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A Comparative Analysis of FOUR Score and Glasgow Coma Scale Using ROC Curves for Mortality Prediction in Pediatric Non-Traumatic Coma : A Prospective Observational Study from a Tertiary Care Center in South India

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Abstract

Background: Non-traumatic coma in children is a common pediatric emergency associated with significant morbidity and mortality. The Glasgow Coma Scale (GCS), though widely used, has notable limitations in intubated and pre-verbal children. The Full Outline of UnResponsiveness (FOUR) score was introduced to address these limitations by incorporating brainstem reflexes and respiratory pattern assessment.

Objectives: To compare the prognostic performance of the FOUR score and GCS in predicting in-hospital mortality in children with non-traumatic coma admitted to the Pediatric Intensive Care Unit (PICU).

Methods: A prospective observational study was conducted over two years (October 2016 – October 2018) at a tertiary care PICU. Seventy-two children aged 1 month to 18 years with non-traumatic coma were enrolled. GCS and FOUR score were recorded within 2 hours of admission. Outcome measures included in-hospital mortality, ICU stay duration, ventilator days, and hospital stay duration. Receiver Operating Characteristic (ROC) curve analysis was used to compare discriminatory ability.

Results: The mean age was 3.55 ± 3.24 years; 59.7% were male. Mortality rate was 13.9% (10/72). Acute bacterial meningitis was the most common etiology (25%). Total FOUR score was significantly lower in non-survivors (mean 3.7 ± 1.76) versus survivors (mean 5.12 ± 1.44; $p = 0.006$). Area under the ROC curve (AUC) for total FOUR score was 0.739 ($p = 0.016$) versus 0.581 ($p = 0.411$) for total GCS. The FOUR respiration (FOUR-R) sub-score showed the highest AUC of 0.765 ($p = 0.008$), with 75.8% sensitivity and 80% specificity at a cut-off of 1.5.

Conclusions: The FOUR score demonstrates superior predictive validity for in-hospital mortality in pediatric non-traumatic coma compared to GCS, particularly due to its respiratory sub-score. It can be reliably used alongside or as an alternative to GCS in PICU settings.

Keywords: FOUR score, Glasgow Coma Scale, pediatric non-traumatic coma, PICU, outcome prediction, mortality

Introduction:

Non-traumatic coma in childhood is a common and serious pediatric emergency with diverse etiologies including infectious, toxic-metabolic, hypoxic-ischemic, post-status epilepticus, and cerebrovascular causes.[1] [2] Neurological outcome ranges from complete recovery to severe disability or death, making early and accurate prognostication essential for both clinical management and family counselling.

Assessment of consciousness by clinical examination remains the simplest, most inexpensive, and widely used tool at the bedside. The Glasgow Coma Scale (GCS), introduced in 1974 and revised in 1976, was originally developed for traumatic brain injury but has since been applied to various neurological conditions.[3] Despite widespread acceptance, GCS has significant limitations in children: the verbal component is difficult to assess in infants and intubated patients, it does not incorporate brainstem reflexes, and it fails to detect locked-in syndrome or different stages of cerebral herniation.[4] [5] [6]

To address these shortcomings, Wijdicks et al.[7] introduced the Full Outline of UnResponsiveness (FOUR) score in 2005, first validated at the Mayo Clinic.[8] The FOUR score is a 17-point scale (0–16) assessing four domains: eye response, motor response, brainstem reflexes, and respiratory pattern. Each domain scores 0–4. It adds eye-tracking to eye opening, detects vegetative state, and uniquely incorporates brainstem and respiratory assessments. It has been validated in Italian,[9] Spanish,[10] and French[11] versions and has demonstrated excellent inter-rater reliability.

While several adult studies have established the FOUR score's superiority over GCS, its validation in the pediatric population remains limited.[12] [13] [14] This study was therefore designed to compare the prognostic ability of the FOUR score and GCS in predicting outcome in children with non-traumatic coma admitted to a tertiary PICU.

Materials and Methods:

Study Design and Setting:

A prospective observational study was conducted in the PICU of Lotus Children's Hospital, Hyderabad, Telangana, India, from October 2016 to October 2018, after obtaining approval from the Institutional Ethics Committee and Scientific Committee. Written informed consent was obtained from parents or legal guardians of all enrolled patients.

Study Population:

Children aged 1 month to 18 years admitted with non-traumatic coma to the PICU were enrolled consecutively.

Inclusion criteria:

All children (1 month – 18 years) with non-traumatic coma admitted to the PICU.

Exclusion criteria:

- Traumatic brain injury
- Children administered sedatives or neuromuscular blocking agents prior to admission
- Pre-existing cerebral palsy, mental retardation, or neurodegenerative disorders
- Visual or hearing impairment
- Ongoing seizures or seizure activity within the preceding 1 hour

Data Collection:
Each patient was assessed within 2 hours of admission to the Emergency Department or PICU. Both the GCS (pediatric modification) and the FOUR score were recorded by an on-duty pediatric resident using a standardized proforma. Assessments were repeated till discharge or death. Outcome parameters recorded included:

- In-hospital mortality (primary outcome)
- Duration of ICU stay
- Duration of mechanical ventilation
- Duration of hospital stay

Sample Size:
Assuming an AUC of 0.85 for GCS and 0.95 for FOUR score, correlation of 0.7 between scores, $\alpha = 0.05$, and power = 0.80, sample size was calculated using MedCalc® version 9.2.0.1 to be 80. A total of 72 patients were analyzed.

