Outcome predictors of nontraumatic coma in children

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Introduction
Nontraumatic coma in children is an important pediatric emergency and accounts for high morbidity and mortality in pediatric-age group. It can cause different etiologies.

Patients and methods
The study was performed at the 'Emergency Unit, Intensive care, Neurologic Unit' Assiut University Children Hospital that included 80 patients.

Results
The mean age of patients enrolled in the study was 37.36 months with maximum age of 15 years. In addition, there was equal percentage of male to female (50.0%). However, there was a significant difference between outcome and age of patients ($P < 0.05$). The mean value of modified Glasgow Coma Scale was 8.73. There was a significant difference ($P < 0.05$) between outcome and vital signs of patients with a higher number of died patients than survival patients. There was 56.25% of patients who had central nervous system infection.

Conclusion
Assessment of vital signs such as low pulse volume, abnormal or respiratory rate, and abnormal oculocephalic reflexes were strong predictors of death following severe nontraumatic coma. The study also reaffirms that clinical variables and Glasgow Coma Scale score remain the most readily available tools for assessment of nontraumatic coma.

Keywords:
children, modified Glasgow Coma Scale, nontraumatic coma

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Introduction

Coma is a state of altered level of consciousness in which there is a loss of both wakefulness and awareness of the self and the environment. A very serious condition necessitates immediate medical decision making upon arrival at the Pediatric Emergency Department or pediatric ICU [1].

The most common scoring system used for assessment of consciousness is the Glasgow Coma Scale (GCS), and a modified version of the GCS is used in pediatric patients [2]. Pediatric coma is generally defined as having a GCS of less than 12 for at least 6 h [3]. Coma, without a history of a traumatic event, is an accompanying feature of many different conditions, including infectious, metabolic–toxic, and epileptic etiologies. These conditions, or the coma resulting from them, can be fatal if they are not swiftly identified and sufficiently treated [4].

Changes in consciousness level in a number of diseases are due to pathologic processes in the central nervous system (CNS). Pediatric GCS was used to assess the mental state of child patients. It is considered coma when the score is less than 12 for more than 6 h [5].

Many children with loss of consciousness will eventually achieve complete neurological recovery. However, depending on the cause of coma, a considerable number of children end in morbidity or mortality [6].

These children need to be hospitalized in the ICU. Coma may be a nonspecific manifestation of different diseases and thus identification of the causes of loss of consciousness can be helpful in prognosis of patients who are in coma [7].

The outcomes of coma are also difficult to predict early in the course of illness, and despite its prevalence and associated poor outcomes, very little information is available from the literature, especially from developing countries. Although many studies showing prognostication parameters of coma are available in adults, limited reviews are available for children [6].

This study attempts to identify the common etiological factors of pediatric comatose patients as well as the predictors of poor outcomes in these patients.

Patients and methods

Type of the study

Prospective observational study on 80 patients.

Study setting

The study was performed at the 'Emergency Unit, Intensive Care and Neurologic Unit' in Assiut University Children Hospital.

Study participants

Inclusion criteria

Patients aged between 2 months and 18 years, admitted with nontraumatic coma to Assiut University Pediatric Hospital.

Exclusion criteria

(1) Children aged in range '2 months: more than 18 years.'
(2) Coma causes by trauma.
(3) Coma causes as part of an anticipated terminal illness.

Sample-size calculation

(1) Sample size calculated in this study by 'EBI' program at power 80%, with confidence 95.0%, alpha 0.5 equal to 80 patients.
(2) Patients signed informed consent.
(3) IRB no: 17100576.

Basic sociodemographic data

Age: from 2 months to 18 years.

Sex: male and female.

Residency: urban or rural.

Socioeconomic status.

Weight.

Plan of the study

(1) The clinical vital signs were
    (a) Heart rate, respiratory rate and pattern, blood pressure (average of three recordings using mercury sphygmomanometer, by auscultatory method), temperature, coma severity (using GCS), pupillary size and response to light, and extraocular movements (by dolls' eye maneuver).
(2) Coma was determined on the basis of history, clinical examination, and relevant laboratory investigations.
(3) The investigations such as lumbar puncture, computed tomography (CT) scan, and metabolic workup were determined by duration of coma before treatment, clinical presentation, evoked potential, and decided by the consultant.

