Research Article

Factors associated with death and predictors of 1-month mortality in nontraumatic coma in a tertiary hospital in Northwestern Nigeria

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Abstract

Background: Coma occurring in the course of an illness ordinarily implies a poor prognosis and early prognostication is important for treatment decisions. The study was undertaken to study the factors associated with mortality in nontraumatic coma in a tertiary institution. **Materials and Methods:** In this prospective observational study, adults with clinically confirmed coma Glasgow coma scale (GCS) score of ≤8, admitted consecutively to the emergency unit of a tertiary hospital in Northwestern Nigeria over a period of 18 months were recruited. Vital parameters, severity of coma by GCS and neurological signs were recorded. The etiology of coma was determined on the basis of history, clinical examination, and laboratory investigations. Outcome was determined within 1 month of onset of coma by patients' death or survival. **Results:** A total of 194 patients (140 males and 54 females) were recruited with mean age was 53.7 ± 1.4. The predominant etiological factors were central nervous system (CNS) infections (28.9%), toxic and metabolic (28.9%), and stroke (23.7%). Overall, 1-month mortality was 49%. On univariate analysis, the factors that showed significant association with outcome were gender, blood pressure, GCS, breathing pattern, pupillary size, pupillary reaction, papiloedema, and abnormal posturing. Abnormal pupillary size, severe hypertension, and GCS score ≤5 were independent predictors of in-hospital 1-month mortality in nontraumatic coma. **Conclusion:** The independent important predictors of nontraumatic 1-month coma mortality in a developing country setting were GCS ≤ 5, abnormal pupillary size, and severe hypertension.

Keywords: Coma, mortality, predictors

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Introduction

Nontraumatic coma is one of the most common presentations in emergency department settings. Coma occurring in the course of an illness traditionally implies a poor prognosis,[1] Because patients admitted to hospital in coma from causes other than trauma have a high mortality, in some situations, comparison has to be drawn between the highly demanding care required and the poor outcome. Thus, early decisions about the intensity of treatment and about the need to use artificial ventilation would be greatly simplified if healthcare givers could select early in the illness factors related to good quality survival and, perhaps more importantly, delineate those patients with almost no chance of independent recovery.[1,2]

However, the number of published studies of adult patients presenting with coma has been surprisingly small in Nigeria despite the relatively high mortality as depicted by a study conducted in Southwestern Nigeria.[3] Consequently, information about prognosis of coma as well as drawing of attention to whether early

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symptoms and signs correlate with outcome is desirable. Such information is essential if clinicians are to identify those comatose patients most likely to regain meaningful function with proper therapy. The information will also assist in taking decisions for further care in the intensive care unit (ICU) to ensure judicious utilization of resources.

Thus, a comprehensive study of history, clinical features, and laboratory parameters that may predict poor outcome in nontraumatic coma is desired. The current study was undertaken to study the factors associated with death and predictors of mortality in nontraumatic coma in a tertiary institution in Kano.

Materials and Methods

In this prospective observational study, adults admitted consecutively to nonsurgical emergency unit of a tertiary hospital in Kano, Nigeria over a period of 18 months (March 2008–September 2009) were recruited. Inclusion criteria was all adult patients in whom there was clinically confirmed coma (Glasgow coma scale (GCS) score of ≤8).[1,3,4] The medical section of accident and emergency unit of the tertiary health institution is a major entry point to the medical department of the hospital where patients with life-threatening conditions requiring urgent medical attention are attended to. It is a high care area offering 24 h daily service. The hospital attracts patients from Kano and the neighboring states in Northwestern Nigeria. Exclusion criteria comprised patients with coma of traumatic cause; patients with coma post anesthesia; patients whose coma was believed to be secondary to sedative drugs or alcohol, as almost all such subjects should recover fully with supportive treatment whatever their early signs;[1] and patients whose relations did not consent to the study.

Assessment of clinical neurological status including cranial and peripheral motor and sensory neurological examination, and cerebella function were carried out on all the patients.

Clinical signs studied were temperature, pulse volume, heart rate, blood pressure, coma severity by GCS, posturing, respiratory pattern, pupillary size, pupillary and corneal reflex, motor patterns, seizures, and findings on fundoscopy. To reduce bias, the clinical signs were studied by more than one investigator and the average findings were documented.

The respiratory pattern considered as abnormal included Cheyne-Stokes respiration, neurogenic hyperventilation, and apneustic and ataxic breathing patterns.

