

Non-traumatic Coma: Causes and Outcome of Adult Patients at University of Gondar Hospital, Northwest Ethiopia

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Abstract: Coma represents a serious, life-threatening medical condition which should be treated effectively. It is important to recognize the underlying causes of coma in order to provide timely medical treatment. There is dearth of data on causes of medical coma in adults in Africa. This research aimed at determining the cause and outcome of coma in University of Gondar Hospital. Methods: A prospective observational descriptive study was conducted from 01/01/2014 to 31/06/2014 G.C in University of Gondar Hospital. All consecutive non trauma patients admitted to the medical wards with a Glasgow Coma Scale of 8 or less were included. An interview administered questionnaire to patient attendants and neurologic examination were employed to collect data like sociodemographics and clinical features. All important laboratory tests and outcome data were documented at patient discharge. Verbal consent from attendants was taken. Data was entered to and analyzed using Epiinfo7. Result: A total of 53 patients constituting approximately 3.4% of the medical emergencies seen during the study period were included in the study. The most common cause of coma were diseases that cause no focal neurologic deficit (FND), occurring in 31 (58.5%) patients. Among the causes with non-localizing signs, the most common causes were intoxications, uremic and hepatic encephalopathies, occurring in 11 (20.8%), 7 (13.2%), and 5 (9.4%) of the patients, respectively. Organophosphate (malathion) poisoning was the most common agent of intoxication responsible for 9 patients out of 11. These were followed by diseases with FND and meningitis syndromes, occurring in 14 (26.4%) and 8 (15.1%) patients, respectively. Among the patients admitted with coma without FND, 17 (54.8%) of the patients died, 6 (19.3%) had disability and 8 (25.8%) patients were discharged with improvement. In contrast, among patients admitted with coma with FND, no patient was discharged with improvement, 7 (50%) died and 7 (50%) were disabled. Among patients admitted with meningitis syndrome, 4 (50%) died, 2 (25%) were disabled and 2 (25%) were discharged with improvement. Conclusion: Diseases presenting without focal neurologic deficit, including toxic and metabolic causes, are the most common causes of coma. Among these, the most common was malathion poisoning which is reversible with appropriate care. Meningitis syndrome was not found to be a prominent cause of coma. Medical coma, regardless of the etiology, was associated with high mortality rate.

Keywords: Focal Neurologic Deficit, Glasgow Coma Scale, Intoxication, Meningitis Syndrome

1. Introduction

Coma is defined as a deep sleeplike state from which the

patient cannot be aroused. Almost all instances of diminished alertness can be traced to widespread abnormalities of the cerebral hemispheres or to reduced activity of the RAS [1, 2].

The causes of coma can be divided into three broad categories: those without focal neurologic signs, meningitis syndromes, and conditions associated with prominent focal signs. In most instances, coma is part of an obvious medical problem, such as drug ingestion, hypoxia, stroke, trauma, or liver or kidney failure. The majority of medical causes of coma can be established without a neuroimaging study and most hospitals in tropical Africa should be able to diagnose up to 90% of cases with non-traumatic coma and simple therapy is likely to be effective in the majority of cases [3, 4]. Coma represents an acute, life-threatening emergency requiring prompt intervention for preservation of life and brain function. 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 particular burdens to the primary disease. Patients admitted to the hospital in coma from causes other than trauma have a high mortality and the survivors have a high morbidity [3, 5-8]. Diseases of medical origin leading to coma account for 3-15% of emergency hospital admissions in developed countries. There is dearth of data on causes of medical coma in adults in Africa. Studies have shown that despite best treatment, only about 15% of patients unconscious from non-traumatic causes made a satisfactory neurologic recovery [9, 10].

