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**Research Article**

# Etiology, Clinical Profile and Outcome of Non-Traumatic in Children

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**Abstract:Background:** Non-traumatic coma in children is a neurological emergency associated with high risk of mortality and undesired consequences.

**Objective:** To investigate the etiology, clinical profile and neurological and clinical outcome in children presented with non-traumatic coma at National Institute of Child Health Karachi.

**Materials and Methods:** A prospective follow-up study was conducted on inpatients visiting pediatric department of National Institute of Child Health Karachi. The study period was six months from 20th December 2022 to 19th June 2023. One hundred and forty-three non-traumatic coma children of age 2 months to 16 years were consecutively selected for investigation. Each child was assessed for vitals, GCS score, duration of unconsciousness and presenting complaints. Laboratory investigations were performed to confirm the etiology of non-traumatic coma. Each child was followed until hospital discharge for final neurologic and clinical outcomes.

**Result:** Out of 143 non-traumatic coma children, male children were 77 (53.8%) and female children were 66 (46.2%) with mean age of 6.74 ± 2.68 years. The most common clinical presentation was fever 123 (86.0%) followed by convulsions 117 (81.8%), headache 112 (78.3%), fast breathing 83 (58.0%), vomiting 70 (49.0%) and abdominal pain 52 (36.4%). Viral encephalitis 41 (28.7%) and acute bacterial meningitis 31 (21.7%) were the most common infectious; while epilepsy 24 (16.8%) and acute poisoning 11 (7.7%) were the most common non-infectious etiologies of nontraumatic coma. The most common neurological outcome was moderate disability 80 (55.9%) children followed by mild and severe disability in 32 (22.4%) and 31 (21.7%) children, respectively. Overall, 112 (78.3%) non-traumatic coma children survived while 31 (21.7%) children died.

**Conclusion:** Infections were the most common cause of non-traumatic coma and also the most common cause of death in children. Meningitis including acute bacterial meningitis and tuberculosis meningitis was the only significant cause of death in children of non-traumatic coma. Death was significantly associated with severe disability.

**Keywords:** Coma, Children, Neurological, Emergency, Mortality, Traumatic injury, Pediatrics.

## INTRODUCTION

In children, coma is considered a neurological emergency with potentially serious consequences. Children with non-traumatic coma are considered a major emergency because of its association with morbidity and mortality [1, 2]. Pediatric coma is simply an unarousable, unresponsive and unconscious state of children. Early and appropriate diagnosis of etiology in pediatric coma is very much important especially in developing countries because it is associated with overlapping clinical presentation, limited diagnostic resources and management facilities [3-5].

In the pediatric emergency, level of consciousness was assessed using the Glasgow Coma Scale (GCS). GCS was divided into three categories-motor, verbal, and eye response-for the assessment of consciousness. A GCS score of three indicates the worst and fifteen the best. A modified type of the GCS score is used for assessment of consciousness in children [6, 7]. Identification of pediatric coma etiology is very much important and distributed into traumatic and non-traumatic etiologies. Most of the researchers worked on traumatic coma; while non-traumatic coma is also a major cause of pediatric emergency department admissions, prolong stay in hospital, morbidity and mortality [8, 9].

In Pakistan, pediatric coma is associated with poor outcome and rate of mortality is high. In order to improve the outcome, clinical symptoms should be identified that will be helpful in early and appropriate diagnosis of pediatric coma, whereas identification of etiologies will be helpful for selecting appropriate therapy. Overall identification of early symptoms and etiologies of pediatric coma will help in decreasing the morbidity and mortality as well decrease the increasing burden on health care system. Therefore, this study was conducted to investigate the etiology, clinical profile and neurological and clinical outcome in children presented with non-traumatic coma at National Institute of Child Health Karachi.

## MATERIALS AND METHODS

A prospective follow-up study was conducted on inpatients visiting pediatric department of National Institute of Child Health

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Karachi. During study period of six months from 20th December 2022 to 19th June 2023, non-traumatic coma children of both genders having age of 2 months to 16 years and GCS of ≤ 12 for at least 6 hours at the time of admission in hospital were consecutively selected in the study whereas children with history of trauma, neurological illness, neuro-developmental delay or children whose parents were unwilling to participate in the study were excluded.

Online Open EPI software was used to calculate sample size of 143 by utilizing study as reference who reported the mortality in 38.7% pediatric coma patients [10], by taking confidential interval 95% and margin of error 8%.

