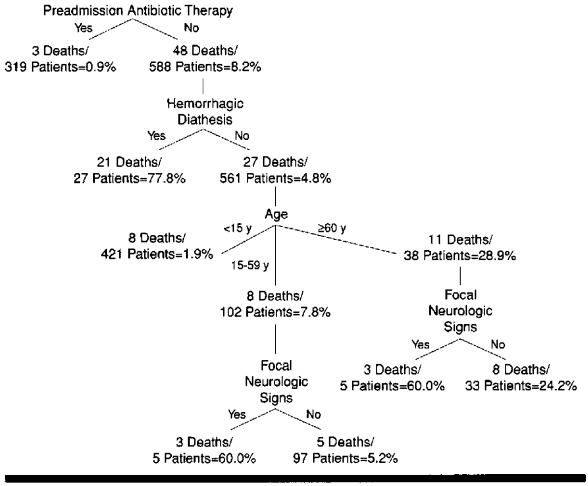

Figure 1.—Algorithm of probability of death in meningococcal disease related to the presence or absence of predictors of death. The fraction expresses the number of deaths/the number of patients with condition, equal to the case-fatality rate.

respiratory tract infection and adequate preadmission antibiotic therapy were associated with a favorable outcome.

Multivariate analysis identified the following independent predictors of poor prognosis in descending order: hemorrhagic diathesis, focal neurologic signs, and age of 60 years or older (Table 3). The clinical form of meningococcal disease and coma were excluded from the multivariate model because of collinearity. Preadmission adequate antibiotic therapy was associated with a favorable prognosis. Although the Hosmer-Lemeshow statistic was not computed for 10 deciles of risk because some cells had zero values, we grouped the observed and expected values in 3 categories ($P=.73$) and found these values to be similar. On the basis of the logistic regression coefficients, 2 points were assigned for hemorrhagic diathesis, 1 point for focal neurologic signs, and 1 point for age of 60 years or older. Receipt of preadmission adequate antibiotic therapy was assigned −1 point (Table 3). The clinical scores ranged from −1 to 3. No patient scored 4 points.

The patients were grouped according to the risk of death based on the presence of predictors of death in a mortality algorithm (Figure 1). Patients with the highest probability of dying were those with hemorrhagic diathesis, whereas those with no predictor of death and who had received preadmission adequate antibiotics had the best prognosis.

Secondary Series of Patients: Validation Set

A total of 298 cases of meningococcal disease were diagnosed in the Barcelona metropolitan area in 1991 and 1992 (average annual incidence rate, 5.01/100 000 inhabitants). Fifteen cases (5.0%) identified by surveillance were excluded from the study because of incomplete data. Of 283 cases available for analysis, there were 124 males (43.8%) and 159 females (56.2%) with a mean (SD) age of 12.7 (18.5) years (median, 5.1 years; range, 45 days-81 years). Ninety-six patients (33.9%) had received preadmission antimicrobials, including β-lactams (mostly amoxicillin alone or combined with clavulanic acid [45 patients]), oral second-generation and third-generation cephalosporins (23), macrolides (24), trimethoprim-sulfamethoxazole (3), and quinolones (1). Two hundred one patients (71.0%) had petechiae. Seventeen patients (6.0%) died, and the average annual mortality rate was 0.29 per 100 000. There were no differences between patients in the primary and secondary series (Table 1), except for an increase in the proportion of patients treated with third-generation cephalosporins in the validation set. However, there were no significant differences between patients treated with penicillin and those who received third-generation cephalosporins with respect to case-fatality rate, both in the derivation set (4.85% vs 7.5%; $P=.33$) and in the validation set (5.7% vs 6.4%; $P=.97$).

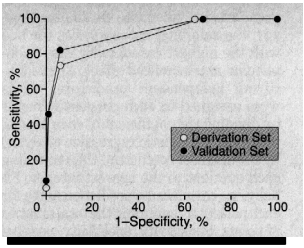

Figure 2.—Receiver operating characteristic curves of bedside scoring system using prognostic factors in meningococcal disease: comparison between derivation set and validation set.