Ethical considerations

The study was approved by the Ethical Committee of the Faculty of Medicine at Assiut University. Informed consent with risk explanation was obtained from each of the all-participating patients. Every patient can refuse metabolic workup of the study without affecting the service or the clinical management. They are free to ask any patient about the study.

Statistical analysis

The collected data were revised, coded, tabulated, and analyzed using the statistical package for the social sciences (SPSS, version 24; IBM SPSS Statistics, Chicago, IL, USA). Data were presented as number, percentage, mean, standard deviation. Chi-square test and was used to compare between qualitative variables. Independent sample t-test was used to compare quantitative variables between two groups. P-value considered statistically significant when $P < 0.05$.

Results

The study was performed at the 'Emergency Unit, Intensive Care and Neurologic Unit' in Assiut University Children Hospital that included 80 patients. In Table 1, there was descriptive data in age and sex, also, there was descriptive data about kidney function and electrolytes, liver function, and complete blood count.

Table 2 shows diagnosis in the study group. There was 56.25% of patients who had CNS infection, as regards, there was 7.5% of patients who had status epilepticus and acute disseminating encephalomyelitis, and there was 6.3% of patients who have metabolic disorders and intracranial hemorrhage.

Table 3 shows imaging investigation in the study group. There was 65% of patients who have no abnormality electroencephalography and 30.0% of patients have diffuse encephalopathy and 5.0% of patients had epilepsy. About CT brain, there as 5.0% of patients who had hemorrhage, 41.25% brain edema, and 22.5% of patients normal CT brain.

Table 4 shows the relation between outcome and clinical data in the study group. There was a significant difference ($P < 0.05$) between outcome and respiratory rate and blood pressure of the patient, with a nonsignificant difference ($P > 0.05$) between outcome with other clinical data.

Table 5 shows the relation between outcome and modified GCS in the study group. There was a

Table 1 Demographic and laboratory data in the study group

Items	Descriptive (*n*=80)
Age (months)	
Mean±SE	37.36±67
Minimum-maximum	1.0-180.0
Sex [*n* (%)]	
Male	40 (50.0)
Female	40 (50.0)
Kidney function and electrolytes	
Urea	32.12±3.25
Creatinine	0.48±0.10
Sodium	141.53±1.46
Potassium	4.28±0.11
Ionized calcium	1.52±0.20
Liver function	
Total protein	6.06±0.13
Albumin	3.43±0.08
Total bilirubin	0.33±0.09
ALT	176.73±66.51
AST	324.08±109.92
ALP	137.83±8.28
RBG	152.55±8.02
Protein glucose	51.79±6.84
CBC	
WBCs	14.74±0.87
Hb	10.60±0.26
Platelets	316.51±15.05
CRP	46.48±6.10

ALT, alanine aminotransferase; ALP, alkaline phosphatase; AST, aspartate aminotransferase; CBC, complete blood count; CRP, C-reactive protein; Hb, hemoglobin; RBG, random blood glucose; WBC, white blood count.

Table 2 Diagnosis in the study group

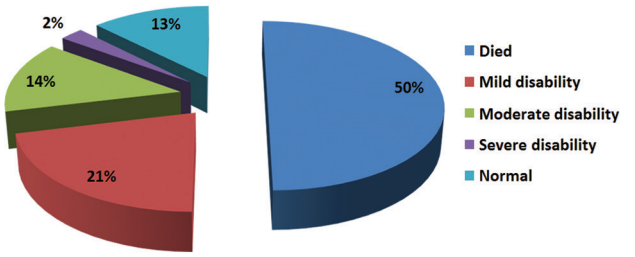
Items	Descriptive (*n*=80) [*n* (%)]
CNS infection	45 (56.25)
Hemorrhagic infarction	8 (10.0)
3 - Metabolic disorders	5 (6.3)
Brain cyst	-
Intracranial hemorrhage	5 (6.3)
6 - Autoimmune hepatitis	1 (1.3)
7 - White matter disease	1 (1.3)
8 - Lupus cerebritis	1 (1.3)
Status epilepticus	6 (7.5)
Typhoid encephalopathy	1 (1.3)
11 - Rabies	2 (2.6)
Post-DPT encephalopathy	1 (1.3)
Acute disseminating encephalomyelitis	6 (7.5)
14 - Brain hypoxia	1 (1.3)

CNS, central nervous system. More than one.

moderate significant difference (P < 0.001) between outcome and modified GCS, there was 38.46% of died patients in the range 3–4 of modified GCS versus 5.55% in survival patients.

