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# Spontaneous community-acquired bacterial meningitis in adults admitted to the intensive care units in the Caribbean French West Indies: Unusual prevalence of *Klebsiella pneumonia*

Pascale Piednoir, Ulrich Clarac, Amélie Rolle, Sylvaine Bastian, Gaelle Gruel, Frédéric Martino, Hossein Mehdaoui, Marc Valette, Sébastien Breurec, Michel Carles

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1 **Title:** Spontaneous community-acquired bacterial meningitis in adults admitted to the  
2 intensive care units in the Caribbean French West Indies: unusual prevalence of *Klebsiella*  
3 *pneumoniae*

4 **Authors :**

5 Pascale Pascale PIEDNOIR<sup>1</sup>, Ulrich CLARAC<sup>1</sup>, Amélie ROLLE<sup>1</sup>, Sylvaine BASTIAN<sup>2</sup>, Gaëlle  
6 GRUEL<sup>3</sup>, Frédéric MARTINO<sup>1</sup>, Hossein MEHDAOUI<sup>4</sup>, Marc VALETTE<sup>1</sup>, Sébastien BREUREC<sup>3,5,6</sup>,  
7 Michel CARLES<sup>1,5,7</sup>

8 **Affiliations :**

- 9 1 Réanimation Polyvalente, CHU de la Guadeloupe 97139 Les Abymes
- 10 2 Laboratoire de Microbiologie Clinique et Environnementale, CHU Guadeloupe 97139 Les  
11 Abymes
- 12 3 Unité Transmission, Réservoir et Diversité des Pathogènes, Institut Pasteur de Guadeloupe,  
13 Les Abymes, France,
- 14 4 Service de Réanimation Polyvalente, CHU de Martinique 97261 Fort-de-France
- 15 5 Faculté de Médecine Hyacinthe Bastaraud, Université des Antilles, Pointe-à-Pitre, France
- 16 6 Centre d'Investigation Clinique 1424 INSERM, Pointe-à-Pitre/Les Abymes, France
- 17 7 Université Côte d'Azur, INSERM, C3M, Nice, France

18

19 **Corresponding author :**

20 Michel CARLES, MD, PhD

21 Mailing address : Service de Reanimation Polyvalente, 28 route de chauvel, CHU de la

22 Guadeloupe 97139 Les Abymes

23 Email : [carles.michel@gmail.com](mailto:carles.michel@gmail.com)

24 Phone : + 33 6 37 37 74 43

25 **Abstract - Word count : 51**

26 An unusual prevalence of *Klebsiella pneumoniae* (24%) was observed in 25 adults admitted to  
27 the intensive care units of two University Hospitals from French West Indies for **spontaneous**  
28 community-acquired bacterial meningitis. All tested isolates had several prominent features  
29 of hypervirulent isolates, including *rmpa* and *iuc* genes, K1 or K2 capsular serotypes.

30 **Running title:** *K. pneumoniae* community-acquired meningitis

31 **Key words:** meningitis – *Klebsiella pneumoniae* - virulence - epidemiology

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38 **Text – Word count : 825**

39 Community-acquired bacterial meningitis (CABM) are rare in Western countries with an  
40 incidence of 0.9 per 100 000 per year, associated with unfavorable outcome in  
41 approximately 40% of cases (1). Most common involved pathogens are *Streptococcus*  
42 *pneumoniae* and *Neisseria meningitidis*, including CABM requiring an intensive care unit (ICU)  
43 admission (1). Guadeloupe and Martinique, two French overseas islands, located in the  
44 Caribbean (about 800 000 inhabitants, mostly Caribbean and European) were considered as  
45 very high-resource countries in 2013 (<http://hdr.undp.org/>). Very few data are available about  
46 CABM epidemiology in this area (2). We report here the clinical and microbiological  
47 characteristics, and outcome of **spontaneous** CABM in adults admitted in the ICU of two  
48 University Hospitals from Caribbean French West Indies.

49 Over a 6 year-period (January 2012 to December 2017), all patients over 18 years admitted  
50 for a diagnosis of CABM with a positive cerebrospinal fluid culture were retrospectively  
51 included. **No post neurosurgical nor device-associated meningitis were included.** API  
52 biochemical galleries (API, BioMerieuxTM, Marcy l'Etoile, France) were used for bacterial  
53 identification. Antibacterial drug susceptibility was determined using the disc diffusion  
54 method, according to the 2018 guidelines of CA- SFM/EUCAST ([http://www.sfm-](http://www.sfm-microbiologie.org)  
55 [microbiologie.org](http://www.sfm-microbiologie.org)). Detection of *iuc* (coding for aerobactin) and *rmpA* (upregulator of capsule  
56 expression) genes, and capsule serotyping of *Klebsiella pneumoniae* isolates were performed  
57 as previously described (3). A standardized specific questionnaire was fulfilled to get  
58 demographic, clinical and biological data, and outcome.

