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Outcome of non-traumatic coma in a tertiary referral hospital in Cameroon

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ABSTRACT

Introduction: Coma is a medical emergency, and optimal management, especially in a resource-poor setting, depends on knowledge of its aetiology and predictors of outcome. This study aimed to provide hospital-based data on the prevalence, etiology, and outcome of non traumatic coma (NTC) in adults at a tertiary level in Cameroon.

Methods: A three year retrospective cohort study of medical records of patients aged 18 years and above, who presented in coma of non-traumatic origin at a Cameroon emergency department (ED) was conducted. Data related to sociodemographic, clinical findings, investigations, etiology of the coma, and outcomes were collected.

Results: A total of 408 patients were recruited, 214 (52.5 %) were males. The mean age was 55.9 ± 16.6 years. NTC accounted for 2.2 % of all consultations at the ED during the period of study. Stroke (29.6 %), infections (19.8 %), and metabolic disorders (12.6 %) were the most frequent cause of NTC. Etiology was unknown in 23.3 % of our participants. The in-hospital mortality was 66.4 %. Duration of hospitalization $\leq$ 3 days, GCS $\langle$ 6, serum creatinine level $\rangle$ 13 mg/L, and administration of adrenergic drugs were predictors of mortality. Overall survival rate was 44.3 % after 5 days of admission.

Conclusion: Non-traumatic coma had various aetiologies. Stroke accounted for almost one third of cases. About three out of five patients died in hospital. Deep coma, high serum creatinine level, short hospital stay and administration of adrenergic medications were independent predictors of mortality.

African relevance

- This study is one of few studies focusing on non-traumatic coma in Africa.
- Stroke, infections, and metabolic disorders are the leading causes of non-traumatic coma.
- In our setting etiology remain unknown in close to one case out of five.
- About two-third of cases of non-traumatic coma die during hospitalization.

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Introduction

Coma is a state of unawareness of self and environment or a suspension of those mental activities by which people are made aware of themselves and their environment, always coupled with a diminished responsiveness to environmental stimuli [1]. It could be as a result of trauma or from non-traumatic causes [2]. It represents an acute, life-threatening emergency requiring prompt intervention for preservation of life and brain function [3]. Seriously impaired states of consciousness, regardless of their causes, are often fatal not only because they represent an advanced stage of many diseases but also because they add their own specific burdens to the primary disease [3].

The global incidence of non-traumatic coma (NTC) is unknown. In USA, approximately 5 % of patients present to the emergency department (ED) with an altered mental state and 1 % of the admissions at the ED are due to coma while in Europe, 5–9 % of all patients in EDs present with acute non-traumatic disorders of consciousness and up to 2 % are reported to be comatose on admission [4,5]. In Asia, a prevalence of 7.3 % was found among intensive care unit admission and 2 % of general admissions [6]. In Africa, the prevalence ranges between 2 and 7.4 % [7, 8].

Patients admitted to hospital in coma from causes other than trauma have a high mortality and the survivors have a high morbidity [9]. The aetiologies of NTC are diverse [3]. According to a systematic review including studies from high and low-middle-income countries, the most common aetiologies of NTC in adults were stroke (6–54 %), post-anoxic coma (3–42 %), poisoning (<1–39 %) and metabolic causes (1–29 %) [10]. In Nigeria, the main causes were stroke (52.2 %), metabolic causes (18.9 %) and infections (18 %) [8]. In Cameroon a study done in the regional hospitals in the South-West region found stroke as the main cause of NTC [7]. The outcome of NTC is often poor. A systematic review reported a mortality rate of 25 to 87 % [10]. In Cameroon, an in-hospital mortality of 84.8 % was reported [7]. The present study aims to provide data on the clinical features, etiologies, and outcome of NTC at a tertiary referral health care center in Cameroon.

Materials and methods

Study design

We retrospectively reviewed medical record of patients admitted from January 2018 to December 2020 in the ED and Intensive Care Unit (ICU) of the Douala General Hospital (DGH). DGH is one of the main referral hospitals in Cameroon, and in the Central African region. The ED of DGH is headed by an intensive care physician. During this study, the ED functioned with 12 medical doctors who worked in two shifts. Three general practitioners (GP) and an internist for the daytime shift and two GPs for the night duty. There were also 12 nurses who also worked in shifts. This department works in close collaboration with the ICU, radiology department, central laboratory, and neurology unit.

