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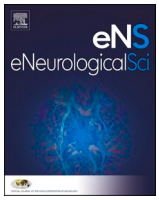

Spontaneous subarachnoid hemorrhage in a referral health Centre in Central Africa

Daniel Gams Massi [a,b,*], Mikael Doufiene Pazeu [c,1], Mathieu Motah [c], Annick Melanie Magnerou [c,d], Caroline Kenmegne [a], Salomon Mbahé [a], Njankouo Yacouba Mapoure [a,c]

[a] Neurology unit, Douala General Hospital, Douala, Cameroon
[b] Faculty of Health Sciences, University of Buea
[c] Faculty of Medicine and Pharmaceutical Sciences, University of Douala, Douala, Cameroon
[d] Neurology department, Douala Laquintinie Hospital, Douala, Douala, Cameroon

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ABSTRACT

Background: Spontaneous subarachnoid hemorrhage (sSAH) is a medicosurgical emergency with high morbidity and mortality. The aimed of this study was to describe the clinical features and outcome of sSAH in Cameroon.
Methods: We reviewed medical records of patients aged ≥15 years old, admitted for sSAH from Januray 2011 to December 2020 in the Douala General Hospital. The diagnosis of sSAH was confirmed by neuroimaging (CT scan or MRI). Clinical and radiological severities were assessed by the WFNS score and the modified Fisher score respectively. Factors associated to in-hospital mortality was identified using cross-table (RR and 95%CI).
Results: Among the 111 cases of sSAH reviewed in emergencies records, we included 70 patients. The mean age was of 55.6 ± 13.6 years. Female were predominant (57.1%). Altered consciousness was the main clinical feature (55.7%). The WFNS score was grade 4–5 in 54.3% of patients. And 75.7% of cases presented a modified Fisher score of 3–4. Ruptured of intracranial aneurysm was the most common etiology (46.2%). Endovascular treatment and/or surgical treatment were not avaible. Hospital-based mortality was 40% and factor associated with death were Altered consciousness (RR: 4.3, 95%CI:1.52–12.33, $p = 0.004$), coma (RR: 23.9, 95%CI:2.85–200.62, $p = 0.004$), WFNS grade 5 (RR: 18.2, 95%CI:3.7–92.3, $p < 0.001$), and hospital length ≤ 7 days (RR: 13.5, 95% CI:4.28–42.56, $p < 0.001$).
Conclusion: Mortality and disability of sSAH are still high in our setting. Further studies with prospective follow up of patients are needed to determine the long-term outcome of these patients.

1. Introduction

Spontaneous subarachnoid hemorrhage (sSAH) is an irruption of blood into the subarachnoid space without traumatic context, generally accompanied by " thunderclap headache" [1,2]. It is a major neurovascular emergency, with mortality estimated at 40% within the first 48 h [3]. Half of survivors suffer from neuropsychological sequelae impacting their quality of life [4]. It affects young patients and causes a significant loss of productive life [4]. sSAH affects more frequently women [5]. The overall incidence of SAH is approximately 9 per 100,000 person-years with variability depending on age, sex and geographic context [5]. The incidence of SAH in the Western countries varies between 3 and 14 per 100,000 person-years [6–8]. In Asia and Latin America this incidence varies between 2.3 and 4.8 per 100,000 person-years [5,9,10]. In Africa, a study conducted in Nigeria reported an incidence of 4.1 per 100,000 person-years [11]. To date, epidemiological data of SAH in Cameroon are scarce.

Patients with sSAH may present with an unusual acute headache [12]. This headache is intense, with a sudden onset, classically described as a "thunderclap in a clear sky" headache and can be accompanied by a

Abbreviations: CT, computed tomography; DGH, Douala General Hospital; DSA, digital substraction angiography; ICA, intracranial aneurysm; MRI, magnetic resonance imaging; MSED, medical-surgical emergency department; MS-ICU, medical-surgical intensive care unit; NU-IMD, internal medicine department including a neurology unit; SAH, subarachnoid hemorrhage; sSAH, Spontaneous subarachnoid hemorrhage; WFNS, World Federation of Neurological Surgeons.

