Clinical & Experimental Pathology

Essayagh et al., J Clin Exp Pathol 2017, 7:4
DOI: 10.4172/2332-0877.1000318

Research Article OMICS International

Vital Prognostic Factors of Bacterial Meningitis in Morocco: A 12-year Study

Essayagh T[1*], Essayagh M[2] and Essayagh S[3]

[1]*Laboratoire de bactériologie, Hôpital Militaire d'instruction Mohamed-V, Rabat, Morocco*

[2]*Military Teaching Hospital Mohamed V, Rabat, Morocco*

[3]*Faculty of Sciences and Techniques, University Hassan Ist, Settat, Morocco*

[*]**Corresponding author:** Touria Essayagh, Laboratoire de bactériologie, Hôpital Militaire d'instruction Mohamed-V, Rabat, Morocco, Tel: 00212669679966; E-mail: essayagh.toula@gmail.com

Received date: July 04, 2017; **Accepted date:** July 22, 2017; **Published date:** July 26, 2017

Abstract

Objectives: Bacterial meningitis remains a life-threatening public health risk in Meknes with the lethality ratio surprisingly increasing from 12.7%, 18.8% to 23.2% in 2007-2009, 2010-2012 and 2013-2015 respectively. However, to our knowledge, there are no published studies analyzing predictor factors of mortality explaining this increase in meningitis-induced mortality in Meknes. Hence, the objective was to identify the predictor factors of mortality of bacterial meningitis in Meknes in order to enhance the case management system.

Study Design: Case series study.

Methods: We conducted a case series study of surveillance data from Meknes collected in 2004-2015 and performed analysis by 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.

Results: The total number of reported meningitis cases was 271. The median age was 6 years. The sex ratio male/female was 1.4. The average case fatality rates per 100.000 populations were 0.35, 0.43 and 0.78 between 2007-2009, 2010-2012 and 2013-2015 respectively. The vital prognostic factors are conscious alterations (AOR: 5.36; p=0.003), probable meningococcal meningitis (AOR: 6.42, p=0.004) and coma (AOR: 21.76, p<0.0001).

Conclusions: All vital prognostic factors we identified are late factors. Unfortunately, the delay before admission to the hospital is reported in days in our current surveillance program and was not found to be a vital prognostic factor. This is probably introducing a limit in the analysis. Hence, to better characterize the underlying factors leading to death, we propose to adjust our management of cases by ensuring delays before admission are shortened and reported within hours and not days. We propose to tackle meningitis by: (i) shortening admission delays, (ii) improving early case management; (iii) strengthening prevention efforts.

Keywords: Meningococcal meningitis; Predictor factors; Meknès; Morocco

Introduction

Infectious bacterial meningitis occurs at an incidence rate of 3 per 100.000 populations in Morocco in 2012 [1]. 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 [2,3]. 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* [4]. Mass vaccination programs targeting *Haemophilus influenzae* and *Streptococcus pneumonia* have been introduced in 2007 and 2010 respectively in Morocco [5]. 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 [1]. 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 and 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). CSF cultures were performed to identify the bacterial vectors of meningitis i.e. *Neisseria meningitidis* (meningococcus), *Streptococcus pneumoniae* (Sp.), and *Haemophilus influenzae* type b (Hib); they allowed positive cases of meningitis to be classified as MMC when meningococcal meningitis was confirmed, pneumococcal meningitis, and *Haemophilus influenzae* meningitis respectively. Cases were classified as presumed 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.

Results

Socio-demographic characteristics of the studied population

Between 2014 and 2015, a total of 271 cases of meningitis were reported in the prefecture of Meknes; 38.7% of total cases were classified as meningococcal meningitis. The median age was 6 years ($p<0.001$). The sex ratio male/female was 1.4. Delay before admission was 3.2 ± 4.8 days. The delay between admission and lumbar puncture was 0.8 ± 1.3 ($p=0.05$). Length of stay at the hospital was 9.4 ± 12.7 days ($p=0.01$). 80.8% of patients were urban residents. 93.7% of total cases were treated in public hospitals (Table 1). The average case fatality rates per 100.000 populations were 0.35, 0.43 and 0.78 between 2007-2009, 2010-2012 and 2013-2015 respectively.

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
Patients median length of stay in days-mean ± SD		9.4 ± 12.7	10.0 ± 13.3	5.5 ± 7.7	0.01
Age in years-mediane (Q1; Q3)		6 (1.0;19.0)	5 (0;15)	28 (7;44)	<0.001
Mean ± SD		14.2 ± 19.1	12.0 ± 17.9	28.0 ± 20.9	
Delay admission/lumbar puncture mean ± SD		0.8 ± 1.3	0.7 ± 1.3	1.2 ± 1.6	0.05
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.					