Every patient who consults at the ED is immediately installed in a consultation room where a medical records file is opened and vital parameters such as blood pressure (BP), pulse, respiratory rate (RR), temperature (To), oxygen saturation (SaO2), blood sugar are taken by a nurse. The patient is examined by a GP. According to the severity of the condition, the patient may be discharged home or admitted either for observation and stabilization or for hospitalization in the appropriate unit after a review by the specialist on call.

Study population and data collection

In this study we included medical records of adult patients (aged ≥ 18 years) who presented with coma of non-traumatic etiology. Incomplete patients' files were excluded. Data extracted from the medical record files included sociodemographic data, relevant past medical history and clinical examination findings, admitting Glasgow coma scale (GCS), available investigation results, diagnosis and the outcome. Diagnosis of coma was based on documentation of a GCS of ≤9. Data extraction was done by an investigator (AHKM) with verification of the principal investigator (DGM).

Ethical clearance was obtained from the Institutional Review Board of the Faculty of Health Sciences of the University of Buea (Ref: 2021/1309/UB/D/FHS). Administrative authorizations were sought from the Dean of the Faculty of Health Sciences, University of Buea and the General Manager of the DGH.

Statistical analysis

Data were coded, entered and analyzed with Statistical Package for the Social Sciences (SPSS) version 23. The hospital-based prevalence was presented as frequency and proportions of NTC on total admission in emergency department. Mortality and disability were presented as frequencies and proportions. Dynamic cross tab with crude odd ratio (95 % confidence interval) was used to determine factors associated to mortality and disability. Statistically significant factors were introduced in the multivariate analysis using binary logistic regression to identify predictive factors [adjusted odd ratio with 95 % confidence interval] of mortality and disability. The level of significance will be set at $p < 0.05$. Survival rates were analyzed using the Kaplan Meier estimator.

Results

A total of 19,819 patients consulted at the ED of the DGH during the study period. Some 432 adults presented in coma of non-traumatic origin giving a hospital-based prevalence of 2.2 %. Just 408 medical records were included in this study with 52.5 % of men and a mean age (SD) was 55.9 ± 16.6 years. Among the included patients, 37.3 % (n = 152) died in the ICU and 33.8 % (n = 138) died at the ED (see Fig. 1).

Patients (65.4 %) were mainly referred from other structures including 21.6 % of cases transported to the DGH by an ambulance (see Table 1). The mean duration at the ED (SD) of patients was 11.2 ± 13.1 h and 35 patients (8.6 %) spent more than 24 h at the ED. The most frequent comorbidities were hypertension (46 %), diabetes (18.4 %), stroke (12.7 %) and HIV (11.8 %) (see Table 2). Clinical features on admission are displayed on Table 3. Among the patients, 28.9 % presented a GCS < 6, and 38 % had a focal motor deficit on admission (see Table 3). Neuroimaging (Brain CT-scan and MRI) was done in 305 cases with 63.3 % of abnormal findings. Serum creatinine was elevated (>13 mg/L)in 57.8 % of the 197 patients who did it (see Table 4).

The commonest aetiologies were stroke (hemorrhagic 18.6 %, ischemic 13.2 %), hypoglycemia (6.4 %) and septic shock (5.6 %). Meningoencephalitis and HIV CNS infections were found in 4.4 % of cases each. The aetiology remained unknown in 18.6 % of patients (see Fig. 2). Non-specific management included: intubation (49.5 %), artificial ventilation (43.6 %), and adrenergic medications (41.7 %).

The in-hospital mortality was 66.4 %. After multivariate analysis, the factors independently associated withmortality were: duration of hospitalization ≤ 3days, GCS < 6, elevated serum creatinine, administration of adrenergic drugs (see Table 5). Survival rate was 56.4 %, 7.3 %, 17.0 % at day 3 (n = 230), day 5 (n = 13) and day 10 (n = 28) of admission respectively. The median of global survival was 6.0 ± 0.7 days. The survival rate at 5 days of admission in patients having a GCS < 6 on admission was higher than those having a GCS ≥ 6. This was statistically significant with a $p = 0.013$ on the Log rank test (see Fig. 3). Patients admitted to the internal medicine department were more likely to survive after 5 days of admission compared to those admitted to the ICU (Log rank test $p < 0.001$) (see Fig. 4).