Table 6 shows multivariate analysis between outcome and clinical parameters as predictor's factors in the study group. There were significant factors of survived age and respiratory rate (P < 0.03; Fig. 1).

Figure 1



Prognosis in the study group.

Discussion

Nontraumatic coma is a significant health problem with considerable morbidity and mortality in children. Timely diagnosis and identification of pathological mechanisms and treatment may be helpful in reducing morbidity and mortality. This study reveals several important results about pediatric nontraumatic coma by reporting characteristics and relationships in its presentation, cause, mortality, and short-term neurological outcome [8].

In the present study, the mean age of patients enrolled in the study was 37.36 months. This agrees with Ibekwe *et al.* [9] who reported that the majority of children who presented with nontraumatic coma were between 1 and 5 years of age.

Also, another study reported higher incidence among young infants (range, 1 month–12 years) [10]. As regards, the study reported 86% patients below 6 years of age [6].

In the present study, there was equal percentage of male to female (50.0%). This agrees with Ibekwe *et al.* [9] who reported not much sex difference. Also, other studies done in nontraumatic coma found that male and female matched in nontraumatic coma [6,11,12].

In the present study, about half of the cases (56.25%) have CNS infection. This agrees with Gowda *et al.* [12] who reported that 65.3% of the patients had CNS infection and it was the important cause of nontraumatic coma in his study. These also agree with a study, which showed that 66% of children with nontraumatic coma had CNS-infectious etiologies [13]. In addition, CNS infection was the prominent cause of coma (64%) [14]. Another study reported the most common cause of nontraumatic coma in children due to CNS infection (41%) [5].

The present study shows that on admission, there was 61.25% of patients who have normal (regular) respiratory pattern and 38.75% of patients have abnormal respiration. Regarding the outcome, there

was 72.2% of survival patients who had normal pattern of respiration versus 40.0% of the died patients with an abnormal pattern of respiration with a statistically significant difference (P < 0.04). This agrees with Berger [15] who reported that abnormal breathing pattern such as apneustic, ataxic, Chyene–Stokes respiration, or neurological hyperventilation had significant association with predicting poor outcome. In addition, his study showed that 57.6% of survival patients had normal pattern of respiration versus 13.5% of the died patients with an abnormal pattern of respiration.

In the present study, as regards the relation between the outcome and the blood pressure, there was a significant difference (P < 0.04). Our study shows that on admission, there was 61.25% of the patients normotensive, 18.75% hypotensive, and 20.0% hypertensive. Regarding the outcome with normotensive patients, there was 77.78% of survival patients with normal blood pressure and 26.92% of died patients with normal blood pressure. Regarding the outcome with hypotensive patients, there was 9.26% of survival patients with hypotension and 38.46% of died patients with hypotension. Regarding the outcome with hypertensive patients, there was 12.96% of survival patients with hypertension and 34.62% of died patients with hypertension. This agrees with Suganthi *et al*. [13] who reported that among the patient's vital signs recorded at the time of admission, blood pressure significantly correlated with the outcome. In addition, other investigators found that hypotension at admission significantly associated with mortality [16].

Table 3 Imaging investigation in the study group

Items	Descriptive (*n*=80)
EEG	
Diffuse encephalopathy	24 (30.0)
No abnormality	52 (65)
Epilepsy	4 (5.0)
CT brain*	
Brain edema	33 (41.25)
Infarction	3 (3.75)
Hemorrhage	4 (5.0)
White matter disease	1 (1.25)
Metabolic disease	1 (1.25)
Brain cyst	1 (1.25)
Tuberous sclerosis	1 (1.25)
Hyrocephalus	1 (1.25)
Hypodens lesion	9 (11.25)
Sturge-Weber	1 (1.25)
Hematoma	3 (3.75)
Atrophic changes	6 (7.5)
Normal	18 (22.5)

CT, computed tomography; EEG, electroencephalography.

