

# Profile and Outcome of Non-Traumatic Coma in a Limited-Resource Setting in the Southwest Region of Cameroon

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## Abstract

**Background:** Non-Traumatic Coma (NTC) almost always poses a diagnostic and therapeutic challenge, even in tertiary hospitals worldwide. We therefore aimed to determine the prevalence, aetiologies, and outcome of non-traumatic coma in two secondary referral centers in Cameroon. **Methods:** A 5-year retrospective hospital-based study was carried out, where medical records of patients aged 18 and above who presented with coma, not associated with physical assault, and were admitted to the medical wards were included. Bivariate and multivariate analyses were employed to identify associations and independent predictors, respectively. Survival rates were analyzed using the Kaplan-Meier estimator. **Results:** A total of 191 patient files were recruited out of 9581, accounting for 2% of admissions. Diseases with No Focal Neurological Deficits (DNFND) were the leading clinical presentation (47.1%). Stroke was the most frequent aetiology of NTC at 31.7% (60/189). The in-hospital mortality of NTC was 84.8% (n = 162/191). 9.9% (n = 19/191) of patients recovered completely. Factors associated with death were: GCS  $\leq$  5, stroke, hypertension, a length of hospitalization of  $\leq$  3 days, and the female gender. A length of hospitalization of  $\leq$  3 days, a GCS of  $\leq$  5, and HIV seropositivity appeared to be predictors of death. Being HIV seronegative or presenting with a GCS  $\geq$  6 conferred a 1.8 times higher odds of survival during admission. **Conclusion:** NTC is associated with higher mortality rates in our setting. It is therefore paramount to adopt a more clinical approach to diagnose the etiology of NTC, given the limitations in establishing diagnoses in these settings.

We have therefore proposed an algorithm which best suits these settings.

## Keywords

Non-Traumatic Coma, Aetiology, Outcome, Focal Neurological Deficit

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## 1. Introduction

NTC accounts for 3% - 7% of admissions in the medical wards, 8% - 10% in the emergency units and as high as 48.99% in the Intensive care units [1]-[4]. Non-traumatic coma (NTC) is a serious condition requiring swift medical or surgical decision-making upon arrival at the emergency department [5]. Comatose states, regardless of their aetiology, are often fatal as a result of the additional burden of coma on the primary disease. A coma is usually acute and a life-threatening emergency requiring prompt intervention for the preservation of life and brain function [1]. The aetiologies of coma are numerous and the window for optimal care is narrow [6] [7]. There is controversy as to which disease is the most common aetiology of NTC [1] [2] [8] [9]. Most studies implicate stroke (diseases with focal deficits) as the most common aetiology of NTC [2] [4] [8], while a few demonstrate metabolic causes (diseases with no focal neurological deficits) as the most common aetiology [1]. In Cameroon, stroke is the most common aetiology of NTC in first category hospitals and the second most common aetiology of neurological disorders at the emergency unit [10] [11]. Survival following NTC tends to increase in high-resource centers that are better equipped to diagnose the aetiology of coma and take immediate action, unlike in resource-limited centers with little or no access to sophisticated medical devices [12]. The outcome following NTC varies from full recovery to ultimately death, with poor outcomes being associated with age, Glasgow score at presentation, aetiology, and vital signs at presentation [3] [8]. Mortality rates associated with NTC are relatively higher in sub-Saharan countries compared to developed countries [3]-[5] [13]. Given the poor prognosis of NTC, with scant attention in resource-limited hospitals, we therefore decided to determine the prevalence of NTC, enumerate its aetiologies, assess its outcome, and identify predictors of death in two secondary referral centers.

## 2. Methods

### 2.1. Study Area/Setting

The Limbe Regional Hospital (LRH) and the Buea Regional Hospital (BRH) both serve as secondary referral centers for the southwest region of Cameroon, receiving patients from across the region.

The LRH has a capacity of 126 beds, 87 nurses, 22 general practitioners, and 18 specialists (1 cardiologist, 1 internist, 1 paediatrician, 1 endocrinologist, 1 nutri-

tionist, 1 anaesthesiologist/ICU physician, 3 radiologists, 2 obstetricians/gynaecologists, 7 surgeons). As of 14 November 2016, the hospital became equipped with an imaging centre and an intensive care unit. The intensive care unit has three beds and only became functional as of the 14<sup>th</sup> of July 2016. Prior to this date, all patients with NTC were managed in the medical wards.