Discussion

In this study, we determined the features and outcome of NTC in adults in a referral hospital in Cameroon. NTC accounted for 2 % of all

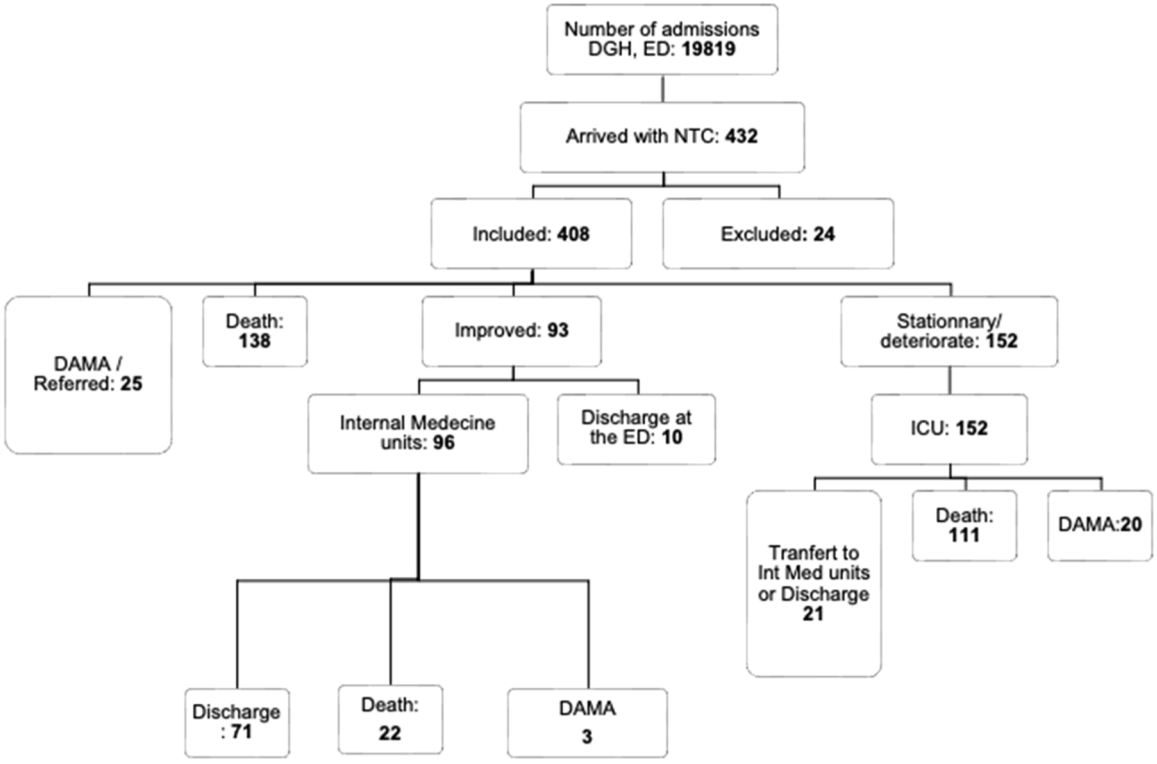

Fig. 1. Fig. 4: Flow chart, NTC patient's circuit and outcome at the DGH (Douala General Hospital). ED: emergency department; DAMA: discharge again medical advice; ICU: intensive care unit; NTC: non-traumatic coma.

Table 1
Mode of admission, duration at the ED and duration of hospitalisation.

Variables			Frequency (n)	Percentage (%)
Mode of admission	Emergency		141	34.6
	Referral	Ambulance	88	21.6
		Other	179	43.8
Duration at Emergency	≤ 24h		373	91.4
	> 24 h		35	8.6
Duration of Hospitalisation	≤3days		299	73.3
	4–7days		68	16.7
	>7days		41	10
Address	Douala		319	78.2
	Other		89	21.8

Table 2
Comorbidities in non-traumatic coma patients.