Different studies have shown different results regarding the causes and outcomes of coma. Studies done in developing countries like India and Africa have shown contrasting results about the causes and outcomes of coma. A study done in India and one in Africa have shown that stroke is the commonest cause of coma [9, 11]. But another study done in Nigeria and Tanzania found that in fact infections to be the commonest causes [12, 13]. There was also contrasting results regarding the outcome of coma patients. A study in Europe showed the mortality to be 26.5%, but in Africa and a study in India showed the mortality to be 51% and 49%, respectively [11, 12, 14]. In Ethiopia, there are no studies about causes and outcome of coma, but one study done on 202 patients about etiology and outcome of non-traumatic altered states of consciousness in Gondar College of Medicine and Health Sciences showed that the commonest cause was infection (55%) followed by metabolic disorders (22.3%), structural lesions (14.9%) and poisoning (3.5%). The etiology was not identified in 4.5% of the patients. Cerebral malaria was the commonest infectious cause followed by chronic meningitis and/ or encephalitis. In hospital mortality rate was 60.4% [15]. Unknown diagnosis, structural neurologic and metabolic causes were associated with increased mortality rate, the same was true for presence of HIV infection [15].

The causes of coma are vast and different studies have shown different results as its causes, outcomes and prognosis. Because coma represents a serious, life-threatening medical condition which should be treated effectively, it is important to recognize the underlying causes of coma in order to provide timely medical treatment. The need for efficiently reaching at a diagnosis and providing appropriate acute care

demands that the physician should have a syndromic approach that leaves none of the common and treatable causes of coma unexplored. There is no data on the causes and outcomes of coma in Ethiopia.

2. Methods

2.1. Study Design and Setting

This is a prospective observational descriptive study conducted in the University of Gondar Hospital medical wards from January 1, 2014 to June 31, 2014. The hospital is situated in North Ethiopia, serving as a referral hospital for over 5 million people. All consecutive adult non trauma patients who were admitted in the medical wards of University Gondar Hospital with a GCS less than 8 from January 1, 2014 to June 31, 2014 were included in the study. Trauma patients and patients whose attendants did not consent to the study were excluded. A pretested questionnaire was prepared and completed by a trained medical resident. Member(s) of the patient's family or care giver(s) were interviewed about the patient's current history, past illness and medication history if there are any. Then a thorough physical examination was done including a detailed neurologic exam. The parameters collected were the patient's vital signs, the GCS, respiratory pattern, corneal reflex, presence of seizure, postural response, gag reflex, and pupillary reflex. The pupils were inspected for the presence of papilledema. Routine laboratory tests available in the hospital such as Random blood glucose were determined for almost all patients. The etiology of coma was then classified into diseases that cause focal neurologic deficit, diseases that cause no focal neurologic deficit, and meningitis syndrome, each having subclasses with a specific cause. The patients were reassessed at the time of discharge and their condition at discharge was classified as full recovery, disability, patient went against medical advice or death. Disability was defined as any impairment in a person's ability to function.

2.2. Data Processing and Analysis

After data was checked for completeness and accuracy, it was entered to and analyzed using EpiInfo 7. Descriptive statistics is presented in means and standard deviation for numerical variables and frequency percentages for categorical variables. Tables and graphs were used to show results.

2.3. Ethical Consideration

The proposal was submitted to the IRB of the school of medicine, University of Gondar and the study was undertaken after approval was obtained. A verbal consent was taken from the patient's family member(s) or care giver(s). Written consent was not taken since the study did not involve any invasive tests. The aim of the study was introduced and they were informed that participation is voluntary and they can decline from the study at any stage. The patient's family member(s) or care giver(s) were assured of the confidentiality

of the information they provide about the patient and privacy will be maintained. Except for the detailed neurologic examination, no other noninvasive or invasive diagnostic tests were done for the study purpose. We utilized the routine medical care laboratory and diagnostic results.

3. Results

A total of 53 patients constituting approximately 3.4% out of 1560 patients admitted to the medical emergencies during the study period were included in the study.

