

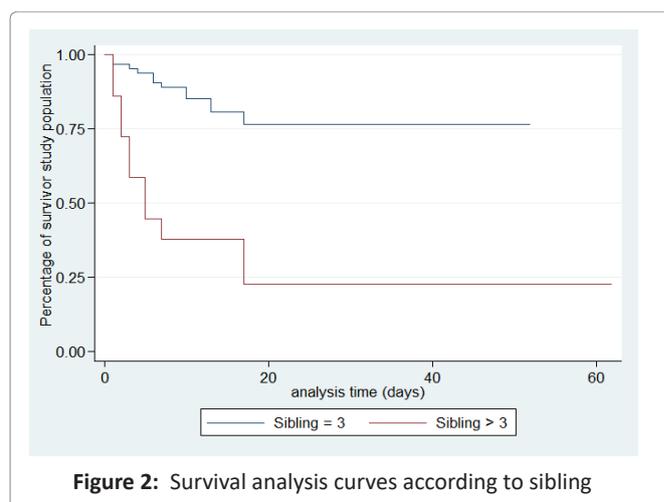
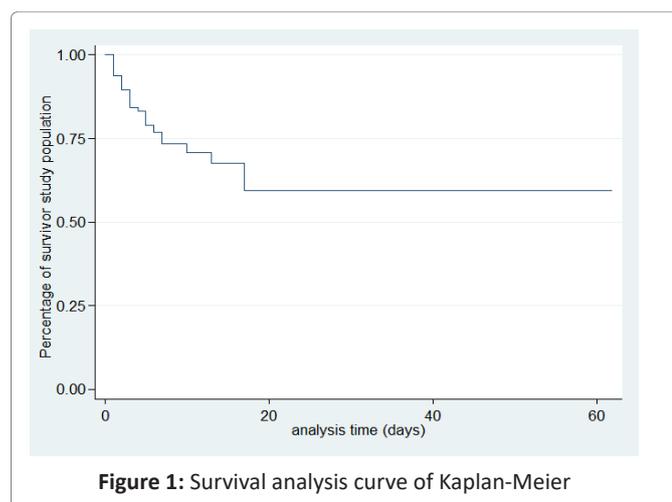
Table 3: Univariate analysis of laboratory parameters

CSF exam	Categories	Cases (32)		Controls (64)		P	OR	IC à 95%
		n	%	n	%			
Germs/ Organisms	<i>N. meningitidis</i>	11	34.38	1	1.56	<0.001*	33	3.00- 361.95
	<i>S.pneumoniae and others**</i>	21	65.63	63	98.44			
CSF glucose	> 20 mg/dl	16	50	39	60.94	0.307		
	≤ 20 mg/dl	16	50	25	39.06			
CSF protein	≤ 400 mg/l	9	28.13	10	15.63	0.147		
	> 400 mg/l	23	71.88	54	84.38			

*Fisher exact test
 **Only *Streptococcus pneumoniae* and *Neisseria meningitidis* were found in the cases, other germs are *Streptococcus B*, *Staphylococcus aureus* and *E. coli*, no *Haemophilus* was found.

Table 4: Adjusted odds ratio of factors associated with BM death

Variables	P	Adjusted OR	95% CI
Age	-		
Sibling	0,003	14,48	2,53- 82,95
Crowding	0,021	9,31	1,39- 62,29
Time before hospitalisation	0,023	9,26	1,36 – 62,92
Altered consciousness	<0,001	47,74	6,24- 364,96
Organism : <i>Neisseria Meningitidis</i>	0,017	36,68	1,90 – 704,97