Statistical Analysis:
Data were analyzed using SPSS version 17.0. Continuous variables were expressed as mean ± SD; categorical variables as frequencies and percentages. Unpaired t-test and ANOVA were used for continuous variable comparisons between groups. Fisher's exact test and chi-square test were used for categorical variables. ROC curve analysis with AUC was used to compare the discriminatory ability of FOUR score and GCS for predicting mortality. A p-value < 0.05 was considered statistically significant.

Results:

Demographic Profile
A total of 72 children were enrolled. The mean age was 3.55 ± 3.24 years (range: 2 months – 14 years). The majority (52.8%) were in the 0–2 year age group. Males comprised 59.7% of patients (male:female ratio 1.48:1).

Table 1: Age Distribution of Study Patients (n = 72)

Age Group (years)	Frequency	Percentage (%)
0 – 2	38	52.8
2.1 – 4	10	13.9
4.1 – 6	10	13.9
6.1 – 8	9	12.5
>8	5	6.9
Total	**72**	**100.0**

Mean ± SD = 3.55 ± 3.24 years

Outcome and Mortality:
Ten patients (13.9%) died during hospitalization. There was no statistically significant difference in mean age between the deceased and surviving groups (p = 0.94). However, mortality was significantly higher in males (90% of deaths were male; chi-square = 4.426, p = 0.035).

Etiology:
The most common diagnosis was acute bacterial meningitis (25%), followed by acute febrile encephalopathy (16.7%), meningoencephalitis (12.5%), dengue encephalopathy (8.3%), and seizure disorders (8.3%). Mortality was significantly associated with inborn errors of metabolism (IEM; 30%), hepatic encephalopathy (20%), brain abscess, enteric encephalopathy, septic encephalopathy, and snake bite (chi-square = 72, p < 0.001).

Table 2: Diagnosis Distribution and Outcome

Diagnosis	Total (n=72)	Dead (n=10)	Alive (n=62)
Acute Bacterial Meningitis	18 (25.0%)	0	18 (29.0%)
Acute Febrile Encephalopathy	12 (16.7%)	0	12 (19.4%)
Meningoencephalitis	9 (12.5%)	0	9 (14.5%)
Dengue Encephalopathy	6 (8.3%)	1 (10.0%)	5 (8.1%)
Seizure Disorder	6 (8.3%)	0	6 (9.7%)
Suspected IEM	3 (4.2%)	3 (30.0%)	0
Hepatic Encephalopathy	2 (2.8%)	2 (20.0%)	0
Brain Abscess	1 (1.4%)	1 (10.0%)	0
Enteric Encephalopathy	1 (1.4%)	1 (10.0%)	0
Septic Encephalopathy	1 (1.4%)	1 (10.0%)	0
Snake Bite	1 (1.4%)	1 (10.0%)	0
Others / Unknown	12 (16.6%)	0	12 (19.3%)

GCS Score and Outcome:

There was no statistically significant difference in any GCS sub-scores (Eye, Verbal, Motor) between survivors and non-survivors (all $p > 0.05$).

Table 3: Mean GCS Sub-scores by Outcome

GCS Component	Dead (Mean ± SD)	Alive (Mean ± SD)	t-value	p-value
GCS-E (Eye)	1.40 ± 0.52	1.66 ± 0.48	1.59	0.116
GCS-V (Verbal)	1.90 ± 0.57	2.02 ± 0.84	0.42	0.675
GCS-M (Motor)	1.80 ± 0.63	1.90 ± 0.80	0.39	0.700
Total GCS	**5.1 ± 1.19**	**5.5 ± 1.31**	1.01	0.315

FOUR Score and Outcome:

The FOUR Eye (FOUR-E) and FOUR Respiration (FOUR-R) sub-scores were significantly lower in non-survivors compared to survivors. Total FOUR score was significantly lower in the non-survivor group (3.7 ± 1.76) versus survivors (5.12 ± 1.44; $p = 0.006$).

Table 4: Mean FOUR Sub-scores by Outcome

FOUR Component	Dead (Mean ± SD)	Alive (Mean ± SD)	t-value	p-value
FOUR-E (Eye)	0.30 ± 0.48	0.66 ± 0.48	2.21	**0.03**
FOUR-M (Motor)	0.80 ± 0.63	0.87 ± 0.82	0.26	0.80
FOUR-B (Brainstem)	1.40 ± 0.97	1.65 ± 0.55	1.16	0.25
FOUR-R (Respiration)	1.10 ± 1.20	1.95 ± 0.88	2.70	**0.01**
Total FOUR	**3.7 ± 1.76**	**5.12 ± 1.44**	2.81	**0.006**

ICU Stay and Ventilation Duration:

There was no statistically significant difference in mean ICU duration (Dead: 5.70 ± 3.27 days vs. Alive: 4.97 ± 2.76 days; $p = 0.45$) or ventilator duration (Dead: 5.40 ± 3.41 days vs. Alive: 5.44 ± 2.50 days; $p = 0.97$) between the two groups.