3.1. Sociodemographic and Clinical Profile

They comprised 32 (60.4%) males and 21 (39.6%) females. The mean age was 41 ± 18.7 years, with the minimum and maximum ages being 15 and 84. Twenty four (45.3%) patients had at least one underlying chronic medical illness. Among these patients, 17 (71%) of them were males. Hypertension, HIV, CKD, and diabetes mellitus were the most common chronic illnesses. Fourteen (58.3%) of these patients were on at least one medication. (Figure 1)

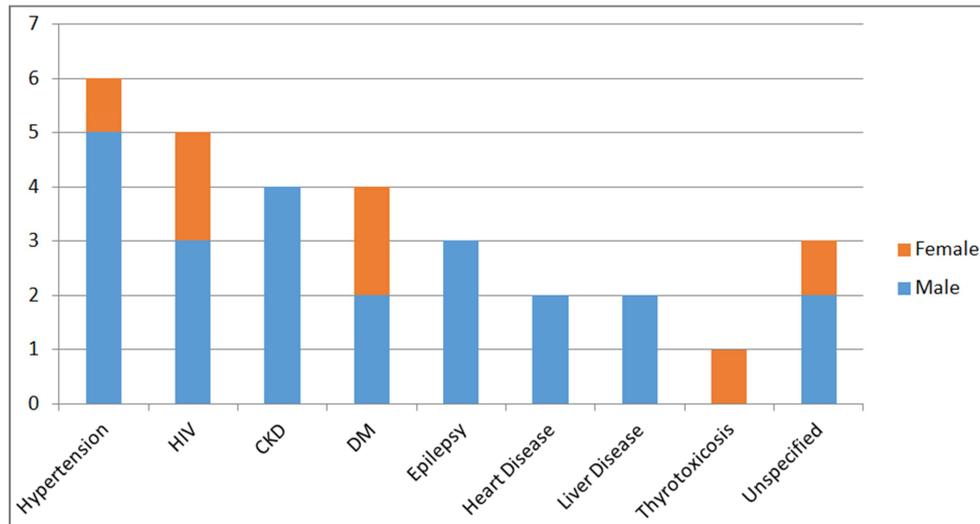
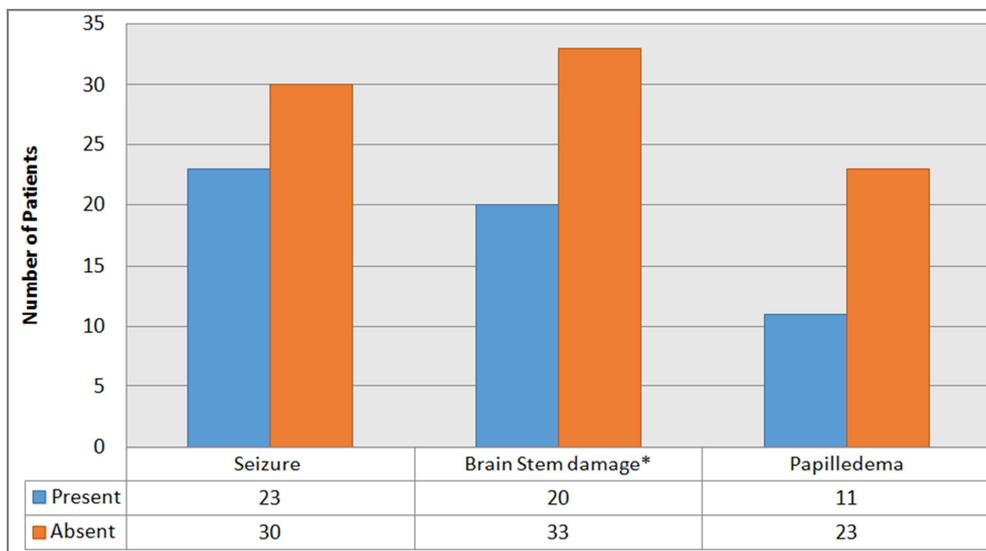


Figure 1. Frequency of previous chronic illnesses in adult non trauma patients with coma admitted to University of Gondar Medical wards during January 1, 2014 to June 31, 2014, Gondar, Ethiopia.



* Brain stem damage: Absent corneal reflex, gag reflex and Doll's eye

Figure 2. Clinical Data on Admission in adult non trauma patients with coma admitted to University of Gondar Medical wards during January 1, 2014 to June 31, 2014, Gondar, Ethiopia.