The etiology of coma was determined on the basis of history, clinical examination, and relevant laboratory investigations. Investigations, such as lumbar puncture, CT scan, and metabolic work-up were carried out depending on the clinical presentation.

Following initial evaluation at the accident and emergency unit, the patients were transferred to medical wards and on few occasions, ICU, where they had further treatment and monitoring on a daily basis for outcome for a minimum of 1 month.

Standard practice guidelines, as contained in the protocol of teaching hospital, were used in the management of patients. Careful attention to medical problems was part of the management protocol for all coma patients. Surgical intervention was undertaken in selected cases based on individualized decisions by the managing team.

Etiology of coma was classified into infectious, toxic-metabolic, stroke, and others.

Outcome, within 1 month of onset of coma, was determined by patients' death or survival.

Data analysis

Analysis of data was carried out using the Statistical Package for Social Sciences (SPSS) program for Windows version 16.0 (SPSS Inc., Chicago, IL). Univariate analysis was carried out using Pearson's Chi-square test for categorical variables. Scores on severity scale were compared using Chi-square for trend and Student's *t*-test for continuous variables. $P < 0.05$ was adopted as a significant level. The variables that were significant on univariate analysis were subjected to multiple logistic regression model and the covariates were adjusted for each independent (regression) variable to find independent predictors of in-hospital mortality. Survival rate was calculated and expressed using the Kaplan-Meier method.

Results

A total of 194 patients comprising 140 males and 54 females were recruited during the study period. Their mean age was 53.7 ± 1.4. The peak age of presentation was between 50 and 60 years. Figure 1 highlights age and sex distribution of the patients. One hundred and sixteen (59.8%) patients presented to the accident and emergency unit of the hospital within 24 h of onset of coma. The predominant etiological factors were central nervous system (CNS) infections which occurred in

56 (28.9%), toxic and metabolic causes in 56 (28.9%), and stroke in 46 (23.7%) [Table 1]. Stroke was the most common singular etiological factor identified.

In 1-month of follow-up, mortality was 49%. The highest case fatality (69%) was recorded among stroke patients that presented in coma. As the GCS decreases, the mortality significantly got worse [Table 2]. Figure 2 showed Kaplan-Meir survival curve pattern for the various etiological categories. Table 3 highlights the factors significantly associated with mortality in coma. A logistic regression model demonstrated that the initial GCS score of less than 5, severe hypertension, and abnormal pupillary size were independent predictors of mortality in coma [Table 4].

Discussion

In resource poor countries, physicians are often faced with the task of predicting the immediate and long term outcome of patients in coma as it is important to efficiently and optimally utilize meager resources. This underscores the need for simple and applicable clinical variables that could serve as determinants of in-hospital mortality in medical coma. Moreover, early prognostication of outcome is relevant for directing rehabilitation treatment and for informing patients and relatives about the prognosis. However, predicting outcome in patients that presented in coma may be difficult due to the variability in etiology presentation and underlying pathophysiological mechanism.

