Vital prognostic factors of mortality in bacterial meningitis in Meknes, Morocco 2004-2015

Sanah Essayagh, PhD [1], Meriem Essayagh DVM, PhD [2], and Touria Essayagh, PhD [3]

Laboratory of Biochemistry and Neuroscience[1], Faculty of Science and Technology Settat, University Hassan I, Department of Bacteriology and Parasitology [2], Teaching Military Hospital Rabat, University Mohamed V, and Epidemiology Cell of the Prefecture of Meknes [3], Ministry of Health, Morocco

Abstract

Infectious bacterial meningitis occured at an incidence rate of 3 per 100.000 populations in Morocco in 2012. Hence, this disease is a serious threat to public health forcing physicians to notify all meningitis cases to the Moroccan "Direction d'Epidémiologie et de Lutte contre les Maladies" via surveillance epidemiology cells spread throughout the Kingdom in an attempt to prevent epidemic scenarii. Bacterial meningitis is an inflammatory disease of the meninges and the cerebrospinal fluid that can be caused by bacterial infection through three main vectors namely *Neisseria meningitidis*, *Haemophilus influenzae*, and *Streptococcus pneumonia*. Mass vaccination programs targeting *Haemophilus influenzae* and *Streptococcus pneumonia* have been introduced in 2007 and 2010 respectively in Morocco. Despite these preventive measures lethality ratios kept increasing since 2004 in Meknes from 12.7%, 18.8% to 23.2% between 2007-2009, 2010-2012 and 2013-2015 respectively. However there is to our knowledge no study characterizing the predictor factors of mortality for a better management of cases. Hence, we sought to analyze data collected over the last 12 years in the epidemiology cell of Meknes to improve meningitis case management in Meknes.

Methods

Protocol of the surveillance system for meningitis in Meknes. Surveillance for meningitis has been established in Meknes following the guidelines established by the Health Ministry of Morocco in accordance with a generic protocol developed by the World Health Organization. Thence, the surveillance program is enforcing the referral of suspected and confirmed cases of meningitis to the provinces' public hospitals. Between January 2004 and December 2015, 271 cases were reported to the epidemiology cell of Meknes.

Case-record forms and data collection. Case-record forms were used to collect data on patient's symptoms and signs on admission, outcome and neurological capacities at discharge. Putative meningitis was diagnosed by sudden onset of intense headache, fever, nausea, vomiting, photophobia and stiff neck. In addition, later neurological signs were also recorded such as lethargy, delirium, coma, and/or convulsion. However infants may have illness without sudden onset of stiff neck but may instead present with bulging fontanel. Patients with presumed bacterial meningitis were given third-generation cephalosporin as primary care treatment. Laboratory investigation of cerebrospinal fluid (CSF), obtained by lumbar puncture, allowed confirmation of meningitis cases and differentiation of the bacterial types of meningitis. Abnormalities of the CSF during meningitis episodes typically comprise pleocytosis, hyperproteinorachia (>3 g/L) and hypoglycorrhachia (>0.2 g/L). Culture of CSF to identify the pathogen that cause meningitis — *Neisseria meningitidis* (meningococcus), *Streptococcus pneumoniae* (S.p.), and *Haemophilus influenzae* type b (Hib) — allowed positive cases of meningitis to be classified as CMM when meningococcal meningitis was confirmed, pneumococcal meningitis and *Haemophilus influenzae* meningitis respectively. Cases were classified as probable bacterial meningitis (PBM) when the CSF displayed at least one of the following features: i. cloudy or purulent aspect of the CSF; ii. CSF leucocyte count >100 cells/µL; iii. CSF leucocyte count of 10-100 cells/µL associated with hyperproteinorachia or hypoglycorrhachia; iv. positive Gram coloration. Cases were classified as presumed meningococcal meningitis (PMM) when the CSF was purulent and the Gram coloration was negative. Cultures where bacterial growth did not match any of the previous criteria were classified as bacterial meningitis with unidentified pathogen.

Data analysis. We conducted a case series study over 12 years to characterize the predictor factors of mortality caused by bacterial meningitis in Meknes. We included all patients admitted in the hospitals of Meknes and for whom meningitis was probable or confirmed. Statistical analysis was performed using Epi Info 7 and Excel 2007. The outcome variable of interest was death. Univariate analysis and logistic regression were conducted to identify vital prognostic factors. The statistical significance of the results obtained was assessed using confidence interval of the estimated odds ratios and the Pearson chi-squared test. The significance threshold was set at $p \leq 0.05$. Quantitative data were expressed as mean and standard deviation (SD) and qualitative data as percentages.

Conclusion

During this analytical study that we performed on the 271 cases reported in Meknes between 2014 and 2015 only conscious alteration, coma and PMM were identified as predictor factors of mortality. Surprisingly the analysis did not highlight any association between the delay before admission and death. This is not concordant with previous results described in the literature. This absence of association in this analysis could be explained by the fact that these delays are reported in days in our current system of surveillance and not hours as is usually done in the literature. Indeed, hourly data are not registered in our reporting system. This has certainly introduced a limit in the study of predictor factors of death. Nevertheless, fulminant bacterial meningitis that lead to death within hours remains impossible to predict and there is not any strategy to prevent its occurrence; in these special instances, delays before admission are not important.