The BRH has a capacity of 108 beds, 10 General Practitioners, and 9 specialists (1 cardiologist, 1 Internist/Nephrologist, 1 Internist/Neurologist, 2 Pediatricians, 2 Obstetrician/Gynecologist, 1 Pathologist, 1 Surgeon). The BRH has no ICU; consequently, patients with NTC are managed in the medical wards. Patients requiring a CT scan are sent to the imaging center in LRH. These hospitals work in synergy and also act as teaching hospitals of the Faculty of Health Sciences, University of Buea.

## 2.2. Patients and Study Design

We conducted a 5-year retrospective study from January 1<sup>st</sup> 2013 to March 31<sup>st</sup> 2018. This study was approved by the Institutional Ethics Committee of Research on Human Health of the Faculty of Health Sciences, University of Buea. Administrative clearance was obtained from the Regional Delegation of Public Health, Southwest. Patients aged 18 and above who presented with NTC prior to admission into the medical wards were included in our study.

## 2.3. Data Collection

The admission records of patients who presented with a Glasgow Coma score of  $\leq 9$  which was not related to physical assault (trauma) were selected for our study. Each selected file was given a code, to ensure confidentiality of data and a one time exploitation of the file. The selected patients' files were evaluated for a detailed history, clinical examination, relevant investigations, diagnosis, and outcome. The files of patients who became comatose while on admission were excluded. Demographic data, including age, sex, duration of coma prior to admission, length of hospitalization, and relevant medical history such as hypertension (HTN), diabetes mellitus (DM), HIV, stroke, epilepsy, and chronic kidney disease (CKD), were collected. Vital parameters such as blood pressure, pulse, respiratory rate, oxygen saturation, and the Glasgow Coma Score on admission were recorded. The GCS on admission was categorized into two groups: 3 - 5 and 6 - 9 [13]-[15]. The diagnosis (etiology) on discharge was recorded, and the outcome of NTC was graded by the Glasgow Outcome Scale.

Data were entered into the Statistical Package for the Social Sciences (SPSS) version 23 and analyzed. Frequencies and percentages were computed for categorical variables. The mean and standard deviation (SD) of all continuous data were reported. Bivariate analysis was employed to identify associations, while multivariate analysis was employed to identify independent predictors. For associations, the variables were defined as follows: **Dependent variables:** non-traumatic coma and outcome. **Independent variables:** socio-demographic factors, ae-

tiologies, and comorbidities. The level of significance for bivariate analysis and multivariate analysis was set at  $p < 0.05$ . Variables with a  $p < 0.2$  were selected for multivariate analysis. Survival rates were analyzed using the Kaplan-Meier estimator.

### 3. Results

#### 3.1. Basic Characteristics of the Study Population

Out of 13,447 patient files which we expected to be seen in the records offices of both hospitals, we found 9581 patient files, implying a total of 3866 missing files. Among the 9581 files viewed, 53 were incomplete and 191 met the inclusion criteria for our study.

The ages ranged from 19 to 109 years with a mean age of  $53.60 \pm 18.32$  years (Table 1). Females were slightly more represented at 50.3% ( $n = 96$ ) (Table 1). A greater proportion ( $n = 102$ , 62.2%) were admitted as elective (emergency) cases, with the mean duration of NTC prior to consultation being  $1.38 \pm 0.74$  days (Table 1), and the majority ( $n = 49$ , 69.0%) presented with a coma duration of less than a day. The mean length of hospitalization was  $4.78 \pm 2.79$  days (Table 1). When categorized, the majority ( $n = 105$ , 62.9%) of patients were admitted for about 3 days (Table 1). The most prevalent comorbidities associated with NTC were hypertension, HIV, and diabetes (Table 1). The mean Glasgow Coma Scale score on admission for patients presenting with NTC was  $6.2 \pm 2.1$  (Table 2).