* Corresponding author at: Neurology unit, Douala General Hospital, PO box: 4856, Douala, Cameroon.
E-mail address: danny.gamsmassi@gmail.com (D. Gams Massi).

[1] Deceased.

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brief loss of consciousness, nausea or vomiting, sign of meningeal irritation, and seizures [13]. Brain computed tomography (CT scan) without contrast is the gold standard for the diagnosis of sSAH [14,15]. A lumbar tap with the 3-tube test can contribute to the diagnosis if the initial brain CT scan is normal [12]. Cerebral angiography can help to identify the etiology of sSAH [16]. These etiologies are dominated by the rupture of an intracranial aneurysm (ICA), responsible for approximately 80 to 85% of cases [15,17]. Other causes incriminated are reversible cerebral vasoconstriction syndrome, amyloid angiopathy, posterior reversible encephalopathy syndrome, inflammatory or infectious arteritis, coagulopathy, cerebral venous thrombosis, and vascular malformations [18]. However, in 1 in 10 cases the etiology remains undetermined [3,18]. The management of sSAH need an urgent multidisciplinary approach [12]. This treatment requires specialized centers that can perform emergency endovascular and interventional neuroimaging and neurosurgical procedure if necessary [19,20]. In a context of adequate technical support, SAH mortality varies from 40 to 50% [21,22]. Half of the survivors will have disabling and debilitating neuropsychological sequelae such as motor deficits, cognitive disorders, psychological, and behavioral disorders [23,24]. In sub-Saharan Africa where the technical platform remains to be improved, the diagnosis of SAH is often made late, thus impacting its management [25–27]. In Cameroon, endovascular procedures and vascular neurosurgery remain limited to some andecdotic cases. Furthermore, data on the epidemiology, clinical presentation, treatment and outcome of sSAH are scarce in our setting. By drawing a clear picture of sSAH in our setting, stakeholders and community leaders would understand the need of appropriate health care facilities and human resources.

2. Materials and methods

2.1. Study setting and design

The Douala General Hospital (DGH) is the main referral health centre in the city of Douala (economic capital of Cameroon). This hospital includes a medical-surgical emergency department (MSED), a medical-surgical intensive care unit (MS-ICU), and an internal medicine department including a neurology unit (NU-IMD). The hospital has a medical imaging department with a 64-slice CT-scan and magnetic resonance imaging (MRI) of 0.4 Tesla available 24/7. This retrospective cohort study was carried out using the medical records of patients admitted from December 2020 to May 2021 in the MSED, MS-ICU, and the NU-IMD. Ethical approval was obtained from the Institutional Ethics Committee of the University of Douala (N°2545/CEI-UDo/04/2021/T).

2.2. Patients and data collection

All medical records of patients over 15 years of age admitted with sSAH confirmed by brain CT scan or MRI. The threshold of over 15 years corresponds to the age below which patients are more likely to be admitted to pediatric emergencies.

Data were collected from the MSED, MS-ICU and NU-IMD registers and recorded in a pre-established data collection form which contained sociodemographic data, medical history, clinical data, paraclinical data, etiologies, treatment and outcome. The World Federation of Neurological Surgeons (WFNS) score on admission was used to grade the clinical severity. A score of 1 to 3 was defined as low grade, while a score of 4 to 5 represented high grade with a greater risk of death. We used the Fisher score to assess severity on imaging. A Fisher score >2 was considered severe.

2.3. Data management and statistical analysis

Data were analyzed using Statistical Package for Social Sciences (SPSS) software version 23.0. The hospital-based prevalence of sSAH was determined using the number of sSAH cases on the total admissions in the MSED. Descriptive statistics included categorical variables (in frequency and percentage) and continuous variables (in means with standard deviations). Univariate analysis using cross-table with relative risk (RR) and 95% confidence interval (CI) helped to identify the factors associated with in-hospital mortality. The results were considered significant for a p-value <0.05.