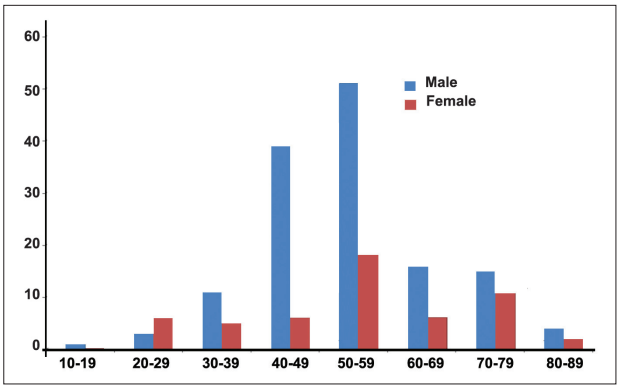

Figure 1: Distribution of gender by age of the patients

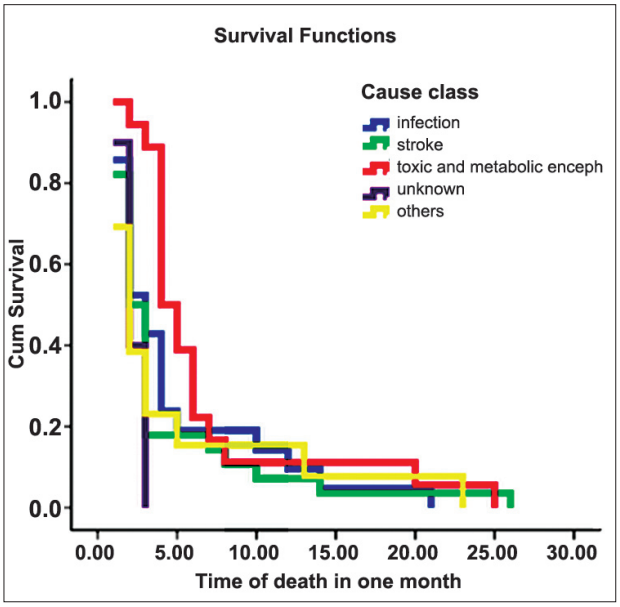

Figure 2: Kaplan-Meier survival curve illustrating the decreasing number of survivors in different coma etiologic categories during the 1-month follow-up

In our study, the predominant causes were infections, toxic and metabolic causes, and stroke. This finding agrees with previous reports within and outside Nigeria in spite of the geographic and technological differences.[1-4] However, when the etiological factors were considered individually, stroke appeared the most common cause. This finding conforms to the report from Southwestern Nigeria,[3] Previous reports from the study centre showed that stroke is a common neurological disorder in Kano, Northwestern Nigeria,[5] accounting for 77.6% of neurological admissions.[6]

Table 1: Distribution of etiology of coma

Etiology	Frequency	Percentage
Infection	56	28.9
Septicemia	24	12.4
Bacterial meningitis	17	8.8
Tuberculous meningitis	9	4.6
Encephalitis	2	1.0
Disseminated tuberculosis	4	2.1
Toxic and metabolic encephalopathy	56	28.9
Chronic kidney diseases	20	10.3
Chronic liver disease	16	8.2
Hypoglycemia	8	4.1
Hyperglycemia	12	6.2
Stroke	46	23.7
Others	20	10.3
Status epilepticus	8	4.1
Other HIV related diseases	8	4.1
Cancers	4	2.1
Undetermined	16	8.2
Total	194	100

Table 2: Association between absolute GC score and outcome

GCS on admission	Outcome		Total
	Died	Survived	
8	1	8	9
7	5	29	34
6	7	29	36
5	29	10	39
4	23	13	36
3	30	10	40
Total	95	99	194

Chi-square for trend=43.99, P=0.001

Table 3: Clinical parameters significantly associated with one-month mortality

Variable (at presentation in accident and emergency)	Proportion of patients who died		OR (95% CI)	*P* value
	Proportion	Percentage		
Age			1.5 (0.83-2.83)	0.14
>50	58/108	53.7		
<50	37/86	43.0		
Sex			5.1 (2.34-11.26)	0.001*
Male	83/140	59.3		
Female	12/54	22.2		
Late presentation			3.6 (1.85-6.85)	0.001*
<24 h	24/78	30.8		
>24 h	71/116	61.2		
Blood pressure (mean >140)			2.5 (1.35-4.69)	0.002*
Abnormal	55/90	61.1		
Normal	40/104	38.5		
Temperature			1.6 (0.86-3.08)	0.114
Abnormal	67/126	53.2		
Normal	28/68	41.2		
Pulse rate			1.4 (0.72-2.61)	0.308
Abnormal	67/130	51.5		
Normal	28/64	43.8		
GCS			12.1 (5.59-26.46)	0.001*
3-5	82/116	70.7		
6-8	13/78	16.7		
Respiratory pattern			1.7 (0.39-3.01)	0.089
Abnormal	44/78	56.4		
Normal	51/116	44.0		
Pupillary size			5.8 (2.35-14.64)	0.001*
Abnormal	32/40	80.0		
Normal	63/154	40.9		
Pupillary reaction			3.9 (1.53-9.96)	0.001*
Abnormal	24/32	75.0		
Normal	71/162	43.8		
Papiloedema			4.6 (2.12-10.04)	0.001*
Present	40/54	74.1		
Absent	43/112	38.4		
Abnormal posturing			2.1 (1.08-4.28)	0.019*
Present	20/56	37.1		
Absent	75/138	54.4		
Seizures			1.5 (0.68-3.22)	0.292
Present	21/37	56.8		
Absent	74/157	47.1		
Co-morbidity			1.3 (0.71-2.37)	0.372
Present	55/106	51.9		
Absent	40/88	45.5		

OR: Odds ratio; CI: Confidence interval; GCS: Glasgow coma scale; *Statistically significant

Table 4: Result of multivariate logistic regression analysis for independent predictors of 1-month mortality