Traumatic come was defined as a GCS score of ≤ 12 for at least 6 hours at the time of admission, while non-traumatic coma was defined as a child diagnosed with coma caused by non-traumatic etiology (without history of trauma). Etiology of pediatric non-traumatic coma was distributed into infective and non-infective etiologies. Infective etiologies include acute bacterial meningitis, cerebral malaria, tuberculosis meningitis, viral encephalitis, sepsis, or Reye's syndrome. Non-infective etiologies include epilepsy, metabolic derangements, neoplastic, accidental poisoning, hypertensive encephalopathy, febrile fit or congenital malformation. A child's level of consciousness was assessed following the modified GCS score parameters.

Outcome of children with non-traumatic was distributed into neurological and clinical outcome. Neurological outcome was further distributed into normal, mild, moderate and severe disability. Normal neurological condition was confirmed on normal neurological examination. Mild disability was confirmed on presence of grade 4 weakness or ataxia, mild alteration of tone, isolated cranial nerve palsy and power or deep tendon reflexes. Moderate disability was confirmed on presence of grade 3 weakness or ataxia and involvement of multiple cranial nerves. Severe disability was confirmed on presence of less than grade 3 weakness or ataxia and tetraplegia or vegetative state. Clinical outcome was further distributed into death of child during non-traumatic coma treatment in hospital and discharge of child from hospital after treatment of non-traumatic coma.

Study permission was taken from institutional ethical review board of National Institute of Child Health Karachi (letter number: IERB-36/2021, Dated: 20-12-2022). Inpatients fulfilling the inclusion criteria of study were selected in study. Demographic details of each child were obtained either from parent or from medical record including name and age of child. Each child was assessed for vitals (temperature, pulse, blood pressure (BP) and respiratory rate (RR). After that GCS score of each child was obtained by using modified GCS score. Duration of unconsciousness was obtained from parents or caregivers. Presenting complaint were also investigated from parents including fever, headache, cough, fast breathing, vomiting, diarrhea, abdominal pain, blindness and convulsions. Laboratory investigations including complete blood count (CBC), arterial blood gas (ABG) analysis, liver function test (LFT), cerebrospinal fluid (CSF) analysis, electroencephalogram, computerized tomography (CT) or magnetic resonance imaging (MRI) were performed whenever necessary to confirm the etiology of nontraumatic coma. Each child was followed until hospital discharge for final neurologic and clinical outcomes.

## STATISTICAL ANALYSIS

All the data was recorded in proforma by researcher and analyzed by using Statistical Package for Social Science (SPSS) software, Version 25. Mean and standard deviation were calculated for quantitative variable and frequency and percentages for qualitative variables. Post-stratification chi-square test was applied by taking p value ≤ 0.05 as significant.

## RESULT

Out of 143 non-traumatic coma children, male children were 77 (53.8%) and female children were 66 (46.2%). The mean age of the children was 6.74 ± 2.68 years; while most 86 (60.1%) of the children were above 5 years of age followed by 52 (36.4%) children of 1-5 years and 5 (3.5%) children of < 1 year. The mean time since unconsciousness was 14.31 ± 3.75 hours; while most 91 (63.6%) of the children were unconscious for more than 12 hours followed by 52 (36.4%) children who were unconscious for equal or less than 12 hours. The mean GCS score was 10.83 ± 1.15; while most 120 (83.9%) of the children were mildly unconscious and 23 (16.1%) children were moderately unconscious. The most common clinical presentation in children with non-traumatic coma was fever 123 (86.0%) followed by convulsions in 117 (81.8%) children, headache in 112 (78.3%) children, fast breathing in 83 (58.0%) children, vomiting in 70 (49.0%) children, abdominal pain in 52 (36.4%) children, cough in 34 (23.8%) children and diarrhea in 20 (14.0%) children (Table **1**).

Most 96 (67.1%) of the non-traumatic coma children were diagnosed with infective etiologies including acute bacterial meningitis in 31 (21.7%) children, viral encephalitis in 41 (28.7%) children, cerebral malaria in 13 (9.1%) children and tuberculosis meningitis in 11 (7.7%) children while 47 (32.9%) of the non-traumatic coma children were diagnosed with non-infective etiology including epilepsy in 24 (16.8%) children, acute poisoning in 11 (7.7%) children, metabolic derangement in 5 (3.5%) children, acute demyelinating brain disease in 4 (2.8%) children and subacute sclerosing panencephalitis in 3 (2.1%) children. Moderate disability was the most common neurological outcome observed in 80 (55.9%) children followed by mild disability in 32 (22.4%) children and severe disability in 31 (21.7%) children. Overall, 112 (78.3%) non-traumatic coma children survived and were discharged from the hospital alive while 31 (21.7%) children died during the hospital stay (Table **2**).