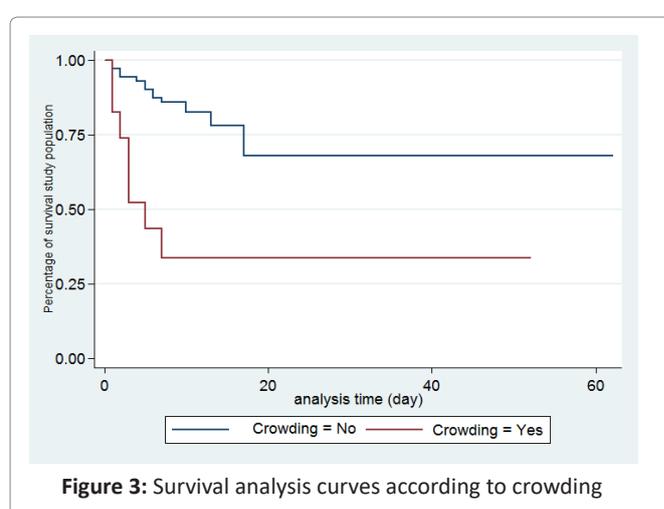
Survival Analysis

In our series, the median duration of hospitalization was 11 days with a maximum of 62 days. For the cases, this median duration is 4, 5 days versus 14 days for the controls. There was a gradual decrease in the survival curve; the decline is most important during the first 5 days (Figure 1)

According to the existence of factors associated with death, survival is shorter if the number of siblings is more than three, with crowding, altered consciousness, and when the causative organism is meningococcal meningitis (Figures 2-6).

Discussion

The mean childhood BM mortality is around 5%



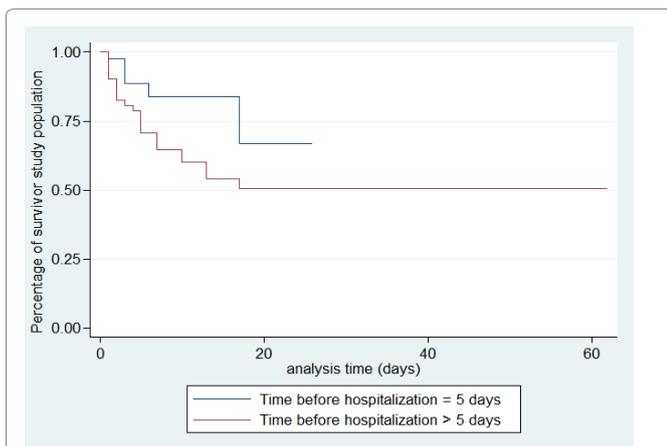


Figure 4: Survival analysis curves according to time before hospitalization

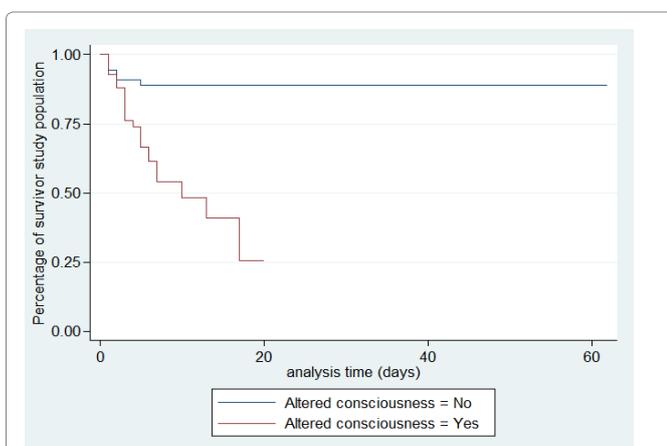


Figure 5: Survival analysis curves according to altered consciousness

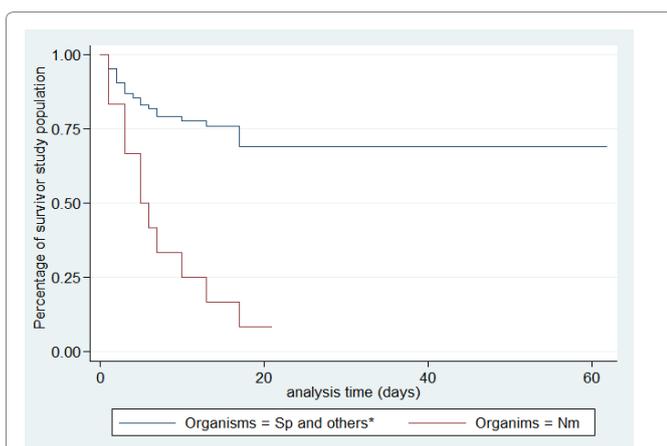


Figure 6: Survival analysis curves according to organisms
*Only *Streptococcus pneumoniae* and *Neisseria meningitidis* were found in the cases, other germs are *Streptococcus B*, *Staphylococcus aureus* and *E. coli*, no *Haemophilus* was found.

worldwide¹⁻⁴ with differences depending on the country and study site. For example it was reported as 28.7% in

Malawi, 33% in Angola, and up to 37% in Latin America⁷⁻¹⁰. In developed countries, this value is much lower as for example in France with a death rate ranging from 5.9 % to 10.2% over the past decade¹¹.