**Table 1.** Basic characteristics of the study population.

Variables	Values
Female, n (%)	96 (50.3%)
Age, years (Mean $\pm$ SD)	53.60 $\pm$ 18.32
Duration of NTC prior to admission ( $\leq 1$ day)	49 (69.0)
Mode of admission: Elective (Emergency)	107 (62.2)
Length of hospitalization ( $\leq 3$ days)	105 (62.87)
Hypertension, n (%)	61 (31.9)
HIV n (%)	43 (22.5)
Diabetes Mellitus, n (%)	40 (20.9)
Hypertension and Diabetes, n (%)	23 (12.0)
Chronic Kidney Disease, n (%)	06 (0 3.1)
Hepatitis B, n (%)	04 (2.1)
Epilepsy n (%)	04 (2.1)
Stroke n (%)	03 (1.57)
Hepatitis C, n (%)	01 (0.53)
Sickle Cell Anaemia, n (%)	01 (0.53)
Parkinson Disease, n (%)	01 (0.53)

**Table 2.** Glasgow coma scale score on admission.

GCS	Mean $\pm$ SD	3 - 5	6 - 9
		n (%)	n (%)
	6.2 $\pm$ 2.1	64 (37.2)	108 (62.8)

### 3.2. Prevalence of NTC

Among 9581 patient files from the internal medicine units, 191 files were included in our study, giving a proportion of 2%.

### 3.3. Aetiology of NTC

Diseases with No Focal Neurological Deficit (DNFND) as a category were found to be the most predominant presentation of NTC, at 47% ( $n = 89/189$ ). Metabolic disorders were found to be the most predominant aetiologies of NTC within the category of DNFND, with the most frequent being hyperglycemic crisis: [*DKA* ( $n = 7$ ), *HONK* ( $n = 7$ ), *hyperglycemia* ( $n = 11$ )] at 13.2% ( $n = 25/189$ ), hepatic encephalopathy at 4.8% ( $n = 9/189$ ), and uremia at 4.8% ( $n = 9/189$ ). Individually, stroke was the most predominant aetiology of NTC, at 31.7% ( $n = 60/189$ ) (**Table 3**).

**Table 3.** Aetiologies of NTC.

AETIOLOGIES	FREQUENCY	PERCENTAGE
	N	(%)
<b>FND</b>	<b>73</b>	<b>38.6</b>
Stroke	60	31.7
Cerebral toxoplasmosis	09	4.7
Cerebral abscess	2	1.1
Subarachnoid haemorrhage	1	0.5
Cerebellar haemorrhage	1	0.5
<b>No FND</b>	<b>89</b>	<b>47.1</b>
Metabolic Disorders	51	29.3
Status epilepticus	7	3.7
Severe malaria	5	2.7
Intoxications	5	2.6
Others***	21	12.2
<b>Meningitis Syndromes</b>	<b>43</b>	<b>22.7</b>
Bacterial meningitis	20	10.4
Cryptococcal meningitis	04	2.1
Tuberculous meningitis	02	1.0
Meningoencephalitis	12	6.2
Encephalitis	05	2.6

**Metabolic Disorders:** Hyperglycaemic crisis = 25 (13.2), Hepatic encephalopathy = 09 (4.8), Uraemia = 09 (4.8), Hypoglycaemia = 7 (3.7), Hyponatremia = 01 (0.5).