Results

Hospital patient enquiry	Variables	N	Survivors	Deceased	p-value
Total in-patients—no. (%)		271 (100)	234 (86.3)	37 (13.7)	
Delay before admission in days—mean ± SD		3.2±4.8	3.2±4.9	3.2±3.8	0.98
Delay admission/lumbar puncture—mean ± SD		0.8±1.3	0.7±1.3	1.2±1.6	0.05
Patients median length of stay in days— mean ± SD		9.4±12.7	10.0±13.3	5.6±7.7	0.01
Age in years—median (Q1; Q3)		6 (1; 19)	5 (0; 15)	28 (7; 44)	<0.001
Age in years—mean ± SD		14.2±19.1	12.0±17.9	28.0±20.9	
Sex —no. (%)	Male	156 (57.6)	139 (89.1)	17 (10.9)	0.12
	Female	115 (42.4)	95 (82.6)	20 (17.4)	
Residence area —no. (%)	Urban	219 (80.8)	189 (86.3)	30 (13.7)	0.96
	Rural	52 (19.2)	45 (86.5)	7 (13.5)	
Host health structure—no. (%)	Public	254 (93.7)	221 (87.0)	33 (13.0)	0.23
	Private	17 (6.3)	13 (76.5)	4 (23.5)	

For qualitative variables, the Pearson chi-square test was used to measure the association between the dependent variable and the independent variables when the conditions for the test were valid. For quantitative variables, a test of comparison of two means was conducted. P-values were considered to be significant when less than 0.05. IQR: interquartile range [Q1-Q3]

Table 1: Meningitis patients' socio-demographic characteristics between 2004 and 2015 in Meknes, Morocco.

		Total patients (N=271)	Survivors (N=234)	Deceased (N=34)	p-value
Symptoms on presentation		**no. (%)**	**no.**	**no.**	
Body temperature ≥38°C		195 (72.0)	161	34	0.01
Vomiting		162 (66.1)	129	23	0.42
Neck stiffness		153 (56.5)	128	25	0.14
Convulsions		49 (18.1)	41	8	0.54
Headache		120 (44.3)	102	18	0.56
Purpura		40 (14.8)	29	11	0.01
Bulging fontanel		20 (7.4)	18	2	0.62
Photophobia		74 (27.3)	65	9	0.66
Indices of CSF inflammation		**no./no. evaluated (%)**	**no.**	**no.**	
Positive CSF culture		52/210 (24.8)	46	6	0.38
Positive soluble bacterial antigen		56/140 (38.8)	49	7	0.91
Proteinorachia	≥3 g/liter	40/239 (16.7)	35	5	0.36
	<3 g/liter	199/239 (83.3)	183	16	
Glycorrhachia	≥0.2 g/liter	178/241 (73.9)	163	15	0.79
	<0.2 g/liter	63/241 (26.1)	57	6	
Score on Glasgow scale		**no.**	**no.**	**no.**	
<14 (conscious alterations)		17	13	4	0.001
<8 (coma)		8	4	4	0.001
Meningitis case classification		**no.**	**no.**	**no.**	
CMM		60 (22.1)	54	6	0.83
PMM		45 (16.6)	32	13	0.006
Haemophilus		20 (7.4)	19	1	0.42
Pneumococcus		19 (7.1)	16	3	0.54
PBM		137 (46.8)	113	14	1

For qualitative variables, the Pearson chi-square test was used to measure the association between the dependent variable and the independent variables when the conditions for the test were valid. For quantitative variables, a test of comparison of two means was conducted. P-values were considered to be significant when less than 0.05. Abbreviations: CSF: cerebrospinal fluid, CMM: confirmed meningococcal meningitis, PMM: presumed meningococcal meningitis, PBM: presumed bacterial meningitis.

Table 2: Meningitis patients' clinical features between 2004 and 2015 in Meknes, Morocco.

	Bivariate analysis	Multivariate analysis, model 1	Multivariate analysis, model 2
	COR (p-value)	AOR (p-value)	AOR (p-value)
Patients' median length of stay in days	0.91(0.01)	0.87 (0.006)	0.89 (0.007)
Age in years	1.03 (<0.001)	1.04 (<0.001)	1.03 (0.006)
Body temperature ≥38°C	5.13 (0.01)	2.38 (0.33)	******
Purpura	2.99 (0.01)	0.48 (0.33)	******
Conscious alterations	15.60 (<0.001)	4.49 (0.012)	5.36 (0.003)
Coma	29.37 (<0.001)	21.00 (0.012)	21.76 (0.003)
CMM	0.89 (0.83)	0.45 (0.31)	0.36 (0.18)
Haemophilus	3.27 (0.006)	9.16 (0.005)	6.42 (0.004)
Pneumococcus	1.51 (0.54)	1.1 (0.92)	1.01 (0.98)
PBM	1	1	

COR: crude odds ratio; AOR: adjusted odds ratio

Table 3: Multivariate odd ratios (p-value) for mortality caused by bacterial meningitis infection, 2004-2015, Meknes, Morocco.

Acknowledgments

No private funding was used to conduct this work.