Variables		Frequency (n)	Percentage (%)
Cardiovascular risks factors	Hypertension	188	46
	Diabetes mellitus	75	18.4
	Stroke	52	12.7
	Cardiopathy	13	3.2
	CKD	24	5.9
	Alcohol & Smoking	23	5.7
Tumour	Brain tumour	10	2.5
	other	24	5.9
HIV		48	11.8
CNS infections		3	.7
Cirrhosis		5	1.2
Previous coma		5	1.2
Epilepsy		8	2

CKD: Chronic kidney disease, CNS: Central Nervous system, HIV: human immunodeficiency virus.

consultations at the ED of the DGH. Similar hospital-based prevalence was reported by Forchap et al. in the Southwest region of Cameroon [7]. Other studies in Africa reported higher prevalence [3,11], but these studies were carried out among medical emergencies only, while we conducted our study in all patients presenting at the ED. The slight male predominance found in this study was consistent with the results reported by Forchap et al. and Dembele et al. [7,12]. Larger male predominance has been reported by other studies in Sub-Saharan Africa [3,8,11]. This male predominance can be explained by the predominance of stroke and diabetes in male population in Cameroon [13].

More than two patients out of five were within the 45 to 65 years. This was consistent with the results of Nwani et al. [8] in Nigeria in 2015, who found 36.9 % of NTC patients within the 40 to 59 years age group. About two third of cases were referred, and one third of them were carried by ambulance. Mapoure et al. reported that 60.9 % of stroke patients in DGH were referred from other health facilities [14]. This was different from Forchap et al. who reported a referral rate of 37.8 % [7]. DGH is a tertiary referral hospital while their Forchap et al., carried out their study in a secondary referral level. DGH represents the highest level of reference in Cameroon. Patients whose treatment is challenging in other health facilities in the region or neighboring regions are referred to the DGH.

Cardiovascular risks factors were the leading comorbidities. Similar results were reported by other studies in Africa, and India [3,7,8,12,11]. History of HIV was found in 11.8 % of cases. Higher rate (22.5 %) was reported in the South-West region of Cameroon [7]. According to the Demographic Health survey 2018, HIV prevalence is higher (3.2 %) in South-West region than Littoral region (2.4 %) where the DGH is located [15]. The high proportions of hypertension, diabetes and HIV observed in African studies could be explained by the double global health burden stemming from the constant threat of infectious diseases and the rising burden of non-communicable diseases due to the epidemiological transition going on in Sub-Saharan countries. On arrival at the ED, more than two thirds of patients had a GCS ≥ 6. Similar results were found by

Table 3
Clinical parameters and signs on admission.

Parameters	Mean ± SD		Frequency (n)	Percentage (%)
Systolic BP (mmHg)	138.1 ± 45.77	High (> 140)	175	42.9
		Normal (90 −140)	178	43.6
		Low (< 90)	54	13.2
Diastolic BP (mmHg)	82.86 ± 27.11	High (> 90)	175	42.9
		Normal (60 – 90)	171	41.9
		Low (<60)	82	20.1
Pulse (Per minutes)	99.5 ± 24.55	High (> 100)	162	39.7
		Normal (60 – 100)	221	54.2
		Low (< 60)	17	4.2
Temperature (°Celsius)	37.45 ± 1.1	High (> 38.5)	48	11.8
		Normal (36.5 – 38.5)	286	70.1
		Low (<36.5)	42	10.3
Glycaemia (g/l)	169.3 ± 114.3	High (> 200)	101	24.8
		Normal (65–200)	235	57.6
		Low (<65)	38	9.3
Respiratory rate (Per minute)	27.39 ± 9.03	High (> 20)	239	58.6
		Normal (≤ 20)	72	17.6
Oxygen saturation (%)	79.92 ± 12.4	Normal (≥ 92 %)	9	2.2
		Low (< 92 %)	66	16.2
Glasgow coma scale	6.53 ± 1.87	6 – 9	290	71.1
		3 – 5	118	28.9
Seizures		Generalized	20	4.9
		Focal	10	2.5
Focal motor deficit			155	38
Meningeal signs			29	7.1
Abnormal pupils			78	19.1
Abnormal cornea			30	7.4
Sensory loss			14	3.4

SD: Standard Deviation.

Table 4
Clinical investigations done in patients with non-traumatic coma.