In this study, the mean value of modified GCS was 8.73 with minimum value 3.0, which shows the significant relation between the outcome and modified GCS in the study group as when decreasing GCS mortality rates that progressively increased. This agrees with Ali *et al*. [10] who found that there is a significant association between GCS and mortality in nontraumatic coma, however, morbidity was higher in patients with lower GCS. This also agrees with a study reporting that in comatose patients with poor score, modified GCS denotes widespread damage to brainstem structures and/or cerebral hemispheres and may predict adverse outcome [17]. Low score of GCS at the time of admission predicted higher mortality. This finding was also observed in other studies reporting that no improvement of GCS over 24 h of hospital stay was also associated with significant high percentage of mortality, this is especially important for

Table 4 Relation between outcome and clinical data in the study group

Items	Died (*n*=26)	Survival (*n*=54)	*P*
1 - Onset 'days'	1.11±0.06	1.25±0.06	*P*=0.144 NS
2 - Duration 'days'	4.57±0.80	4.88±0.80	*P*=0.809 NS
3- Respiratory rate 'RR'	45.77±0.51	40.82±2.16	*P*<0.03*
4 -Temperature [*n* (%)]			
Normal	11 (26.83)	6 (15.38)	
Hyperthermia	3 (7.32)	2 (5.13)	*P*=0.249 NS
Hypothermia	13 (31.70)	15 (38.46)	
High-grade fever	14 (34.15)	16 (41.03)	
5 - Blood pressure [*n* (%)]			
Normotensive	7 (26.92)	42 (77.78)	
Hypotensive	10 (38.46)	5 (9.25)	
Hypertensive	9 (34.61)	7 (12.96)	*P*<0.04*
6 - Heart rate [*n* (%)]			
Normal	5 (19.23)	15 (27.78)	
Bradycardia	3 (11.53)	1 (1.85)	*P*=0.438 NS
Tachycardia	18 (69.23)	38 (70.37)	
Family history '+convulsion'	2 (7.7)	8 (14.8)	*P*=0.790 NS
8 - History of fever	22 (27.5)	43 (53.75)	*P*=0.243 NS

Table 5 Relation between outcome and modified Glasgow Coma Scale in the study group

Items	Died (*n*=26) [*n* (%)]	Survival (*n*=54) [*n* (%)]	*P*
MGCS			
Mean±SD	7.38±0.66	9.38±3.85	
3-4	10 (38.46)	3 (5.55)	*P*<0.001**
5-6	9 (34.62)	8 (14.82)	
7-8	3 (11.54)	11 (20.37)	
9-19	3 (11.54)	11 (20.37)	
>10	1 (3.84)	21 (38.89)	

MGCS, modified Glasgow Coma Scale.

Table 6 Relation between outcome and clinical parameters as predictor factors in the study group

Items	*P*	Odds ratio	95% CI
1- Age	*P*<0.02*	3.45	1.21-14.77
2 - Sex	*P*=0.237 NS	1.79	0.82-4.2
Onset 'days'	*P*=0.144 NS	1.66	0.38-3.52
Duration 'days'	*P*=0.809 NS	1.24	0.27-1.46
Respiratory rate	*P*<0.03*	4.79	1.01-1.98
6- Temperature	*P*=0.691 NS	1.11	0.39-2.01
7 - Systolic blood pressure	*P*=0.614 NS	1.86	0.42-1.67
8 - Diastolic blood pressure	*P*=0.515 NS	1.08	0.31-1.64
9 - Family history 'convulsion'	*P*=0.790 NS	1.86	0.26-1.37
10- History of fever	*P*=0.243 NS	1.36	0.17-1.64
11- EEG	*P*=0.447 NS	1.28	0.22-2.04
12- Respiratory pattern	*P*<0.04*	6.72	1.89-21.22

EEG, electroencephalography.

developing countries due to limited resources set up for early identification of this important general danger sign [6,18]. Another study in nontraumatic coma has indicated that high when the GCS is less than 8 that was significantly high with the mortality [19]. Also, in another study, the use of brainstem reflexes increased the prediction of mortality [20]. Another study found that when the ocular and verbal response score is less than 2, motor response 1, and brainstem score less than 1, the mortality was higher [21]. So periodical evaluation of brainstem reflexes is an important investigation in nontraumatic coma. Also, another study reported that clinical features such as GCS less than 8, nonreactive pupils, and abnormalities in tone that increased association with mortality include *P* value less than 0.01 [16].

Conclusion

Infections in cerebrospinal fluid were the leading cause of nontraumatic coma as well as the leading cause of mortality in our study.

Low GCS, clinical signs such as poor pulse volume, abnormal oculocephalic reflexes, or abnormal respiratory pattern were strong predictors of mortality following severe nontraumatic coma. From this study, clinical variables and GCS score remain the most used tools for assessment of nontraumatic coma. In addition, they are the causes of nontraumatic coma in children.

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Nil.

Conflicts of interest

None declared.

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