After examining different clinical scores (Table 4), we chose a score of 2 or greater for our final model because of its highest overall accuracy (96.1%). Prospective validation revealed that a score of 2 or greater had positive and negative predictive values of 80.0% and 96.7%, respectively. No patient with a score greater than 2 points survived. The areas under the ROC curves for the derivation set and the validation set were 0.89 (95% CI, 0.83-0.95) and 0.91 (95% CI, 0.83-0.99), respectively (Figure 2). No statistically significant differences were found when comparing both curves ($P=.36$). The reliability and the discriminatory power of the model was good. The distribution of predicted likelihood of death for patients in the validation set who died was as follows: mean, 0.81; median, 0.95; 10%, 0.04; and 90%, 0.95. For survivors, these data were mean, 0.17; median, 0.04; 10%, 0.00; and 90%, 0.95. The probability of death for the 907 study patients according to the observed score is shown in Table 5.

COMMENT

Even in developed countries, meningococcal disease is a serious disease with a significant case-fatality rate (approximately 5% in several studies[6,12,16]). To our knowledge, our model and scoring system are the first validated instruments that predict the outcome in patients with microbiologically proven meningococcal disease. Death was reliably predicted by the presence of hemorrhagic diathesis, focal neurologic signs, and age of 60 years or older, and by the absence of receiving adequate antibiotic therapy prior to admission. These data can be obtained easily by the physician or another well-trained health professional (eg, a nurse or paramedic) and not just in the hospital emergency area, but even in the physician's office or the patient's home.

Table 4.—Clinical Parameters for Prediction of Outcome in Meningococcal Disease: Comparison of Models With Different Prediction Scores

Prediction Score	Primary Series* Sensitivity	Specificity†	PPV‡	NPV‡	Overall Accuracy	Secondary Series* Sensitivity	Specificity†	PPV‡	NPV‡	Overall Accuracy
≥−1	100	. . .	5.4	. . .	5.4	100	. . .	6.0	. . .	6.0
≥0	100	34.1	8.0	100	37.7	100	33.1	8.7	100	37.1
≥1	73.5	94.6	43.9	98.4	93.4	82.4	94.0	46.7	98.8	93.3
≥2	47.1	99.0	72.7	97.0	96.2	47.1	99.2	80.0	96.7	96.1
≥3	2.9	100	100	94.7	94.7	5.9	100	100	94.3	94.3

*For the primary series, the derivation set included 624 patients. For the secondary series, the validation set included 283 patients.
†Ellipses indicate data not applicable.
‡PPV indicates positive predictive value (probability of death); and NPV, negative predictive value (probability of not dying).

The goodness of fit of the logistic regression model could not be calculated because in several groups of deciles of risk there were zeros, a situation quite frequent when logistic regression models are validated.[25] Thus, following Hosmer-Lemeshow methods,[26,27] we found that observed and expected values were similar, thereby giving validity to our model. Had the scoring system been used for all our patients, the outcome would have been predicted correctly in 96.1% of the patients. Furthermore, the lower 95% confidence limits of the ROC curves are 83% in both the derivation set and the validation set, indicating that the model prediction is better than chance prediction.[22]

The ability to predict the likelihood of death may be helpful in the management of patients with suspected meningococcal disease to prioritize the transfer of the patient to the hospital, prioritize admission to an intensive care unit, classify patients according to their prognosis, and institute experimental therapies. According to our scoring system, a patient with a score of 1 point or more should have priority for admission to an intensive care unit to maximize surveillance and detect complications early or to treat complications that have occurred. For these patients, extremely aggressive management may be necessary, even with therapies such as monoclonal antibodies, immunomodulators, leukapheresis, and plasmapheresis.[28-30] With a high cutoff value and a score validated as almost ideal, this aim is theoretically attainable. However, any study of new forms of management of meningococcal disease should have strict entry criteria to ensure that treatment and control groups are of equal disease severity. Our predictive model and scoring system may be useful for such an assessment and may help to improve understanding and communication between health care staff (eg, to express the severity of the disease or to stratify patients in clinical trials). Moreover, our scoring system is readily interpretable by the clinician and, because it is based entirely on data available at the bedside, may be applicable in the important initial stages before and at the time of admission to the hospital.