### 3.4. Outcome of NTC

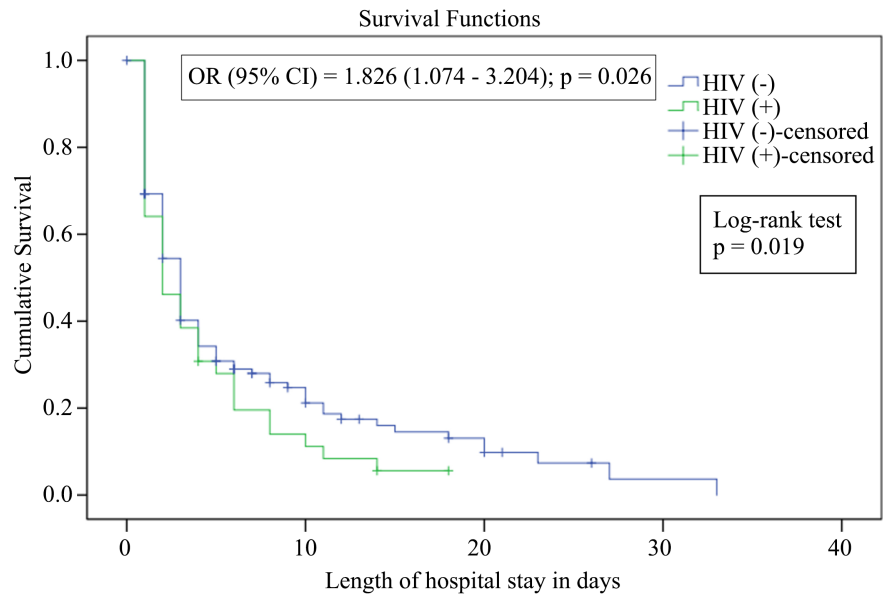
The in-hospital mortality rate was 84.8% (Table 4). Mortality was highest among stroke (DFND) patients, as 57 out of 60 (95%) stroke patients who presented with NTC died. GCS  $\leq 5$  [OR: 2.571 (CI = 1.053 - 6.277;  $p = 0.0240$ )], Stroke [OR: 4.796 (CI = 1.391 - 16.543;  $p = 0.007$ )], Hypertension [OR: 4.833 (CI = 1.402 - 16.661;  $p = 0.007$ )], length of hospitalization of  $\leq 3$  days [OR: 5.333 (CI = 1.743 - 16.322;  $p = 0.002$ )], and female gender [OR: 2.578 (CI = 1.107 - 6.002;  $p = 0.025$ )] were associated with death. Female sex [AOR = 5.316 (CI: 1.334 - 21.77;  $p = 0.001$ )], length of hospitalization of  $\leq 3$  days [AOR = 13.899 (CI: 3.028 - 63.802;  $p = 0.001$ )], GCS of  $\leq 5$  [AOR = 5.759 (CI: 1.183 - 28.038;  $p = 0.030$ )], and HIV seropositivity [AOR: 8.326 (CI = 1.288 - 53.811;  $p = 0.026$ )] appeared to be independent predictors of death on admission of patients with NTC (Table 4). Patients who were HIV negative or who had a Glasgow Coma Scale score  $\geq 6$  had 1.8 odds of surviving (Table 5) (Figure 1 and Figure 2).

**Table 4.** Outcomes of NTC using the glasgow outcome score.

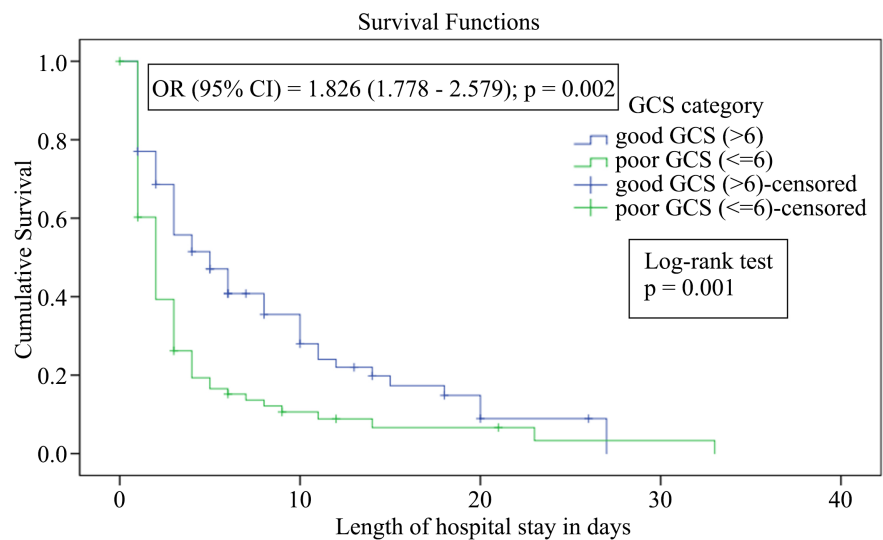
VARIABLE	FREQUENCY (n)	PERCENTAGE (%)
Death	162	84.8
Persistent Vegetative State	0	0.0
Severe Disability	2	1.0
Moderate Disability	8	4.0
Good Recovery	19	9.9