Variables	Mean ± SD		Frequency (n)	Percentage (%)
Creatinine (mg/L)	39.41 ± 42.01	≤ 13	87	21.3
		> 13	110	26.9
Sodium (meq/L)	142.6 ± 9.54	< 136	9	2.2
		136 - 146	31	7.6
		>146	12	2.9
Potassium (meq/L)	4.13 ± 1.38	< 3.5	21	5.1
		3.5 - 5	18	4.4
		> 5	14	3.4
WBC count (per mm^3)	15,978.46 ± 13,416.15	<4000	2	0.5
		4000–10,000	63	15.4
		>10,000	122	29.9
Haemoglobin (g/dl)	12.2 ± 3.37	≥ 12	85	20.3
		< 12	102	25
CRP (mg/l)	111.35 ± 65.26	Negative	1	0.2
		Positive	22	5.4
Procalcitonin (ng/ml)	29.46 ± 52.41	Negative	2	0.5
		Positive	20	4.9
Brain CT-scan		Normal	78	35.8
		Abnormal	140	64.2
Brain MRI		Normal	34	39
		Abnormal	53	61

WBC: White blood cells, CRP: C-reactive protein, CT: Computed Tomography, MRI: Magnetic resonance imaging.

Forchap et al. [7]. However, this was higher than 41.5 % reported by Abdulkadir et al. in Ethiopia [3]. Their study was conducted at the ICU where severe cases are being transferred.

The most common etiology in our study was stroke accounting for 31.8 % of cases. This is consistent with a systematic review done in 2015 [10]. In Africa, Adeloye et al. reported an increase in incidence of more than 10 % between 2009 and 2013 [16]. This trend is reflected in a study carried out in the Department of Internal Medicine at DGH where non-communicable diseases represented more than two thirds of admissions [17]. This highlight the epidemiological transition ongoing in Sub-Saharan Africa with an increase burden of NCDs. For Ibekwe et al., 85 % of NTC patients were due to infections [2]. This latest study included the paediatric population. The predominance of infectious causes in non-traumatic childhood coma was also reported by Ali et al. [18]. Infectious causes were predominant in those less than 45 years, while metabolic disorders were more common in the 45 to 65 age group. HIV related neurological infections represented 24.7 % of infectious causes of NTC and carried a mortality rate of 66.7 %. With a prevalence of 2.7 % in 2018, Cameroon remains an endemic country for HIV [19]. Despite free HIV treatment and monitoring, the rate of non-adherence to treatment still remains high, thus exposing patients to opportunistic infections [20]. Covid-19 was found in 3.2 % of patients. The mortality rate of Covid-19 was 100 % in comatose patients in this study. In a meta-analysis of Covid-19 mortality in ICU, Armstrong et al. reported in March 2021 a mortality rate of 41.6 % [21]. Patients with a metabolic condition had better outcome as compared to other groups of etiologies. Horsting et al. and Fichet et al. in France in 2009 found similar results [10,22]. The cases of convulsive status epilepticus in this study reflect the severity of the clinical manifestations of the different etiologies of NTC. A study carried out in the same center found strokes and infections among the most common causes of convulsive status epilepticus [23]. The aetiology was not found in a large number of cases, reflecting the difficulty of accessing appropriate diagnostic tools in our setting.

About two third of patients died in the hospital. This was consistent with the in-hospital mortality of 66.7 % reported by Abdoukadir et al. [3]. Lower mortality rate was reported by Nwani et al. in a medical ward [8]. A higher mortality for most causes of NTC is expected in the ED where both severe and less severe cases are received. Patients are transferred to a medical ward when they have been stabilized. Lower in-hospital mortality rate was reported in Europe [21,22]. Availability of human and material resources and better organization of pre-hospital and in-hospital management of patients may contribute to this lower mortality in Europe [24,25]. In a more resource-constrained setting Forchap et al. reported an in-hospital mortality (84.8 %) [7]. In addition to the lack of suitable resources, more than two-thirds of patients transferred from a health facility to our referal center were transported by non-medical means. Several studies have demonstrated the positive impact of specialized critical care transport units for patients undergoing interhospital transport on the outcome of patients [26-28]. The setting up of an optimal organized medical transport service could contribute to significantly reducing this mortality.