Random blood sugar was done for 46 (86.8%) patients. It was elevated in 19 patients and one patient was hypoglycemic. Seven (13.2%) patients presented with a low blood pressure (hypotension), 11 (20.6%) of patients presented with high blood pressure, 8 (15.1%) patients of

which had a blood pressure in the malignant hypertension range ($BP \geq 180/120$ mmHg), and the rest 35 (66.2%) patients had a normal blood pressure. The GCS at presentation was 8 in 7 (13.2%) patients, 7 in 7 (13.2%) patients, 6 in 8 (15.1%) patients, 5 in 6 (11.3%) patients, 4 in 6 (11.3%) patients, and

3 in 19 (35.9%) patients, and the average being 5. Seizure at admission or before admission was present in 23 (44.4%) patients. Papilledema was present in 11 (32.4%) of the 34 patients in which funduscopy was done. It was not possible to do a funduscopic examination in 19 (35.8%) patients because of conditions precluding visualizing of the fundus like corneal scarring and cataract. (Table 1 and Figure 2)

Table 1. Clinical and laboratory features at admission in adult non trauma patients with coma admitted to University of Gondar Medical wards during January 1, 2014 to June 31, 2014, Gondar, Ethiopia.

	Low	Normal	High
Blood pressure (mmHg)	7 (13.2%)	11 (20.6%)	35 (66.2%)
Pulse rate (beats/min)	2 (3.8%)	24 (45.3%)	27 (50.9%)
Respiratory rate (breaths/min)	2 (3.8%)	11 (20.6%)	40 (75.5%)
Temperature (°C)	2 (3.8%)	34 (64.2%)	17 (32.1%)
Random blood glucose (mg/dL) (n=46)	1 (2.17%)	26 (56.5%)	19 (41.3%)
Serum creatinine (mg/dL) (n=31)	-	19 (61.3%)	12 (38.7%)
White blood cells (cells/mm3) (n=39)	3 (7.7%)	23 (60%)	13 (33.3%)
Hematocrit male (%) (n=20)	0	11 (55%)	9 (45%)
Hematocrit female (%) (n=19)	4 (21.1%)	13 (68.4%)	2 (10.5%)
Platelet (cells/mm3) (n=39)	15 (38.5%)	23 (59%)	1 (2.6%)

3.2. Etiology of Coma

The most common causes of coma were diseases that cause no FND followed by diseases that cause FND and meningitis syndrome. Among the causes of coma without a localizing sign, the most common cause of coma was malathion poisoning, followed by uremia and hepatic coma. Almost all of the patients who presented with coma and FND were diagnosed to have hemorrhagic stroke and only one patient was diagnosed to have brain abscess. None of the patients was diagnosed as ischemic stroke. Acute bacterial meningitis and tuberculous meningitis were the only causes of coma in patients presenting with meningitis syndrome. (Table 2 and Figure 3)

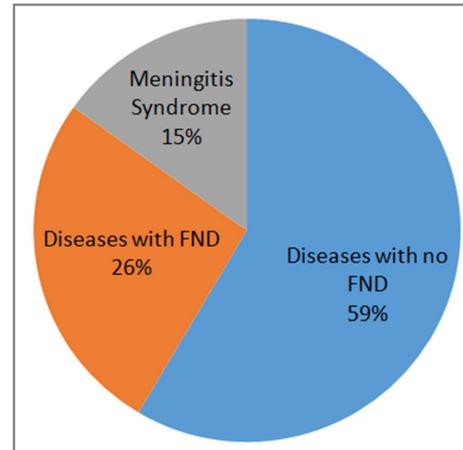


Figure 3. Causes of Coma in adult non trauma patients with coma admitted to University of Gondar Medical wards during January 1, 2014 to June 31, 2014, Gondar, Ethiopia.

Table 2. Causes of coma in adult non trauma patients with coma admitted to University of Gondar Medical wards during January 1, 2014 to June 31, 2014, Gondar, Ethiopia.