59 Chi-2 or Fisher's exact tests (if required) and Student's t test were used to compare categorical  
60 and continuous variables, respectively. A p-value under 0.05 was significant. The ethical  
61 committee of the University Hospital in Guadeloupe approved the protocol (registration  
62 number: n° A1\_18\_06-01\_MEN).

63 After exclusion of 7 patients because alternative diagnosis or lack of microbiological  
64 confirmation, a total of 25 patients with culture-proven bacterial meningitis were included.

65 General data including underlying comorbidities for 17 (68%) patients are reported in the  
66 Table. Main involved bacteria were *S. pneumoniae* (n=7, 28%), *K. pneumoniae* (n=6, 24%), *S.*  
67 *aureus* (n=5, 20%) and *E. coli* (n=3, 12%). One patient displayed a mixed infection with *E. coli*  
68 and *Streptococcus* spp. No difference has been shown regarding the bacterial epidemiology  
69 between the two hospitals (p>0.05). Suppurative complications of the CABM-related bacteria  
70 occurred in 4 patients: a cerebral abscess in two patients (due to *S. aureus* and a combination  
71 of *E. coli* and *Streptococcus* spp., respectively), a *K. pneumoniae* liver abscess in one patient  
72 and a *S. aureus* pulmonary abscess in another one. Moreover, an endocarditis was diagnosed  
73 for 4 out of the 5 *S. aureus* CABM. The overall mortality was 52% (13 patients).

74 According to previous data (1,2), *S. pneumoniae* was the most frequent pathogen (28%) in our  
75 study. Unexpectedly for CABM, we described a high prevalence of CABM- associated *K.*  
76 *pneumoniae* (24%), mostly described as one of the main CABM-related pathogens in Asia (4,  
77 5). In Taiwan, *K. pneumoniae* was even the first involved pathogen in adult CABM with  
78 prevalence rates up to 50% (6). The identification of Gram negative bacillary and *S. aureus*  
79 among the leading cause of bacterial adult's CABM is unusual and several hypothesis could be  
80 considered: specific local epidemiology in the Caribbean with high frequency of *K. pneumoniae*-

81 related infections (reservoir issue), the role of the introduction of conjugated vaccines for *S.*  
82 *pneumoniae* and *Neisseria meningitidis* as suggested elsewhere (7).

83 The emergence of severe community-acquired hypervirulent *K. pneumoniae* (CA-HvKp)  
84 disease has been reported during the past three decades, usually pyogenic liver abscess, but  
85 also meningitis, brain abscess or ophthalmitis, initially in Asia and more recently in Western  
86 countries (8). Out of the 4 isolates investigated, all harbored *rmpa* and *iuc* genes. These two  
87 genes coding for an increased expression of capsular material and an increased efficiency of  
88 iron-acquisition, respectively, are two major hvKp-specific virulence factors (8). In addition, all  
89 but one (K2) were assigned to the K1 capsular serotype. This serotype is strongly associated  
90 with the Sequence Type 23, the most commonly genetic background recovered worldwide  
91 associated to CA-HvKp (9). We did not find any significant difference of the clinical  
92 presentation or outcome between patients with *K. pneumoniae* CABM versus others (after  
93 exclusion of those displaying *S. aureus* endocarditis), related in part to the small sample size  
94 ( $p>0.05$ ) (Table 1). We noticed that 2 of the 4 *K. pneumoniae*-infected patients have  
95 predisposing risk factors of CA-HvKp infection in our population (8), i.e. diabetes mellitus and  
96 alcoholism. Taking into account that diabetes and alcoholism are overrepresented public  
97 health issues in the Caribbean (10), a survey of such infections (CA-HvKp) is urgently needed.  
98 The mortality is high (around 50%) with a short delay after admission. In term of antimicrobial  
99 resistance, a recent rise of extended spectrum beta-lactamase - and carbapenemase-  
100 producing HvKp has been reported. In our study, all isolates were susceptible to all  
101 antimicrobials tested except for ampicillin and ticarcillin. Altogether, our data suggests the  
102 need for comprehensive epidemiologic studies focused on CA-HvKp infections in the

103 Caribbean. A better understanding of environmental niches that act as reservoirs of these  
104 isolates may enable preventive interventions.