Independent predictors	Beta	Standard error	Odds ratio (95% CI)	*P* value
GCS <5	2.366	0.790	10.7 (2.40-47.32)	0.002
Mean BP >140	2.001	0.761	7.4 (1.57-34.79)	0.011
Abnormal pupillary size (dilated or small pupil)	–4.195	1.214	11.9 (1.01-16.30)	0.001

GCS: Glasgow coma scale; BP: Blood pressure; CI: Confidence interval; *Statistically significant

The mortality rate of 49% recorded in the present study, although comparable to report from other places,[4,7,8] was less than 76% previously reported in Ibadan,[9] southwestern Nigeria. This difference could be ascribed to a higher proportion of coma from metabolic encephalopathy with a better recovery rate in our study. Nonetheless, the figure is less than those reported in certain developed countries where patients received better emergency and intensive care. For instance, a study conducted in Stockholm, Sweden; mortality rate of 26.5% was reported, but in that study, 30% of the study patients received treatment in the ICU.[10] On the contrary, ICU of the study hospital is a 4-bedded facility serving as a general ICU for Kano, Jigawa, and Katsina states; all in Northwestern Nigeria which is grossly inadequate. Access to this vital care is often very competitive and bed occupancy is 75-100%.

On univariate analysis, the factors that showed significant association with outcome in medical coma were gender, blood pressure, GCS, breathing pattern, pupillary size, pupillary reaction, papiloedema, and abnormal posturing. This result parallels those obtained in patients with traumatic coma.[11-14]

In the present study, despite a higher proportion of poor outcome among the older groups of patient, there was no statistically significant association between age and outcome. Previous reports on effect of age on medical coma in children and adults revealed conflicting findings.[9,15] Nonetheless, our finding suggests that the prognosis for recovery from nontraumatic cerebral insult as one ages may not necessarily be a function of the aged brain, but the type of insult that occurs frequently in each age group.

As reported in previous studies,[1,2] abnormal breathing pattern was significantly associated with mortality in nontraumatic coma. Different abnormal respiratory pattern may be seen in coma depending on the part of brain that is involved. Abnormal breathing pattern recorded in this study included apneustic, ataxic, and Cheyne-Stokes respiration.

An abnormal neuro-ophthalmological sign at presentation is known to forecast a bad prognosis.[1,2,4,16] In this study, statistically significant association was obtained between pupillary size, pupillary reactivity, and outcome of nontraumatic coma. The parasympathetic, pupilloconstrictor, light reflex pathway mediated by the third cranial nerve is anatomically adjacent to brainstem areas controlling consciousness and medial temporal lobe. Therefore, damage to midbrain third nucleus or efferent third nerve by temporal lobe compression produces dilation of the pupil. If the damage or compression is significant, the pupil will be

unresponsive to a light stimulus. The pupillary light reflex and size equality of pupils had been shown to have a high interobserver reliability.[17] Therefore, the use of pupillary size and light reflex are indirect measures of dysfunction to pathways subserving consciousness and; thus, important clinical parameters in assessing outcome from traumatic coma. However, effort should be made to exclude direct occulomotor neuropathy before pupillary reactivity or size is considered a prognostic indicator.

In this study, severe systemic arterial hypertension was found to be a statistically significantly associated with mortality which agrees with report from elsewhere.[9] However, in similar studies conducted on patients with traumatic coma hypotension was rather found to be predictive of poor outcome.[11,12]

We found an increasing probability of poor outcome with decreasing GCS, in a stepwise manner in this study. Besides, GCS < 5 was found to be predictive of 1-month mortality. This finding concurs with previous reports in both traumatic and nontraumatic coma.[1,2,8,11,12,18] The GCS has been shown to have adequate information to identify specific levels of consciousness and to categorize the severity of coma. In previous report, GCS was found to be a reliable predictor of 2-week outcome.[19] In the report, patients with GCS scores of 3 to 5 had a greater risk of death or persistent coma at 2 weeks than patients with higher scores of 6 to 8.[19] The estimated probability of waking from nontraumatic coma by 2 weeks was seven times higher in those with a higher initial GCS score.[19]

Although physicians usually attempt to take a wide range of factors into account when making clinical decisions and assessing prognosis, there is probably a redundancy in this effort to be complete. Nevertheless, in clinical practice, relatively few features have been found to contain most of the prognostic information.[20] In the present study, adjusting for all other factors, GCS of less than 5, pupillary size, and severe hypertension were found to be independent predictors of nontraumatic coma.