**Table 5.** Predictors of death in non-traumatic coma.

Variables	Dead (n = 29)	Alive (n = 232)	Univariate analysis		Multivariate analysis	
			Unadjusted OR (95% CI)	p value	Adjusted OR (95% CI)	p value
Age $\geq 65$ years	46 (28.2)	05 (17.2)	1.903 (0.684 - 5.291)	0.211		
Female gender	87 (53.7)	09 (31.0)	2.578 (1.107 - 6.002)	<b>0.025</b>	<b>5.316 (1.334 - 21.177)</b>	<b>0.018</b>
Duration of Coma prior to admission ( $\leq 1$ day), n (%)	40 (69.0)	9 (69.2)	1.013 (0.275 - 3.725)	0.985		
Length of Hospitalization ( $\leq 3$ days)	98 (69.5)	7 (26.9)	5.333 (1.743 - 16.322)	<b>0.002</b>	<b>13.899 (3.028 - 63.802)</b>	<b>0.001</b>
Mode of admission (Emergency)	91 (62.3)	16 (61.5)	1.313 (0.275 - 3.725)	0.939		
GCS $< 6$	60 (53.3)	4 (16.0)	2.571 (1.053 - 6.277)	<b>0.024</b>	<b>5.759 (1.183 - 28.038)</b>	<b>0.030</b>
Hypertension	58 (35.8)	3 (10.3)	4.833 (1.402 - 16.661)	<b>0.007</b>	3.046 (0.446 - 20.830)	0.256
HIV seropositive	40 (24.7)	3 (10.3)	2.84 (0.816 - 9.891)	0.088	<b>8.326 (1.288 - 53.811)</b>	<b>0.026</b>
Diabetes Mellitus	6 (20.7)	34 (21.0)	1.018 (0.384 - 2.699)	0.971		
Epilepsy	2 (6.9)	2 (1.2)	0.169 (0.023 - 1.249)	0.110		
CKD	5 (3.1)	1 (3.4)	0.892 (0.100 - 7.923)	0.918		
Stroke	57 (35.6)	3 (10.3)	4.796 (1.391 - 16.543)	<b>0.007</b>	<b>23.227 (1.091 - 494.574)</b>	<b>0.044</b>
Metabolic imbalance	42 (19.8)	9 (32.1)	0.527 (0.218 - 1.276)	0.151		
Meningitis	33 (20.6)	3 (10.3)	2.252 (0.642 - 7.899)	0.303		



**Figure 1.** Kaplan-Meier survival rate of HIV-positive patients compared with HIV-negative patients with NTC.



**Figure 2.** Kaplan-Meier survival rate of NTC patients with GCS  $\leq 6$  compared with that of those with GCS  $> 6$ .

#### 4. Discussion

The aim of this study was to determine the prevalence, aetiology, and outcome of NTC in the only two referral hospitals in the southwest region of Cameroon.

NTC accounted for 2% of admissions into the medical wards. Our findings were low but were expected because our study was limited to the medical wards, thereby excluding patients who died in the emergency units or who were immediately referred to a tertiary health facility upon arrival. Our findings were lower than those recorded in other African contexts [1] [2] [10] [13]. The higher prevalence can be explained by the following reasons: the studies were carried out in tertiary hospi-

tals, which had the capacity to manage comatose patients, whereas that was not the case in our study; variation in inclusion criteria; and variation in the study design and settings.

Diseases with No Focal Neurological Deficits (DNFND) as a category were the leading clinical presentation (43.0%) of NTC, among which metabolic disorders were the most frequent: Hyperglycemic crisis (13.2%), Hepatic Encephalopathy (4.8%), and Uraemia (4.8%). These findings corroborate the study carried out by Mohamed *et al.* (Nigeria, 2015) but are divergent from that of Owolabi *et al.* (Nigeria, 2012), who documented meningitis syndromes (28.9%) as the leading clinical presentation of NTC. Looking at the aetiologies of NTC individually in our study, stroke was the leading aetiology of NTC, 31.7% (n = 60/189). This finding is consistent with publications from other African settings [2] [4] [10] [14]. These similar findings could be explained by similar socio-demographic characteristics.

We reported an in-hospital mortality rate of 84.8%. We expected this rate to be high, given the lack of an intensive care unit and the limited scope of investigations, thereby prompting delay or inability to make a proper diagnosis and management. Our findings were thrice that recorded by Forsberg *et al.* (Sweden, 2010) who reported a mortality rate of 26.7% [13]. Our findings were higher than those of other studies in Africa [1] [2] [9]. Moreover, mortality was highest amongst stroke patients as 57 out of 60 (95%) stroke patients died. This finding was consistent with other studies [2] [8] [16]. A GCS of 3 - 5 was significantly associated with death as 60 out of 64 patients with a GCS  $\leq$  5 died. This finding was convergent with other studies [8] [10] [14] [15].