The mortality in our study was 17, 71%, which is lower than for the other African countries, but it could be revised upwards due to the relatively small sample size as a result of exclusion of children with missing data. Also one retrospective study such as ours cannot provide an accurate estimation of the mortality due to BM in Madagascar.

In France, Nigeria, Guatemala and Malaysia, the category mainly affected by BM is children less than 12 months¹¹⁻¹⁴. Basri in Malaysia shows that children less than 12 months are at increased risk of death due to BM (OR = 3.13 [1.33 to 7.24])¹⁴. These results are in agreements with our study, children suffering from BM and less than six months of age have twice the risk of death. Young infants are a population at risk for BM death and may require a more tailored support.

The majority of BM impact studies found a male predominance of 50 to 60%, as MacCormick in Malawi⁸, Kuti in Nigeria¹², and Basri in Malaysia¹⁴ have reported. The sex ratio depends on the socio-demographic breakdown of each country. However, sex is not a death risk factor related to BM.

Our study found a strong association between the number of siblings and death among children with BM. Our findings thus confirmed what the literature clearly established and reported, an association between the risk of developing BM and the number of siblings^{15, 16}. However, no study has shown the effect of siblings on the survival of children with BM. In our study, the effect of the number of siblings on the survival of children with BM could be explained by the assumption of difficulty of a hospitalized child from a large family in a developing country. It's very difficult for parents devoting time because of economic difficulties to take care all their children.

The same applies to overcrowding. Huljer highlights that children staying in a nursery have twice the risk of acquiring BM, but the association with death has not been established. Overcrowding exposes the child to more virulent organisms, and once again, the large family cannot cope with the hospital charge or fee due to demands of the family. This may explain the strong association of deaths and number of of siblings or overcrowding in our study.

In several countries in Latin America, Garcia and his team have demonstrated the protective effect of the haemophilus vaccine on the risk of meningitis, with a relative risk ranging from 0.07 to 0.21¹⁷. Suarez demonstrates that the efficacy of pneumococcal vaccine on mortality in pneumococcal diseases including meningitis

from admission. Further studies are necessary, given the limitations of the present study, among other things, the establishment of the childhood BM severity score, and the assessment of care in emergency is particularly essential.

Competing interests

SAM, RMRR, RM and ALR are in the Faculty of Medicine of Antananarivo, Madagascar. The authors declare no financial competing interests.

Authors' contributions

SAM wrote the first draft of the study and conceived the study with ALR. SAM, RMRR and RM contributed the data. SAM, RMRR, RM and ALR were responsible for data interpretation. All authors edited the final version of the manuscript and approved its submission for publication.