The correlation between neurological and clinical outcome and risk factors of non-traumatic coma are presented in Table **3** and **4** Acute bacterial meningitis and tuberculous meningitis were significantly more common in severe disability while viral encephalitis, cerebral malaria and epilepsy in moderate

disability (P-value <0.001). Meningitis including acute bacterial meningitis and tuberculosis meningitis was the only significant cause of death in children of non-traumatic coma (P-value <0.001). Death was significantly associated with severe disability (P-value <0.001).

**Table 1.** Demographics, Vitals and Clinical Profile of Non-Traumatic Coma Patients (n=143).

| Variables | | Frequency | Percentage |
|---|---|---|---|
| **Gender** | Male | 77 | 53.8 |
| | Female | 66 | 46.2 |
| **Age (Years)** | Mean ± SD | 6.74 ± 2.68 | |
| | < 1 | 5 | 3.5 |
| | 1-5 | 52 | 36.4 |
| | > 5 | 86 | 60.1 |
| **Time Since Unconscious (Hours)** | Mean ± SD | 14.31 ± 3.75 | |
| | ≤ 12 | 52 | 36.4 |
| | > 12 | 91 | 63.6 |
| **Vitals** | Temperature | 102.36 ± 1.16 °F | |
| | Pulse | 124.95 ± 8.46 beats/min | |
| | Systolic Blood Pressure | 108.90 ± 8.02 mmHg | |
| | Diastolic Blood Pressure | 65.21 ± 5.40 mmHg | |
| | Respiratory Rate | 18.34 ± 1.85 breaths/min | |
| **GCS** | Mean ± SD | 10.83 ± 1.15 | |
| | Mild | 120 | 83.9 |
| | Moderate | 23 | 16.1 |
| **Clinical Profile** | Fever | 123 | 86.0 |
| | Convulsion | 117 | 81.8 |
| | Headache | 112 | 78.3 |
| | Fast Breathing | 83 | 58.0 |
| | Vomiting | 70 | 49.0 |
| | Abdominal Pain | 52 | 36.4 |
| | Cough | 34 | 23.8 |
| | Diarrhea | 20 | 14.0 |

**Table 2.** Etiology and Outcome of Non-Traumatic Coma Patients (n=143).

| Variables | | Frequency | Percentage |
|---|---|---|---|
| **Etiology & Its Type** | **Infective** | 96 | 67.1 |
| | Acute Bacterial Meningitis | 31 | 21.7 |
| | Viral Encephalitis | 41 | 28.7 |
| | Cerebral Malaria | 13 | 9.1 |
| | Tuberculosis Meningitis | 11 | 7.7 |
| | **Non-Infective** | 47 | 32.9 |
| | Epilepsy | 24 | 16.8 |
| | Acute Poisoning | 11 | 7.7 |
| | Metabolic Derangement | 5 | 3.5 |
| | Acute Demyelinating Brain Disease | 4 | 2.8 |
| | Subacute Sclerosing Panencephalitis | 3 | 2.1 |

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|---|---|---|---|
| **Neurological Outcome** | Mild disability | 32 | 22.4 |
| | Moderate disability | 80 | 55.9 |
| | Severe disability | 31 | 21.7 |
| **Clinical Outcome** | Death | 31 | 21.7 |
| | Discharged | 112 | 78.3 |