	Number of patients (%)
Diseases that cause no FND	31 (58.5%)
Metabolic causes	15 (28.3%)
Uremia	7 (13.2%)
Hepatic encephalopathy	5 (9.4%)
Hypoglycemia	2 (3.8%)
Intoxications	11 (20.8%)
Organophosphate (Malathion)	9 (17.0%)
Chlorpromazine	1 (1.9%)
Wernicke encephalopathy	1 (1.9%)
Systemic infections (Cerebral malaria)	1 (1.9%)
Status epilepticus	4 (7.6%)
DKA	1 (1.9%)
Diseases that cause FND	14 (26.4%)
Hemorrhagic stroke	13 (24.5%)
Brain abscess	1 (1.9%)
Meningitis syndrome	8 (15.1%)
Acute bacterial meningitis	5 (9.4%)
Tuberculous meningitis	3 (5.7%)

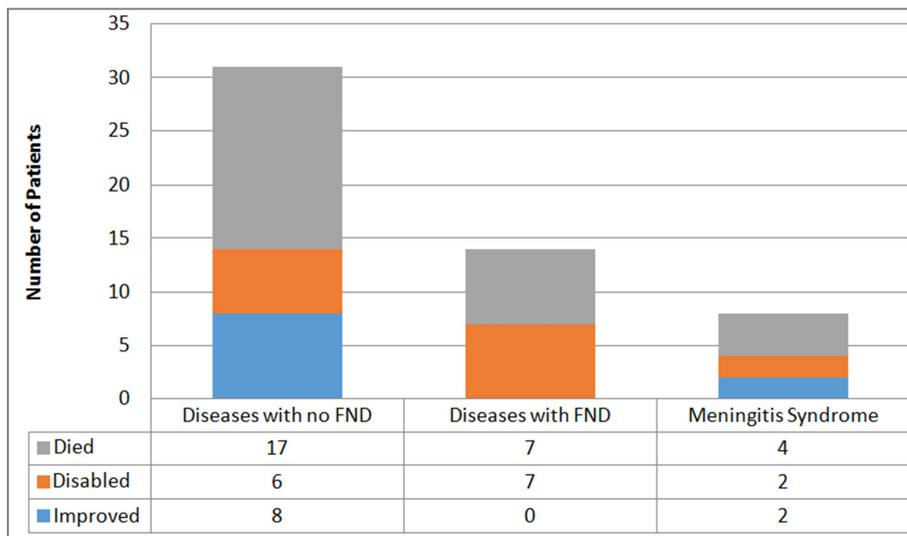


Figure 4. Outcome of Coma in adult non trauma patients with coma admitted to University of Gondar Medical wards during January 1, 2014 to June 31, 2014, Gondar, Ethiopia.

3.3. Outcome

Among the patients admitted with coma without FND, 17 (54.8%) patients died, 6 (19.3%) had disability and only 8 (25.8%) patients were discharged with improvement. In contrast, patients admitted with coma and FND, no patient was discharged with improvement, 7 (50%) died and 7 (50%) were discharged with disability. Among patients admitted with meningitis syndrome, 4 (50%) died, and 2 (25%) were disabled and 2 (25%) were discharged with improvement.

4. Discussion

This study showed that approximately 3.4% of medical emergencies seen at this tertiary health facility presented in coma. This figure is in contrast to two studies done in Nigeria which was 8.1% and 10%, respectively [9, 12]. But this figure may underestimate the true reflection of the population as many comatose patients, for reasons of lack of awareness, poverty and poor means of transportation, may not make it to the hospital. In this study, the majority of the patients were males. Many studies had also reported a high male to female ratio in medical coma. This male dominance may portray the belief that males have more risky or disease promoting lifestyles than females and so are more likely to fall sick and present to hospital. The median age of patients was 41 ± 18.7 years which agrees with the Nigerian study and other studies as well [9]. This shows that coma is affecting the productive age group of the community.

Diseases that cause no FND, including toxic and metabolic causes, were by far the most common causes of coma. This is in contrast to the studies done in India and Nigeria which showed stroke to be the commonest cause of coma, accounting for 33% each [11, 12]. This difference is likely to be explained by the fact that the causes of coma which are likely to be treatable like malathion poisoning and uremic coma are being addressed in these countries and causes of coma that are less likely to be easily treated are taking the large share as a cause of coma.