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

Clinical feature of bacterial meningitis patients in Meknes

Symptoms on presentation: In 72.0% of cases, meningitis was associated with a febrile state (p=0.01). Other symptoms registered upon admission were vomiting (56.1%), neck stiffness (56.5%), convulsions (18.1%), headache (44.3%), purpura (14.8%; p=0.01), a bulging fontanel (7.4%) and photophobia (27.3%). On admission, 27.0% (p<0.001) of patients presented with conscious alterations and 11.4% (p<0.001) were in coma (Table 2).

		Total patients (N=271)	Survivors (N=234)	Deceased (N=37)	p-value
Symptoms on presentation		no. (%)	no.	no.	
Body temperature ≥ 38°C		195 (72.0)	161	34	0.01
Vomiting		152 (56.1)	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)		73 (27.0)	44	29	<0.001
<8 (coma)		31 (11.4)	10	21	<0.001
Meningitis case classification					
CMM		60 (22.14)	54	6	0.83
PMM		45 (16.6)	32	13	0.006
Hémophilus		20 (7.38)	19	1	0.42
Pneumococcus		19 (7.01)	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, 2004-2015, Meknes, Morocco.

Indices of CSF inflammation: Biochemical and cytological CSF analyses are key tests for diagnosing bacterial meningitis. These emergency tests have been conducted as soon as possible. Lumbar punctures were performed in 210 cases. CSF indices of inflammation that were evaluated included pleocytosis, hyperproteinorachia, hypoglycorrhachia, positive CSF cultures and/or the detection of positive soluble bacterial antigens in the CSF using a latex agglutination test, and the appearance of CSF cultures (clear, cloudy, hematic, purulent). Results are summarized in Table 2. In all cases, CSF pleocytosis was recorded. Bacterial meningitis was confirmed with pathogen identification in the CSF or in blood cultures and/or with the presence of soluble bacterial antigens when the latex agglutination test was available. Briefly, 210 samples of CSF were cultured: 24.8% were positive for bacterial growth. In parallel, the latex agglutination test evaluating the presence of soluble bacterial antigen in the CSF show that out of 140 samples tested for agglutination, 56 were positive (38.8%; Table 2). In 9.1% of the cases, CSF culture was not performed suggesting under-estimations in reported results.

Multivariate analysis

Three independent variables were kept in the final model. The severity of these 3 clinical features upon admission was the factor the most associated to death. These 3 factors were conscious alterations (AOR: 5.36; p=0.003), probable meningococcal meningitis (AOR: 6.42, p=0.004) and coma (AOR: 21.76, p<0.0001) (Table 3).

	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	15.6 (<0.001)	4.49 (0.012)	5.36 (0.003)

Coma	29.37 (<0.001)	21 (<0.001)	21.76 (<0.001)
CMM	0.89 (0.83)	0.45 (0.31)	0.36 (0.18)
PMM	3.27 (0.006)	9.16 (0.005)	6.42 (0.004)
Hémophilus	0.42 (0.42)	0.32 (0.49)	0.31 (0.45)
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.

Discussion

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 [6-8]. 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 their occurrence [9]; in these special instances, delays before admission are not important. Hence, to better characterize the underlying factors leading to death, we propose to adjust our management of cases by ensuring delays before admission are shortened and reported within hours and not days. We propose to tackle meningitis by: (i) shortening admission delays, (ii) improving early case management; (iii) strengthening prevention efforts.

References

1. Moroccan-Government (2010) Guide de la lutte contre les méningites bactériennes communautaires. In: Ministry of Health M.
2. Faucon R, Halatchev N, Zannotti P, Lefevre M, Menard M, et al. (1969) Cerebrospinal meningitis in Fes en 1966-1967. II. Epidemics of Fes. Medecine tropicale : revue du Corps de sante colonial 29: 308-329.
3. Olyhoek T, Crowe BA, Achtman M (1987) Clonal population structure of Neisseria meningitidis serogroup A isolated from epidemics and pandemics between 1915 and 1983. Rev Infect Dis 9: 665-692.
4. Sabatini C, Bosis S, Semino M, Senatore L, Principi N, et al. (2012) Clinical presentation of meningococcal disease in childhood. J Prev Med Hyg 53: 116-119.
5. Moroccan-Government (2013) Programme National d'Immunisation-Aspects pratiques de la vaccination-Manuel de formation. In: Ministry of Health M.
6. Proulx N, Frechette D, Toye B, Chan J, Kravcik S (2005) Delays in the administration of antibiotics are associated with mortality from adult acute bacterial meningitis. QJM 98: 291-298.
7. Koster-Rasmussen R, Korshin A, Meyer CN (2008) Antibiotic treatment delay and outcome in acute bacterial meningitis. J Infect 57: 449-454.
8. Namani S, Milenkovic Z, Kuchar E, Koci R, Mehmeti M (2012) Mortality from bacterial meningitis in children in Kosovo. J Child Neurol 27: 46-50.
9. Radetsky M (2014) Fulminant bacterial meningitis. Pediatr Infect Dis J 33: 204-207.