Duration of hospitalization ≤ 3days, GCS < 6, elevated serum creatinine, administration of adrenergic drugs were predictive factors of mortality. Acharya and Amatya, in Nepal found association between increase duration of stay at the ED and increased hospital stay, increased mortality and increased inpatient transfer for ICU [29]. Several studies reported different predictors of poor outcome. Almost all reported that GCS < 6 was associated with poor outcome [2,3,6,7,8,12,14,15,30]. The global survival rate was 67.4 %, 44.3 %, 35.1 % at day 3, day 5 and day 10 respectively. Mapoure et al. found almost similar results in Senegal, where they found a survival rate of 50.3 % and 33.7 % at day 5 and day 10 of admission respectively [31]. Creatinine appears as a significant biomarker, closely associated with heightened in-hospital mortality in critically ill patients [32,33]. If low GCS might have contributed to increase the mortality, the provision of adrenergic medications, or short duration of stay were probably functions of irretrievable patient condition on presentation. One third of our participants died before reaching either the ICU or the internal medicine department. Patients admitted to the internal medicine department were more likely to

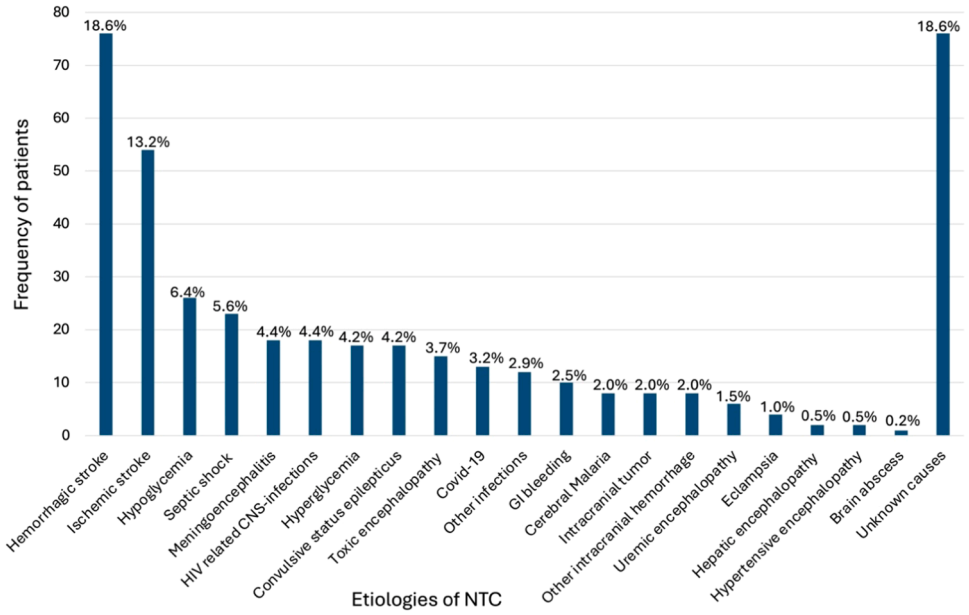

Fig. 2. Etiologies of non-traumatic coma (NTC). (GI: gastrointestinal)

Table 5
Predictors of mortality in non-traumatic coma.

Variables	aOR	95 % CI		*p*-value
		lower	Upper	
Hospitalisation ≤ 3 days	10.325	4.687	22.747	<0.001
GCS < 6	2.359	1.183	4.705	0.015
Systolic BP < 90 mmHg	1.070	0.326	3.516	0.911
Diastolic BP < 60 mmHg	1.394	0.544	3.571	0.489
Elevated serum creatinine	9.216	2.195	38.696	0.002
Infectious causes	1.934	0.845	4.428	0.118
Abnormal WBC	1.150	0.725	5.013	0.803
Intubation	2.737	0.810	9.248	0.105
Artificial respiration	2.425	0.638	9.214	0.193
Admission in ICU	0.425	0.198	0.931	0.028
Adrenergic	13.297	5.804	30.463	<0.001

aOR: adjusted Odd ratio, WBC: white blood cells, ICU: Intensive care unit, GCS: Glasgow coma scale.

survive after 5 days of admission compared to those admitted to the ICU.

This is one of the pioneer studies in the field of NTC in adults in Cameroon. We were able to identify predictive factor of mortality among comatose patients. However, some limitations need to be highlighted. The study was carried out in a single center, and thus results may not reflect the reality of NTC in the whole country. In addition, the outcome was only assessed during hospital admission and discharge from the DGH. This may underestimate deterioration following discharge.