Other factors associated with death included: gender, length of hospitalization  $\leq$  3 days, stroke, hypertension, and HIV seropositivity. These findings were similarly recorded in other studies [9] [17]-[21]. Independent prognostic predictors of death in our study were: female gender, length of hospitalization  $\leq$  3 days, stroke, GCS  $\leq$  5, and HIV seropositivity. These findings were consistent with those of Owolabi *et al.* (Nigeria, 2013), who reported GCS  $\leq$  5 and hypertension [9] [22]. These results are similar due to the similar socio-demographic characteristics of the study settings. The clinical implication of these predictors of NTC in simple words is that if you have a patient with stroke or on an HIV terrain, who comes to a secondary referral Hospital in a context such as ours, with a GCS  $\leq$  5, will die within 3 days of admission. This outlines the importance of early recognition of the aetiology of NTC, prioritizing referral for admission in the intensive care unit.

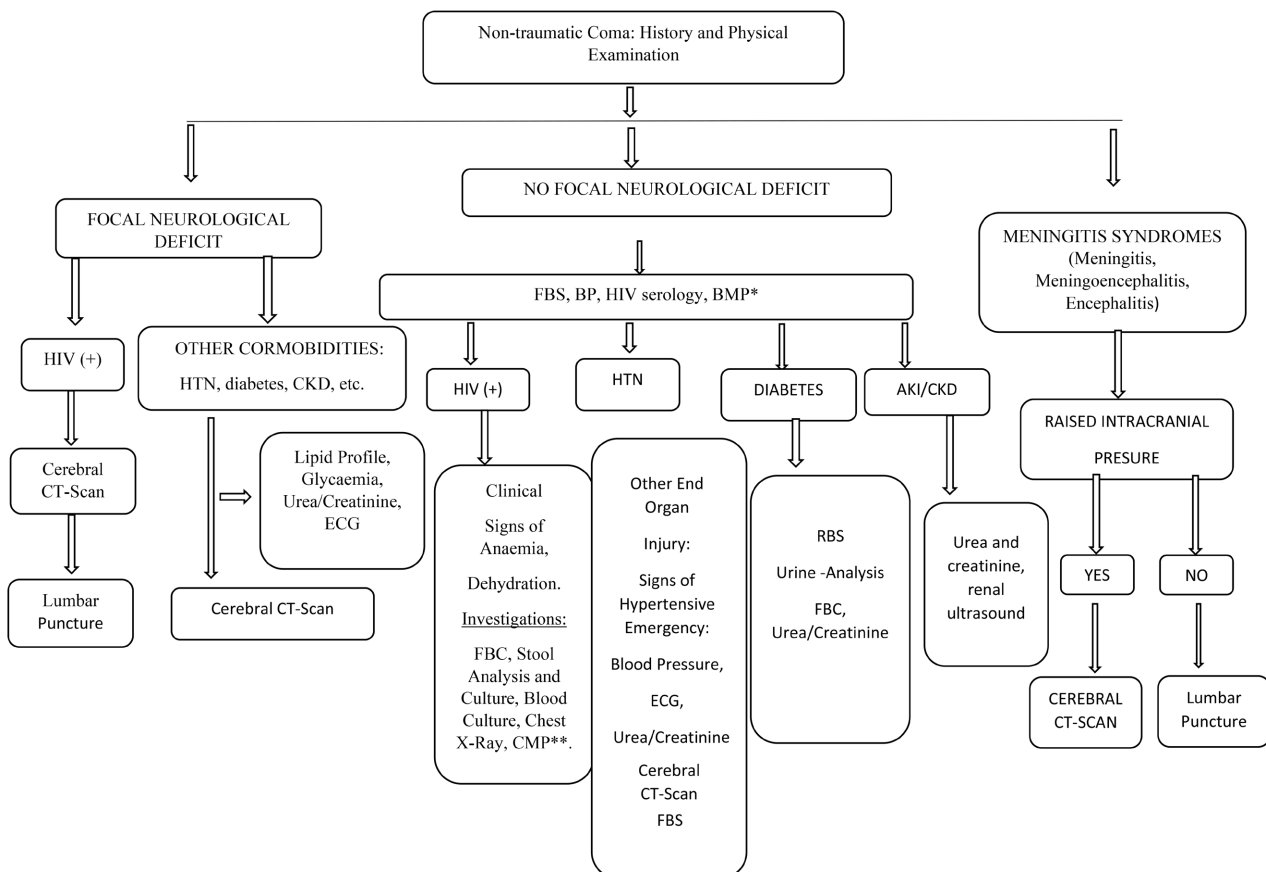
Our results simply show that NTC is not a far-fetched presentation in resource-limited hospitals. This study also demonstrates that mortality rates associated with NTC are very high in low-resource settings. These findings were anticipated, given the lack of an ICU, a stroke unit, limited scope of investigations, and the absence of universal health coverage.