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107 **Conflict of interest** : none

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109 **Ethical approval** : The ethical committee of the University Hospital in Guadeloupe approved  
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156 **Table:** Demographic characteristics, predisposing factors, clinical features upon hospital admission,  
157 outcomes parameters and associated complications among the total population of community-acquired  
158 bacterial meningitidis (All CABM) and *Klebsiella pneumoniae* meningitidis (KP CABM). Categorical  
159 variables were expressed as percentages and continuous variables as medians (25th and 75th  
160 percentiles).

Characteristics	All CABM		KP CABM	
	n=25		n=6	
Age (years) median [Q1-Q3]	60.0	[54–70]	60	[55–68]
Male, <i>n</i> (%)	16	64.0	4	67.0
Underlying disease				
Remote head trauma <i>n</i> (%)	0	0.0	0	0.0
Otitis/Sinusitis <i>n</i> (%)	3	12.0	2	33.0
Diabetes mellitus <i>n</i> (%)	7	28.0	1	16.0
Chronic alcoholism <i>n</i> (%)	4	16.0	1	16.0
Immunosuppressive status <i>n</i> (%)	5	20.0	0	0.0
Cirrhosis <i>n</i> (%)	0	0.0	0	0.0
Malignancy <i>n</i> (%)	4	16.0	0	0.0
Severe chronic renal insufficiency <i>n</i> (%)	2	8.0	0	0.0
Chronic respiratory insufficiency <i>n</i> (%)	0	0.0	0	0.0
Signs and symptoms upon presentation				
Headaches <i>n</i> (%)	14	56.0	6	100.0
Fever <i>n</i> (%)	25	100.0	6	100.0
Septic shock <i>n</i> (%)	7	28.0	0	0.0
Generalized seizure <i>n</i> (%)	5	20.0	3	33.0
Focal neurological deficit <i>n</i> (%)	0	0.0	0	0.0
Neck stiffness <i>n</i> (%)	13	52.0	4	66.0
Glasgow Coma scale, median [Q1-Q3]	10	[9–14]	9	[7–13]
Severity scores				
IGS II median [Q1-Q3]	56	[36-57]	43	[36-47]
Charlson's Score median [Q1-Q3]	3	[2-4]		
Outcome parameters				
Length of stay in ICU, (days) median [Q1-Q3]	10	[3–17]	13	[16–21]
Mechanical ventilation (VM) <i>n</i> (%)	18	72.0	5	83.0

Total duration of VM (days) median [Q1-Q3]	5	[0–17]	7	[2–21]
In-hospital mortality <i>n</i> (%)	13	52.0	3	50.0
Delay of mortality occurrence (days) median [Q1-Q3]	10	[4–22]	3	[1–24]
Initial cerebrospinal fluid results				
Glucose (mmol/L) median [Q1-Q3]	0.40	[0.02–3.83]	0.25	[0.03-4.75]
Protein (g/L) median [Q1-Q3]	5.25	[2.21–7.50]	6.60	[5.62-8.40]
Leukocytes/mm <sup>3</sup> median [Q1-Q3]	2350	[282–5745]	5990	[4795-6660]
PNN percentage median [Q1-Q3]	94	[90–95]	95	[91-97]
Gram's stain-positive (total) <i>n</i> (%)	20	80.0	6	100.0
Culture-positive <i>n</i> (%)	25	100.0	6	100.0
<i>Streptococcus pneumoniae</i>	7	28.0	-	
<i>Klebsiella pneumoniae</i>	6	24.0	6	
<i>Staphylococcus aureus</i>	5	20.0	-	
<i>Escherichia coli</i>	2	8.0	-	
<i>Neisseria meningitidis</i> B	2	8.0	-	
<i>Streptococcus spp</i>	1	4.0	-	
<i>Pseudomonas aeruginosa</i>	1	4.0	-	
<i>Escherichia coli</i> + <i>Streptococcus spp</i>	1	4.0	-	
Associated Complications				
Bacteremia <i>n</i> (%)	18	72.0	4	66.0
<i>Streptococcus pneumoniae</i>	7			
<i>Klebsiella pneumoniae</i>	4			
<i>Staphylococcus aureus</i>	4			
<i>Escherichia coli</i>	1			
<i>Pseudomonas aeruginosa</i>	1			
Cerebral abscess <i>n</i> (%)	2	8.0	0	0.0
Other abscess <i>n</i> (%)	2	8.0	1	16.0