3. Results

Among the 60,097 patients admitted in the MSED, 111 cases of sSAH were recorded (hospital-based prevalence of 0.18%). 41 medical records were excluded (no data availble in 26, and non-confirmed diagnosis in 15). A total of 70 medical records met our criteria. The mean age of patients was 55.6 ± 13.6 years. Female represented 57.1% of cases. More details on general charateristics of patients can be found in Table 1. The major risk factors were hypertension (70%) and alcohol consumption (10%). The most frequent reasons for consultation were altered consciousness (55.7%) and headache (25.7%). The WFNS score was 4–5 in 54.3% of patients, and the Fisher grade was 3–4 in 75.71% of cases (***see in*** Table 2). Ruptured ICA (17.1) was the most common etiology (***see*** Fig. 1). However, 62.9% of patients did not perform any etiological workup. (See Fig. 2.)

No endovascular and/or surgical treatment was available during the study period. 55.7% of patients were managed in MS-ICU. Details on treatment options available are found in Table 3.

Hydrocephalus (14.3%) and convulsive status epilepticus (14.3%) were the most common acute neurological complications. 40% of sSAH cases died during the hospital stay. Altered consciousness (RR: 4.3, 95% CI:1.52–12.33, $p = 0.004$), coma (RR: 23.9, 95%CI:2.85–200.62, $p = 0.004$), WFNS grade 5 (RR: 18.2, 95%CI:3.7–92.3, $p < 0.001$), and hospital length ≤ 7 days (RR: 13.5, 95%CI:4.28–42.56, $p < 0.001$) were significantly associated with in-hospital mortality (see Table 4).

4. Discussion

This pioneering study aimed to provide data on clinical features, etiologies, therapeutic options and short-time outcome on sSAH in Cameroon. More than half of the patients had a high grade WFNS score and more than three-quarter of cases had a Fisher score greather than 2. No patient received any endovascular and/or surgical treatment. Two out five patients died during the hospitalization.

The frequency of sSAH found in our study was similar to those found

Table 1
General characteristics of patients.

Variables	Frequency (%)
Age groups (years)	
≤ 45	16 (22.9)
46–60	28 (40)
> 60	26 (37.1)
Sex	
Female	40 (57.1)
Male	30 (42.9)
Marital status	
Couple	55 (78.6)
Single	8 (11.4)
Widow	7 (10)
Location	
Douala	48 (68.6)
Out of Douala	22 (31.4)
Occupation	
Unemployed	28 (12.9)
Employed	42 (8.6)
Risk factors	
Hypertension	49 (70)
Alcohol consumption	7 (10)
Diabetes	5 (7.1)
Smoking	3 (4.3)
Oral anticoagulants	1 (1.4)

Table 2
Clinical features of sub-arachnoid hemorrhage.

Variables	Frequency (%)
Clinical reasons of admission	
Headache	39 (55.7)
Altered consciousness	18 (25.7)
Motor weakness	4 (5.7)
Confusion	4 (5.7)
Seizures	3 (4.3)
Speech disturbances	1 (1.4)
Vomiting	1 (1.4)
Clinical signs on admission	
Delirium	20 (28.6)
Meningism	13 (18.6)
Coma (GCS* $\leq$ 8)	11 (15.7)
Headache	10 (14.3)
Raised ICP	8 (11.4)
Focal neurological deficit	8 (11.4)
WFNS † score	
Grade 1	24 (34.3)
Grade 2	6 (8.6)
Grade 3	2 (2.9)
Grade 4	23 (32.9)
Grade 5	15 (21.4)
Fisher score	
Grade 0	–
Grade 1	5 (7.1)
Grade 2	12 (17.1)
Grade 3	31 (44.3)
Grade 4	22 (31.4)
Hospital length (days)	
$\leq$ 7	29 (41.4)
8–14	16 (22.9)
$>$ 14	25 (35.7)

*Glasgow coma scale. †World Federation of Neurological Surgeons.