Conclusion

Features of non-traumatic coma at the Douala General Hospital show some similarities with the literature. The commonest etiologies were stroke, metabolic disorders and infectious diseases. Three out of five patients died in the hospital, especially patients with severe coma on admission, elevated serum creatinine level, and those requiring

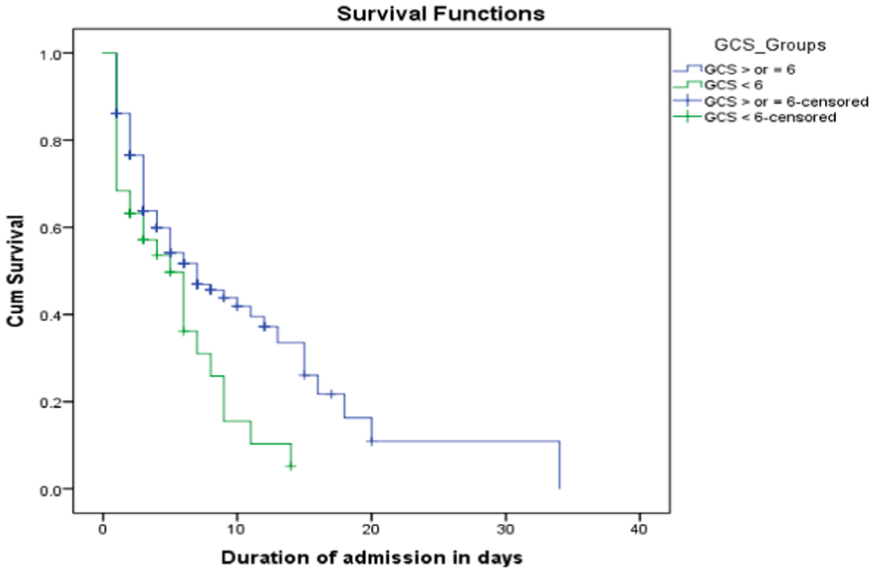

Fig. 3. Kaplan-Meier survival curves of NTC patients with GCS < 6 compared to those with GCS ≥ 6. GCS: Glasgow coma scale.

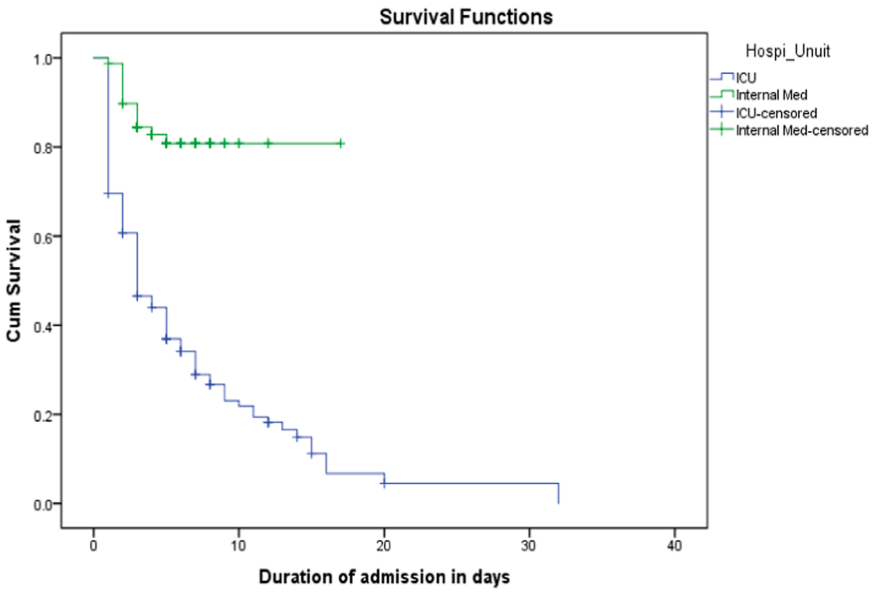

Fig. 4. Kaplan-Meier survival curves of NTC patients according to the unit of admission. ICU: intensive care unit; NTC: non-traumatic coma.

adrenergic drugs on admission. This raises the need to reinforce the structural and functional organization of ED in our setting.

Dissemination of results

Results from this study was shared with staff members of the ED, ICU, and internal medicine department at the DGH. The results were also presented as ePoster during the World Congress of Neurology 2023.

Authors' contribution

Authors contributed as follow to the conception or design of the work, the acquisition, analysis, or interpretation of data for the work; and drafting the work or revising it critically for important intellectual content: DGM, AHKM, MNY contributed 20 % each; and VVS, JAMM, AMM, EGBL, VS, PCMC, JD, and CKT contributed 5 % each. All authors approved the version to be published and agreed to be accountable for all aspects of the work.

Declaration of competing interest

The authors declared no conflicts of interest.

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