In Sub-Saharan Africa with inadequacy and/or escalating costs of intensive care, such variables, as reported in this study, that provide some prognostic information can aid in decisions about allocation of resources as well as assist in clinical therapeutic decisions and counseling patients' relatives regarding the prognosis.

Conclusion

In conclusion, the present study provides information on the important predictors of nontraumatic coma mortality in a developing country setting. GCS of less than 5, abnormal pupillary size, and severe hypertension were independent predictors of nontraumatic coma.

References

1. Bates D, Caronna JJ, Cartlidge NE, Knill-Jones RP, Levy DE, Shaw DA, *et al*. A prospective study of nontraumatic coma: Methods and results in 310 patients. Ann Neurol 1977;2:211-20.
2. Levy DE, Bates D, Caronna JJ, Cartlidge NE, Knill-Jones RP, Lapinski RH, *et al*. Prognosis in nontraumatic coma. Ann Intern Med 1981;94:293-301.
3. Obiako OR, Oparah S, Ogunniyi A. Causes of medical coma in adult patients at the University College Hospital, Ibadan Nigeria. Niger Postgrad Med J 2011;18:1-7.
4. Diango D, Moghomaye M, Maiga Y, Beye SA, Dembele AS, Coulibaly Y, *et al*. Coma in the elderly: Etiological factors, management, and prognosis in the department of anesthesia and intensive care. Anesth Essays Res 2011;5:153-7.
5. Owolabi LF, Nagoda M. Stroke in developing countries: Experience at Kano, Northwestern Nigeria. Sudan J Med Sci 2012;7:9-14.
6. Owolabi LF, Shehu MY, Shehu MN, Fadare J. Pattern of neurological admissions in the tropics: Experience at Kano, Northwestern Nigeria. Ann Indian Acad Neurol 2010;13:167-70.
7. Matuja WB, Matekere NJ. Causes and early prognosis of non-traumatic coma in Tanzania. Muhimbili Medical Centre experience. Trop Geogr Med 1987;39:330-5.
8. Sinclair JR, Watters DA, Bagshaw A. Non-traumatic coma in Zambia. Trop Doct 1989;19:6-10.
9. Obiako OR, Ogunniyi A, Anyebe E. Prognosis of non traumatic coma: The role of some socio-economic factors on its outcome in Ibadan, Nigeria. Ann Afr Med 2009;8:115-21.
10. Forsberg S, Höjer J, Ludwigs U. Prognosis in patients presenting with non-traumatic coma. J Emerg Med 2012;42:249-53.
11. Jennett B, Teasdale G, Braakman R, Minderhoud J, Heiden J, Kurze T. Prognosis of patients with severe head injury. Neurosurgery 1979;4:283-9.
12. Fleminger S, Ponsford J. Long term outcome after traumatic brain injury. BMJ 2005;331:1419-20.
13. Perel P, Edwards P, Wentz R, Roberts I. Systematic review of prognostic models in traumatic brain injury. BMC Med Inform Decis Mak 2006;6:38.
14. Willemse-van Son AH, Ribbers GM, Verhagen AP, Stam HJ. Prognostic factors of long-term functioning and productivity after traumatic brain injury: A systematic review of prospective cohort studies. Clin Rehabil 2007;21:1024-37.
15. Bansal A, Singhi SC, Singhi PD, Khandelwal N, Ramesh S. Non traumatic coma. Indian J Pediatr 2005;72:467-73.
16. Tokuda Y, Nakazato N, Stein GH. Pupillary evaluation for differential diagnosis of coma. Postgrad Med J 2003;79:49-51.
17. van den Berge JH, Schouten HJ, Boomstra S, van Drunen Littel S, Braakman R. Interobserver agreement in assessment of ocular signs in coma. J Neurol Neurosurg Psychiatry 1979;42:1163-8.
18. Zafonte R, Hammond FM, Mann NR. Relationship between Glasgow coma scale and functional outcome. Am J Phys Med Rehabil 1996;75:364-9.
19. Sacco RL, VanGool R, Mohr JP, Hauser WA. Nontraumatic coma: Glasgow coma score and coma etiology as predictors of 2-week outcome. Arch Neurol 1990;47:1181-4.
20. Braakman R, Gelpke GJ, Habbema JD, Maas AI, Minderhoud JM. Systematic selection of prognostic features in patients with severe head injury. Neurosurgery 1980;6:362-70.

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