in sub-Saharan Africa, varying between 0.15 and 0.55% [28–30]. This frequency would have been higher if it had been exclusively carried out in a neurology or intensive care unit like the other studies. The mean age of the patients was around fifty with a predominance of 46–60 years. This was consistent with the mean age of 55 years reported in other studies [4,29,31–33]. Female predominance was similarly found in several studies in Africa and out of the continent [31,34]. In woman, oral contraceptives and menopause increases the risk of sSAH [35,36]. The major risk factors found were hypertension, alcohol consumption, and smoking. In Burkina Faso, hypertension and chronic alcohol consumption were the most common risk factors [34]. The risk of sSAH is increased by 3 for smoking, by 2.5 for hypertension, and by 1.5 for

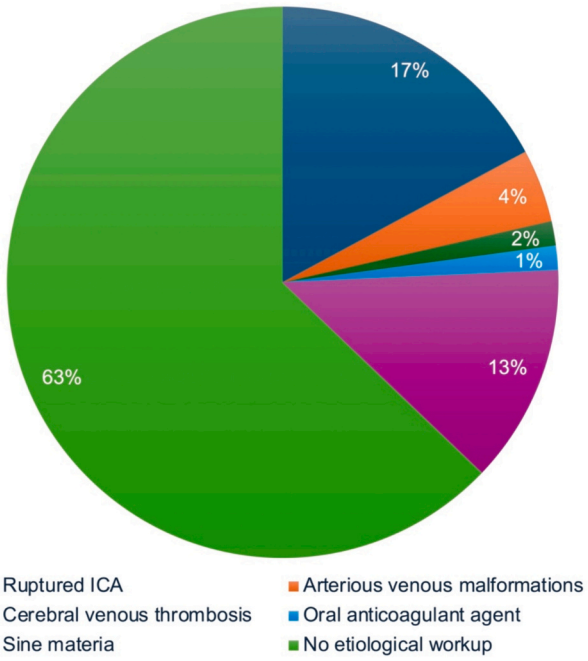

Fig. 2. etiologies of spontaneous subarachnoid hemorrhage including the percentage of patients without etiological workup.

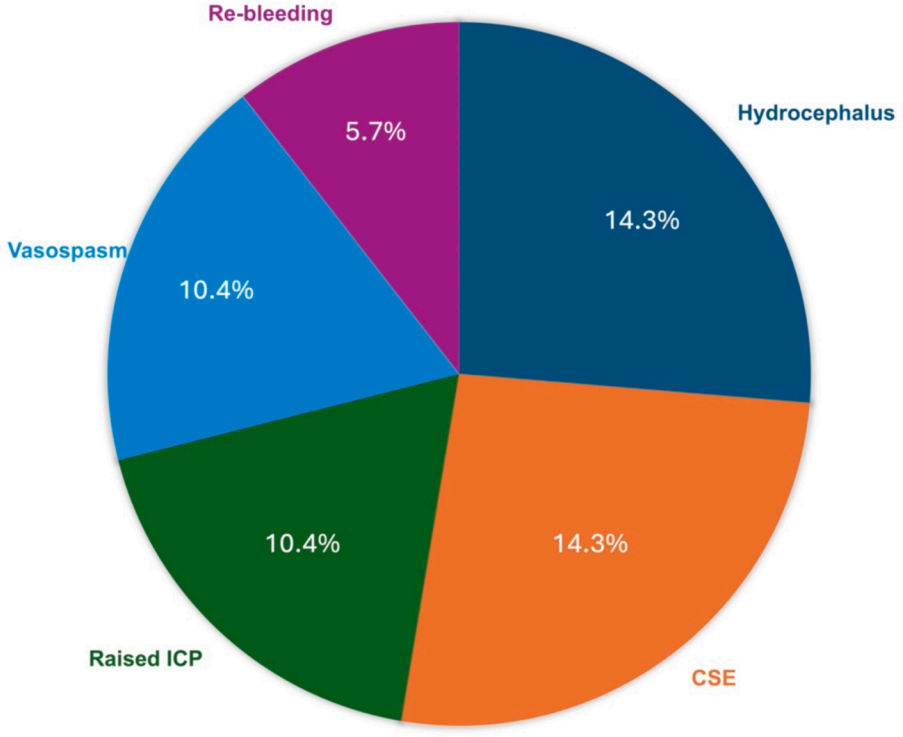

Fig. 1. acute neurological complications in patients with spontaneous subarachnoid hemorrhage.