ROC Curve Analysis:

The AUC for total FOUR score (0.739, $p = 0.016$) was significantly higher than total GCS (0.581, $p = 0.411$) for predicting in-hospital mortality. Among individual sub-scores, FOUR-R showed the highest discriminatory ability (AUC = 0.765, $p = 0.008$) with a best cut-off of 1.5, yielding a sensitivity of 75.8% and specificity of 80%.

Table 5: ROC Curve Analysis – GCS vs. FOUR Score

Score	AUC	p-value	95% CI	Best Cut-off	Sensitivity (%)	Specificity (%)
GCS-E	0.631	0.187	0.441 – 0.820	1.5	66.1	60
GCS-V	0.525	0.801	0.360 – 0.690	1.5	71.0	20
GCS-M	0.523	0.820	0.346 – 0.699	1.5	66.1	30
Total GCS	**0.581**	**0.411**	0.395 – 0.768	6.5	90	24.2
FOUR-E	0.681	0.068	0.502 – 0.860	0.5	66.1	70
FOUR-M	0.508	0.935	0.334 – 0.683	0.5	62.9	30
FOUR-B	0.573	0.464	0.347 – 0.798	1.5	61.3	50
FOUR-R	0.765	**0.008**	0.577 – 0.952	1.5	75.8	80
Total FOUR	**0.739**	**0.016**	0.538 – 0.939	3.5	60	87.1

Discussion

This study evaluated the comparative prognostic utility of the FOUR score and GCS in 72 children with non-traumatic coma. The FOUR score demonstrated superior discriminatory ability (AUC 0.739) over GCS (AUC 0.581) for predicting in-hospital mortality, consistent with findings from both adult and pediatric literature.

Bruno et al.[12] in a prospective study of 176 pediatric ICU patients with severe brain damage found FOUR score to be a valid tool with prognostic value comparable to GCS and Glasgow-Liège Scale (GLS), with FOUR score not inferior to GLS in prognostic capacity. Cohen et al.[13] reported better inter-rater reliability and higher predictive value for FOUR score than GCS in PICU patients. Sankhyan et al.[14] studied children aged 5–12 years and concluded FOUR score was as good as GCS for predicting in-hospital and 3-month mortality. Kochar et al.[22] compared GCS and FOUR score in children aged 5–18 years and found both were good predictors of in-hospital mortality with no significant difference between the two.

Wijdicks et al.[15] noted that FOUR score provided greater neurological detail than GCS by detecting locked-in syndrome and varying stages of herniation. Phuping et al.[16] demonstrated AUC values of 0.88 and 0.92 for poor outcome and in-hospital mortality using FOUR score in 68 patients. Stead et al.[20] concluded that FOUR score could be reliably used by non-neurological staff in the emergency setting. Khajeh et al.[24] in 200 PICU children reported good to excellent inter-rater reliability and confirmed FOUR score as a good predictor of in-hospital mortality.

The finding that FOUR-R (respiratory sub-score) was the most significant predictor of mortality (AUC = 0.765, sensitivity 75.8%, specificity 80%) highlights the clinical importance of incorporating respiratory pattern assessment, something not captured by GCS. Respiratory pattern reflects brainstem integrity at the pontine and medullary levels, making it a sensitive indicator of neurological deterioration.

The higher specificity of total FOUR score (87.1% at cut-off 3.5) compared to GCS (24.2% at cut-off 6.5) is particularly valuable in reducing false positives in mortality prediction, which has critical implications for resource allocation and counselling in resource-limited PICU settings.

Conclusion

The FOUR score is a superior predictor of in-hospital mortality compared to GCS in children with non-traumatic coma, particularly due to its respiratory sub-score component. At a total FOUR score cut-off of ≤ 3.5, it achieves a specificity of 87.1% for mortality prediction. The FOUR score should be considered as a standard neurological assessment tool in pediatric intensive care settings alongside or in place of GCS, especially in intubated and pre-verbal patients.

Limitations

A limitation of this study is the relatively small sample size (n = 72), single-centre design, and the inability to assess inter-rater reliability formally. Additionally, long-term neurodevelopmental outcomes

beyond hospital discharge were not assessed. Future multicentric studies with larger sample sizes and functional outcome measures at 3 and 6 months are warranted.

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Author Contributions

Dr. A. Sanjana: Study design, data collection, analysis: Dr Santhi Meher Peddi, data validation, and manuscript writing and review: Dr. V.S.V. Prasad: Concept, protocol approval, manuscript review

Conflict of Interest

None declared.

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Ethical Approval

Approved by the Institutional Ethics Committee and Scientific Committee, Lotus Children's Hospital, Hyderabad.