Authors' information

ALR is director of the CHUMET of Madagascar

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WHO-DPEV Madagascar

References

1. VanDemark. Acute Bacterial Meningitis Current Review and Treatment Update. *Crit Care Nurs Clin N Am*. 2013; 25: 351–361. <http://dx.doi.org/10.1016/j.ccell.2013.04.004>
2. World Health Organization. Global health estimates 2014 summary tables: deaths by cause, age and sex, by who region, 2000-2012. June 2014. World Health Organization Geneva, Switzerland. Acces at http://www.who.int/healthinfo/global_burden_disease/en/
3. Watt JP, Wolfson LJ, O'Brien KL, et al. Burden of disease caused by Haemophilus influenzae type b in children younger than 5 years: global estimates. *Lancet*. 2009; 374: 903–11.
4. O'Brien KL, Wolfson LJ, Watt JP, et al. Burden of disease caused by Streptococcus pneumoniae in children younger than 5 years: global estimates. *Lancet*. 2009; 374: 893–902.
5. Goldman L, Schafer A. Goldman's Cecil medicine (Twenty-Fourth Edition). Chapter 420 Meningitis: bacterial, viral, and other. Elsevier Health Sciences. 2012; 2355-2371.
6. McIntyre PB, O'Brien KL, Greenwood B, et al. Bacterial Meningitis. Effect of vaccines on bacterial meningitis worldwide. *Lancet*. 2012; 380: 1703–11.
7. De Jonge, van Furth AM, Wassenaar M, et al. Predicting sequelae and death after bacterial meningitis in childhood: A systematic review of prognostic studies. *BMC Infectious Diseases*. 2010; 10: 232.
8. McCormick DW, Wilson ML, Mankhambo L, et al. Risk Factors for Death and Severe Sequelae in Malawian Children with Bacterial Meningitis, 1997–2010. *Pediatr Infect Dis J*. 2013 February; 32(2): e54–e61. doi:10.1097/INF.0b013e31826faf5a.
9. Pelkonen T, Roine I, Monteiro L, et al. Risk Factors for Death and Severe Neurological Sequelae in Childhood Bacterial Meningitis in Sub-Saharan Africa. *Clinical Infectious Diseases*. 2009; 48: 1107–10. DOI: 10.1086/597463.
10. Roine I, Peltola H, Fernandez J, et al. Influence of Admission Findings on Death and Neurological Outcome from Childhood Bacterial Meningitis. *Clinical Infectious Diseases*. 2008; 46: 1248–52. DOI: 10.1086/533448.
11. Levya C, Varond E, Tahae MK, et al. Change in French bacterial meningitis in children resulting from vaccination. *Archives de Pédiatrie*. 2014; 21: 736-744 0929-693X/ 2014 Elsevier Masson SAS. <http://dx.doi.org/10.1016/j.arcped.2014.04.025>.
12. Kuti BP, Bello EO, Jegede TO, et al. Epidemiological, clinical and prognostic profile of childhood acute bacterial meningitis in a resource poor setting. *J Neurosci Rural Pract*. 2015 OctDec; 6(4): 549–557. doi: 10.4103/09763147.165424 PMID: PMC4692015.
13. Olson D, Lamb MM, Gaensbauer JT, et al. Risk Factors for Death and Major Morbidity in Guatemalan Children with Acute Bacterial Meningitis. *The Pediatric Infectious Disease Journal*. July 2015; Volume 34: Number 7. DOI: 10.1097/INF.0000000000000720.
14. Basri R, Zueter AR, Mohamed Z, et al. Burden of bacterial meningitis: a retrospective review on laboratory parameters and factors associated with death in meningitis, kelantan malaysia. *Nagoya J Med Sci*. 2015; 77: 59 ~ 68.
15. Goldacre MJ, Wotton CJ, Maisonneuve JJ. Maternal and perinatal factors associated with subsequent meningococcal, Haemophilus or enteroviral meningitis in children: database study. *Epidemiology and Infection*. 2013 May 10; 142(2): 371–8. Doi: 10.1017/S095026881300099X.
16. Case-Control Study. Hjuler T, Wohlfahrt J, Simonsen J, et al. Perinatal and Crowding-Related Risk Factors for Invasive Pneumococcal Disease in Infants and Young Children: A Population-Based. *Clinical Infectious Diseases*. 2007; 44: 1051–6. DOI: 10.1086/512814.
17. Garcia S, Lagos R, Munoz A, et al. Impact of vaccination against Haemophilus influenzae type b with and without a booster dose on meningitis in four South American countries. *Vaccine*. 2012; 30: 486–492.
18. Suarez V, Michel F, Toscano CM, et al. Impact of pneumococcal conjugate vaccine in children morbidity and mortality in Peru: Time series analyses. *Vaccine*. 2016; 34: 4738–4743.
19. Roine I, Pelkonen T, Bernardino L, et al. Factors Affecting Time to Death From Start of Treatment Among Children Succumbing to Bacterial Meningitis. *Pediatr Infect Dis J*. 2014; 33: 789–792.
20. World Health Organisation. Madagascar: WHO and UNICEF estimates of immunization coverage: 2015 revision – DRAFT. May 13, 2016.
21. Shinjoh M, Iwata S, Yagihashi T, et al. Recent trends in pediatric bacterial meningitis in Japan- A country where Haemophilus influenzae type b and Streptococcus pneumonia conjugated vaccines have just been introduced. *J Infect Chemother*. 2014; 20: 477e483.