**Table 3.** Neurological Outcome with Risk Factors (n=143).

| **Variables** | | **Neurological Disability** | | | **P-Value** |
|---|---|---|---|---|---|
| | | **Mild n(%)** | **Moderate n(%)** | **Severe n(%)** | |
| **Gender** | Male | 17 (53.1) | 46 (57.5) | 14 (45.2) | 0.502 |
| | Female | 15 (46.9) | 34 (42.5) | 17 (54.8) | |
| **Age (Years)** | < 1 | 3 (9.4) | 0 (0.0) | 2 (6.5) | 0.104 |
| | 1-5 | 9 (28.1) | 32 (40.0) | 11 (35.5) | |
| | > 5 | 20 (62.5) | 48 (60.0) | 18 (58.1) | |
| **Time Since Unconscious (Hours)** | ≤ 12 | 9 (28.1) | 28 (35.0) | 15 (48.4) | 0.230 |
| | > 12 | 23 (71.9) | 52 (65.0) | 16 (51.6) | |
| **GCS** | Mild | 32 (100.0) | 78 (97.5) | 10 (32.3) | <0.001 |
| | Moderate | 0 (0.0) | 2 (2.5) | 21 (67.7) | |
| **Etiology & Its Type** | Infective | 17 (53.1) | 48 (150.0) | 31 (96.9) | <0.001 |
| | Non-Infective | 15 (46.9) | 32 (100.0) | 0 (0.0) | |
| | Acute Bacterial Meningitis | 3 (9.4) | 4 (12.5) | 24 (75.0) | |
| | Viral Encephalitis | 9 (28.1) | 32 (100.0) | 0 (0.0) | |
| | Cerebral Malaria | 3 (9.4) | 10 (31.3) | 0 (0.0) | |
| | Tuberculosis Meningitis | 2 (6.3) | 2 (6.3) | 7 (21.9) | |
| | Epilepsy | 7 (21.9) | 17 (53.1) | 0 (0.0) | |
| | Acute Poisoning | 3 (9.4) | 8 (25.0) | 0 (0.0) | |
| | Metabolic Derangement | 2 (6.3) | 3 (9.4) | 0 (0.0) | |
| | Acute Demyelinating Brain Disease | 2 (6.3) | 2 (6.3) | 0 (0.0) | |
| | Subacute Sclerosing Panencephalitis | 1 (3.1) | 2 (6.3) | 0 (0.0) | |
| **Clinical Outcome** | Death | 0 (0.0) | 0 (0.0) | 31 (100.0) | <0.001 |
| | Discharge | 32 (100.0) | 80 (100.0) | 0 (0.0) | |

**Table 4.** Clinical Outcome with Risk Factors (n=143).

| **Variables** | | **Outcome** | | **P-Value** |
|---|---|---|---|---|
| | | **Death n(%)** | **Discharge n(%)** | |
| **Gender** | Male | 14 (45.2) | 63 (56.3) | 0.273 |
| | Female | 17 (54.8) | 49 (43.8) | |
| **Age (Years)** | < 1 | 2 (6.5) | 3 (2.7) | 0.599 |
| | 1-5 | 11 (35.5) | 41 (36.6) | |
| | > 5 | 18 (58.1) | 68 (60.7) | |
| **Time Since Unconscious (Hours)** | ≤ 12 | 15 (48.4) | 37 (33.0) | 0.116 |
| | > 12 | 16 (51.6) | 75 (67.0) | |

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|---|---|---|---|---|
| **GCS** | Mild | 10 (32.3) | 110 (98.2) | <0.001 |
| | Moderate | 21 (67.7) | 2 (1.8) | |
| **Etiology & Its Type** | Infective | 31 (100.0) | 65 (58.0) | <0.001 |
| | Non-Infective | 0 (0.0) | 47 (42.0) | |
| | Acute Bacterial Meningitis | 24 (75.0) | 7 (6.3) | |
| | Viral Encephalitis | 0 (0.0) | 41 (36.6) | |
| | Cerebral Malaria | 0 (0.0) | 13 (11.6) | |
| | Tuberculosis Meningitis | 7 (21.9) | 4 (3.6) | |
| | Epilepsy | 0 (0.0) | 24 (21.4) | |
| | Acute Poisoning | 0 (0.0) | 11 (9.8) | |
| | Metabolic Derangement | 0 (0.0) | 5 (4.5) | |
| | Acute Demyelinating Brain Disease | 0 (0.0) | 4 (3.6) | |
| | Subacute Sclerosing Panencephalitis | 0 (0.0) | 3 (2.7) | |
| **Neurological Outcome** | Mild disability | 0 (0.0) | 32 (28.6) | <0.001 |
| | Moderate disability | 0 (0.0) | 80 (71.4) | |
| | Severe disability | 31 (100.0) | 0 (0.0) | |

## DISCUSSION

Non-traumatic coma is one of the most common pediatric presentations to emergency department (ED) or intensive care unit (ICU) throughout the world. Non-traumatic coma requires early and appropriate diagnosis and immediate management in the ED or ICU [11, 12]. One of the most frequent causes of admission to an ICU or ED is impaired consciousness due to non-traumatic coma [13, 14]. Non-traumatic coma is significantly associated with undesired complications and mortality [15, 16].