Table 5.—Probability of Death According to Observed Score

Prediction Score	Deaths, No./ Patients, No.	Case-Fatality Rate, %	OR (95% CI)*	P Value
−1	0/287	0	0 (0-0.6)	.02
0†	12/533	2.3	1 (. . .)	. . .
1	15/55	27.3	16.3 (6.6-40.1)	<.001
≥2‡	24/32	75.0	119.4 (40.4-368.9)	<.001

*OR indicates odds ratio; and CI, confidence interval.
†Reference category. Ellipses indicate data not applicable.
‡A total of 22 of the 30 (73.3%) patients who scored 2 points died. The 2 patients who scored 3 points died.

Although most of the predictors identified have been previously recognized as factors of prognostic importance in meningococcal disease,[5-7,9-12,31-34] one novel aspect of our model is the independent association with preadmission adequate antibiotic therapy. However, in our patients, out-of-hospital antimicrobials usually were given to treat symptoms that clinicians thought represented an upper respiratory tract infection and were administered orally and at doses not usually used to treat meningococcal disease. However, our findings suggest that preadmission adequate antibiotic therapy was associated with a beneficial effect in these patients, as other authors have reported.[35,36] Preadmission antibiotic therapy is the only prognostic factor that can be modified; therefore, when a diagnosis of meningococcal disease is considered, antimicrobials should be initiated, especially when the distance to the hospital is substantial.

Although previous studies have examined symptoms, signs, and abnormal laboratory values as predictors of the outcome in meningococcal disease, a number of studies failed to validate the clinical usefulness of many of these predictors[5-7,11-13,28,31,33] and multivariate analyses of possible independent predictors of outcome have not been performed in others.[5,6,8,14,31,38] Some studies are only applicable to certain forms of the disease (meningococcemia or meningitis)[14,32] or to selected populations (children or adults)[11,16,31,33]; in others, scores have been chosen arbitrarily.[6,10,14] In contrast, our multivariate model was an accurate predictor of outcome in all forms of meningococcal disease and all age groups, since age was an independent predictor of death. We also validated the usefulness of our scoring system prospectively.

Laboratory test values have been included in many scoring systems of meningococcal disease[6-7,9-11,16,31,32] and have the theoretical advantage of early detection of relevant pathophysiological alterations for which they frequently represent surrogate markers, such as thrombocytopenia or low fibrinogen level in consumption coagulopathy or acidosis in shock. In other cases, laboratory studies are used as confirmatory tests of abnormalities that usually can be diagnosed on clinical grounds. Except for selected measurements, obtaining laboratory data is often only possible in the hospital setting and is frequently time-consuming. Moreover, even when laboratory tests improve a bedside clinical score, the improvement is seldom great. Because laboratory parameters cannot be included in the initial evaluation of the patient, the goal of our model was to use simple clinical findings, which can be easily assessed at the bedside by physicians or health care workers who first attend the patients, for prognostic purposes. The simplicity of our predictive model and scoring system makes it more clinically suitable than laboratory or mixed laboratory and bedside scores; consequently, it may be useful in developing countries, which are most affected by meningococcal disease.

The complexity of the pathophysiological mechanisms leading to multiple organ failure and the diversity of causes of death in meningococcal disease make it highly unlikely that a simple formula will predict death or survival in all cases. However, the most powerful predictors of death identified in our study clearly point to 2 main causes: death from a neurologic cause (focal neurologic signs) and death secondary to the systemic effects of infection (hemorrhagic diathesis).

The results of our study should be interpreted in the light of several potential limitations. First, even though we believe our findings are generally applicable in meningococcal disease, such generalizations should be made with caution. Our results may not apply to cases without microbiological proof of infection. Preadmission antibiotic therapy is the most common cause of microbiologically unproven meningococcal disease,[37,38] and the case-fatality rate is generally lower in this form of disease.[35,36,38] In addition, our findings must be validated in a population of this kind because the use of preadmission antibiotic therapy alters the clinical presentation of meningococcal disease.[35,36,38]

Second, recall bias may have affected some of our data: patients, relatives, or both were asked to recall symptoms or signs at the time of admission to the hospital. If recall bias existed, we believe it would cause a nondifferential misclassification. Because nondifferential misclassification bias tends to skew results toward nonassociation, this potential bias should not have invalidated our positive findings.

In summary, we derived and validated a clinical model that can predict the outcome of meningococcal disease. The scoring system is based on readily observable bedside findings, may be useful to help guide intensive therapy, and may provide a useful tool for evaluating the impact on survival of new therapeutic strategies.

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