Our study had a wide range of limitations, including the poor record keeping of these hospitals, which resulted in a large number of missing files that might have had a significant impact on our results. Our study did not take into consid-

eration the files of patients who presented with NTC who may have died at the hospital emergency unit, or transferred to tertiary Hospitals, which would likely have had an impact on the prevalence and outcome. Secondly, the retrospective nature of our study might not reflect current trends. However, this is one of the very few studies carried out in a secondary referral center and is most likely the first in Cameroon. This might serve as a starting point for more research on this subject.

## 5. Conclusion

Stroke remains the leading aetiology of NTC even in resource-limited settings of Cameroon. Our findings also suggest that 8 in 10 adults presenting with NTC in such a setting are likely to die. A length of hospitalization of  $\leq 3$  days, female gender, a GCS of  $\leq 5$ , and HIV seropositivity are predictors of death among patients presenting with NTC. The very high mortality rates and the overwhelming list of factors associated with poor outcomes of NTC simply outline the importance of preventive measures, the creation of a comprehensive clinical approach (algorithm) to identify the diagnosis of NTC in these settings, and also the need to provide these hospitals with the minimum (both human and material) resources (See **Figure 3**).



**Figure 3.** Algorithm for the diagnosis of NTC.

### 5.1. What Is Already Known on This Topic

- Stroke is the most frequent aetiology of NTC both in the Western world and Africa.
- The mortality rates associated with NTC are higher in African hospital settings compared to those in developed countries.
- A GCS  $\leq 5$  is a predictor of death.

### 5.2. What This Study Adds

- NTC is a frequent presentation in resource-limited hospitals and is associated with higher in-hospital mortality.
- The predictors of death associated with NTC in resource-limited settings include HIV seropositivity, GCS  $\leq 5$ , and female gender.
- This study is the first ever to be conducted in Cameroon and therefore, could be used as baseline data for future studies on this topic.

## 6. Recommendations

We propose a simple algorithm that is more clinical in its approach to the diagnosis of NTC, which can orient health staff in resource-limited settings, especially in Sub-Saharan Africa. The algorithm focuses on a rapid initial clinical assessment of the patient presenting with NTC, in a resource-limited setting. With these three simple questions, the health personnel will be able to situate the patient; Is my patient having a focal neurological deficit? Is my patient present with signs of meningeal irritation or an infectious syndrome? Is my patient presenting with NTC, not associated with either a focal neurological deficit or an infectious syndrome? This algorithm was proposed given the very high mortality rates and identified the predictors. The team reflected on what could be done in such a setting, within the first three days: Referral to higher levels of care, counselling the patient caregivers on prognosis and eventually drawing the attention of policy makers to the creation of the required infrastructure and human resources. It is worth noting that this algorithm has not been prospectively validated.

## 7. Definition of Operational Terms

1) **Coma:** An alteration in the level of consciousness with a GCS  $\leq 9$  for more than 6 hours.

2) **Hyperglycaemic crises:** A patient diagnosed with any of the following: isolated hyperglycaemia, DKA, or HONK.

3) **Systemic symptoms:** Non-specific symptoms that are present in any systemic disease.

4) **Low disability:** Light damage with minor neurological and psychological deficits.

5) **Moderate disability:** Low disability with no need for assistance in everyday life; employment is possible but may require special equipment.

6) **Severe disability:** Severe neurological injury with permanent need for help

in daily living.

**7) Persistent vegetative state:** Severe neurological damage with a prolonged state of unresponsiveness and lack of higher mental functions.

**8) Death:** Irreversible cessation of vital signs (heart rate, respiration, fixed dilated pupils).

**9) Non-traumatic Coma:** Coma resulting from any aetiology except trauma (physical assault).

**10) Poor outcome:** Patient with a who died or whom upon recovery was severely disabled.

**11) Stroke:** A focal neurological deficit lasting more than 24 hours with the aetiology being vascular in origin.

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## Conflicts of Interest

The authors have no conflicts of interest to declare.

## Authors' Contribution

Yacouba Njankouo Mapoure, Forchap Nkemanjong Milton, and Nkouonlack Cyrille developed the research questions. Chia Mark Ayeah analyzed and interpreted the data. Forchap Nkemanjong Milton and Nkouonlack Cyrille wrote the original manuscript, while Yacouba Njankouo Mapoure reviewed it for corrections.

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