Table 3
Therapeutic measures and outcome.

Variables	Frequency (%)
Neurosensorial isolation	70 (100)
Resuscitation measures	39 (55.7)
Drugs	
Nimodipine	70 (100)
Nicardipine	51 (75)
Analgesics (WHO*)	70 (100)
ladder 1	4 (5.7)
ladder 2	59 (84.3)
ladder 3	7 (10)
Sedatives	46 (65.7)
Antiseizure medications	25 (35.7)

* World Health Organization.

Table 4
Factors associated with in-hospital mortality of sSAH.

Variables	n (%)	RR (95%CI)	p-value
≤ 45 years	28 (40)	0.96 (0.9–1.02)	0.37
Male	11 (15.7)	0.9 (0.32–2.24	0.469
Female	17 (24.3)	1.4 (0.54–3.69)	0.324
Altered consciousness	21 (30)	4.3 (1.52–12.33)	0.004
Motor weakness	3 (4.3)	5.2 (0.51–52.31)	0.16
Alcohol	2 (2.9)	0.6 (1.1–3.33)	0.439
Diabetes	3 (4.3)	2.5 (0.39–16.13)	0.293
Menigism	4 (5.7)	0.7 (0.18–2.35)	0.369
Coma	10 (14.3)	23.9 (2.85–200.62)	<0.001
Delirium	9 (12.9)	1.4 (0.5–4.05)	0.346
Focal neurological deficit	4 (5.7)	1.7 (0.38–7.29)	0.374
WFNS* grade 1	2 (2.9)	0.1 (0.02–0.36)	<0.001
WFNS* grade 4	12 (17.1)	2.3 (0.82–6.20)	0.093
WFNS* grade 5	13 (18.6)	18.2 (3.7–92.3)	<0.001
Fisher grade 2	3 (4.3)	0.5 (0.12–1.9)	0.229
Fisher grade 3	12 (17.1)	0.9 (0.38–2.57)	0.587
Fisher grade 4	12 (17.1)	2.6 (0.91–7.13)	0.062
≤ 7	21 (30)	13.5 (4.28–42.56)	<0.001
> 14	4 (5.7)	0.2 (0.05–0.61)	0.003
Vasospasm	4 (5.7)	2.3 (0.47–11.05)	0.259
Hydrocephalus	2 (2.9)	0.4 (0.07–1.77)	0.167
CSE †	6 (8.6)	2.7 (0.69–11.71)	0.131
Re-bleeding	2 (2.9)	1.6 (0.21–12.18)	0.508

*: World Federation of Neurological Surgeons. †Convulsive status epilepticus.

excessive alcohol consumption [7,37].

Altered consciousness and headaches were the most frequent reasons for consultation. Disorder of consciousness and headache are the commonest symptoms according to studies [9,32]. More than half of patients had a high grade WFNS score. In France, 40% of patients presented high WFNS score [29]. In this latest study, patients transferred to another center for the etiological management were excluded. This clinical severity score on admission could reflect a late arrival of patients in dedicated centers. In Cameroon, the prehospital care and patient transfer sector are not well structured. In addition, patients and their families receive very little education about neurological diseases and will prioritize self-medication or traditional medicine before being referred to a health facility.

Brain CT scan without contrast is the gold standard for the diagnosis of SAH with a sensitivity close to 100% if performed early [14,15]. To investigate the cause of sSAH, digital substraction angiography (DSA) by arterial catheterization remains the reference. However, it is no longer systematically performed [38]. DSA is not available in our health facility. However, brain CT angiography and magnetic resonance angiogram may help to identify the etiological diagnosis of sSAH with sensitivity <86% and a negative predictive value of 65% [39]. Three-quarter of patients presented a severe radiological severity score (Fisher score 3–4). Dabilgou et al. reported >80% of patients with a Fisher score 4 [34]. Ruptured ICA was the most common etiology among our patients. Other studies in Sub-Saharan Africa (SSA) found lower proportion of ruptured ICA [32,34]. This contrasts with the proportion of ruptured ICA (80% to 85%) identified in the Western world [15,17,29]. Access to limited diagnostic tools in SSA explains the difference in identifying the causes of sSAH compared to Western countries. If CT scan are more available in SSA, increasing. However, DSA and MRI are difficult and expensive to access. Many efforts must be made by stakeholders to improve access to appropriate diagnostic tools and to train health care professionals to better care for patients.