In this study, rate of mortality was high (21.7) in non-traumatic coma children. Similarly high rate of mortality was reported from Pakistan and throughout the world. Pakistani studies [10, 17, 18] who reports the 38.7, 29.0 and 26.12 mortality in non-traumatic coma children, respectively. Studies from other parts of the world also reports the higher mortality rate [19-23] who reports the 8.2, 16.0, 18.2, 33.9, 29.8, 16.6 mortality in non-traumatic coma children, respectively. In this study, meningitis including acute bacterial meningitis and tuberculosis meningitis was the only significant cause of death in children of non-traumatic coma. Bacterial meningitis is a serious infection with a mortality rate of about 30.0 while neurological sequelae develop in 50.0 of survivors [24, 25].

In this study most (53.8) of the children were male and 46.2 were female with mean age of 6.74 ± 2.68 years (80.8 months); while most 86 (60.1) of the children were above 5 years of age followed by 52 (36.4) children of 1-5 years and 5 (3.5) children of < 1 year. The results were comparable with other studies, which also report a male predominance, [10] reports 66.3 male with mean age of 3.66 ± 3.49 years, [17] reports 59.0 male with mean age of 44 ± 45 months, [26] reports 50.9 male with mean age of 55 months and [21] reports 55.7 male. In contrast study [19, 20, 23], who reports the higher female 59.6, 55.4 and 58.0 in non-traumatic coma children, respectively.

This study also identifies the common clinical presentation of non-traumatic coma in children. The most common clinical presentation in children with non-traumatic coma was fever 123 (86.0) followed by convulsions 117 (81.8), headache 112 (78.3), fast breathing (58.0) children, vomiting (49.0), abdominal pain (36.4), cough (23.8) and diarrhea (14.0). Different other researchers also reported the similar clinical findings [26] reports the seizure (52.2), vomiting (41.5), fever (40.9) and headache (18.9), [19] reports the convulsion (90.0) and fever (68.0) and [23] reports the seizure (34.8), nausea and vomiting (16.4) and fever (14.2) as most common clinical symptoms of non-traumatic coma. All similar studies have shown that convulsion and fever are the most common clinical presentation of non-traumatic coma.

This study also identifies the common etiologies of non-traumatic coma in children. Most (67.1) of the non-traumatic coma children were diagnosed with infective etiologies including acute bacterial meningitis (21.7), viral encephalitis (28.7), cerebral malaria (9.1) and tuberculosis meningitis (7.7) while 32.9 of the non-traumatic coma children were diagnosed with non-infective etiology including epilepsy (16.8), acute poisoning (7.7), metabolic derangement (3.5), acute demyelinating brain disease (2.8) and subacute sclerosing panencephalitis (2.1). Similar high infective etiology was reported by different other researcher [10] reports the 63.75 infective etiology with higher prevalence of acute bacterial meningitis (33.3), cerebral malaria (31.4), viral encephalitis (19.6), tuberculosis meningitis (11.8) and 36.25 non-infective etiology with higher prevalence of metabolic derangement (34.5), accidental poisoning (27.6) and epilepsy (20.7). Another study [17], reports the 65.0 infective etiology with higher prevalence of acute bacterial meningitis (31.0), cerebral malaria (29.0), viral encephalitis (18.0), tuberculosis meningitis (12.0) and 34 non-infective etiology with higher prevalence of metabolic derangement (26.0), accidental poisoning (15.0)

and epilepsy (15.0). One more study [26] reports the neuro-infection as most common cause (31.4), toxic-metabolic causes (25.8), epileptic causes (15.1) and viral encephalitis (15.0). A study [19] reports the 58.0 infective etiology with higher prevalence of acute bacterial meningitis (22.0), tuberculosis meningitis (16.0) and viral encephalitis (14.0). These etiological findings of non-traumatic coma in children were also comparable with other studies [18, 20-23]. All similar studies have shown that infection is the most common cause of non-traumatic coma in children and that acute bacterial meningitis, viral encephalitis, cerebral malaria and tuberculosis meningitis are the most common infectious etiologies.

## CONCLUSION

All study findings help to conclude that infections were the most common cause of non-traumatic coma and also the most common cause of death in children. Meningitis including acute bacterial meningitis and tuberculosis meningitis was the only significant cause of death in children of non-traumatic coma. Death was significantly associated with severe disability.

## AUTHORS' CONTRIBUTION

- **Asma Majeed**: Study conceptualization, Literature search, Designed study protocol, Initial drafting of manuscript.
- **Muhammad Ashfaq**: Designed study protocol, Critically reviewed and revised the initial manuscript.
- **Zara Shoukat and Mariam Aijaz**: Literature search, Designed study protocol, Initial drafting of manuscript.
- **Badar u Nisa**: Data collection, Data analysis, Result writing.

## CONFLICT OF INTEREST

Declared none.

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