Hepatic and uremic encephalopathies were among the most common causes of diseases presenting without FND, which agrees with the study done in Nigeria [12]. Among the admitted patients, 24 (45.3%) of the patients had at least one previous underlying medical illness, which probably have predisposed these patients to coma. HIV, DM, hypertension and CKD are the most common ones. This shows that much effort has to be done to address these underlying risk factors.

Seizure at admission or a history of seizure before admission was found in 23 (44.4%) patients and it was more common in patients who presented with coma without localizing sign. Over a third of patients had signs of advanced brain damage in the form of brain stem involvement at admission. This finding might have attributed to a higher proportion of disability and death.

Only one patient was admitted with the diagnosis of cerebral malaria, which is in contrast to the study in Tanzania

in which cerebral malaria was the most common cause of coma [13]. Paucity of coma secondary to malaria in the present study is probably because of the general trend of the decrease of malaria prevalence as a cause of coma. But this may also be a result of the timing at which this research was done. Despite the expected high burden of infectious disease in our set up, infectious cause of coma were rather not common compared to intoxications, metabolic causes and cerebrovascular disorders. Acute bacterial meningitis was diagnosed in 5 (9.4%) of the patients. Gondar, the study site, is situated within the sub-Saharan meningitis belt but the study was conducted outside meningitis epidemics suggesting that sporadic acute bacterial meningitis is not an uncommon cause of coma in Gondar.

The mortality rate of 66.7% recorded in the present study, is higher than reports from the studies done in similar settings like Nigeria (49%) and also significantly higher than reports from Europe which reported mortality rate of 26.5%. [12, 14]. However, in the later study, 30% of the study population was treated at an intensive care unit in Sweden. The Intensive Care at the University of Gondar Hospital is a 4-bedded facility and serves as a general ICU for Gondar and its catchment area of almost 5 million people. Access to the ICU is often very competitive and bed occupancy is very high. Moreover, insufficient diagnostic facilities as well as lack of intensive care facilities have most likely accounted for the higher mortality recorded in our hospital.

A trend of higher rate of poor outcome (i.e. death and disability) was observed with patients admitted with coma with FND. All the patients admitted with coma and FND had seemed to have poor outcome compared with patients admitted with coma without FND and meningitis syndrome.

5. Conclusion

Diseases that present without a localizing sign, including toxic-metabolic causes were the most common causes of coma, the most common one being malathion poisoning. Patients who presented with coma and FND had a higher trend of poor outcome (death and disability). Medical coma, regardless of the etiology, was associated with high mortality rate.

Recommendation

Appropriate investigational modalities for patients with coma, including neuroimaging and blood tests, should be available for these patients. Standard care for comatose patients, including ICU care, should be provided to improve the outcome. The most common cause of coma was malathion poisoning which is reversible with appropriate care. Therefore, important drugs used for intoxications should be available in the hospital in general and at the medical emergency in particular. Larger studies are required to confirm the observations of this study and to determine prognostic factors in comatose patients.

Limitations of the Study

The small sample size of the study did not allow assessment of factors associated with mortality. Neuroimaging was obtained in only a single patient and was not obtained when it was indicated because the machine was broken. Important investigations like renal function tests, electrolytes, etc. were not complete for all patients because of lack of resource. A bigger prospective study with complete investigations is recommended to clearly understand the causes of non-traumatic coma and determinants of mortality.

Abbreviations

AIDS: Acquired Immunodeficiency Syndrome
 BP: Blood Pressure
 CKD: Chronic Kidney Disease
 DKA: Diabetic Ketoacidosis
 DM: Diabetes Mellitus
 FND: Focal Neurologic Deficit
 GCS: Glasgow Coma Scale
 HIV: Human Immunodeficiency Virus
 ICU: Intensive Care Unit
 IRB: Institutional Review Board
 RAS: Reticular Activating System

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