Standard treatment for sSAH ue to ruptured ICA includes endovascular coiling or surgical clip as early as possible [40]. In the absence of endovascular and surgical procedures, patients in DGH received supportive treatment including neurosensorial isolation, nimodipine for the vasospasm prevention, high bloop pressure, pain management, and antiseizure medication. The most common acute neurological complications were hydrocephalus, seizure, raised ICP, and vasospasm. Indeed, these complications are those usually found in the literature [17]. hydrocephalus and raised ICP are factors of poor neurological outcome of sSAH [41,42]. Two out of five cases died during the hospital stay. Same mortality rate was found in Portugal by Papadimitriou et al. in 2019 [21]. Lower mortality rate has been reported in France (25%) where high standard treatment are available [29]. This highlights the interest of developing access to quality care to improve patients' outcome. This can be done through the training of qualified human resources to increase neurosurgeons / population ratio (1.07/1,000,000 Cameroonians, *unpublished data*) and the optimization of technical platform, allowing them to practice in a better environment.

Disorders of consciousness, WFNS grade 5, and hospital length ≤ 7 days were significantly associated with the in-hospital mortality. Indeed, in the literature, loss of consciousness, rupture ICA, vasospasm, hydrocephalus, rebleeding, delayed cerebral ischemia, and WFNS grade 4–5 are associated with high mortality and a poor functional outcome [43–45]. The short hospital length reflects the high risk of death during the days following the sSAH. More than half of death had occurred by SAH day 7 according to Lantigua et al. [46]. This study described with some details the features of sSAH in Cameroon. However, there were several limitations such as missing data. We were unable to contact a significant number of patients by telephone and those contacted could be subject to memory bias making the reliability of the results difficult to assess. This demonstrates the need for a more robust medical data collection system. This study was carried out in one center and the results cannot be generalized to the community.

5. Conclusions

Spontaneous sub-arachnoid hemorrhage is responsible for significant intra-hospital mortality and frequent acute neurological complications. Disorders of consciousness and high WFNS score may contribute to the poor outcome of patients in our setting. Further need to be conducted on the impact of standardized diagnosis and management protocol on the outcome of spontaneous sub-arachnoid hemorrhage in our setting.

Authors contribution

(1) Conception and design of the study, or acquisition of data, or analysis and interpretation of data: DGM, MDP†, MM, NYM.

(2) drafting the article or revising it critically for important intellectual content: DGM, MDP†, AMM, CK, SM.

(3) final approval of the version to be submitted: DGM, MM, NYM, AMM, CK, SM.

CRediT authorship contribution statement

Daniel Gams Massi: Writing – review & editing, Writing – original draft, Validation, Software, Methodology, Investigation, Formal analysis, Data curation, Conceptualization. **Mikael Doufiene Pazeu:** Writing – original draft, Software, Methodology, Investigation, Formal

analysis, Data curation, Conceptualization. **Mathieu Motah:** Writing – review & editing, Validation, Supervision, Project administration, Methodology, Conceptualization. **Annick Melanie Magnerou:** Writing – review & editing, Writing – original draft, Visualization. **Caroline Kenmegne:** Writing – review & editing, Writing – original draft. **Salomon Mbahé:** Writing – review & editing, Writing – original draft. **Njankouo Yacouba Mapoure:** Writing – review & editing, Writing – original draft, Visualization, Validation, Supervision, Project administration, Methodology, Data curation, Conceptualization.

Declaration of competing interest

None.

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In the loving memory of MDP[†] died in 13/09/2022 in Cameroon.

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