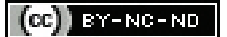


# Association of Mean Arterial Pressure and Outcome in Children with Acute Non Traumatic Neurological Illnesses in Paediatric Intensive Care Unit: A Prospective Cohort Study

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## ABSTRACT

**Introduction:** The course of outcome in non traumatic neurological illnesses, such as acute encephalitis syndrome, meningitis, paediatric stroke, metabolic encephalopathy, etc., can be affected by various risk factors. While there have been many studies evaluating the effects of blood pressure on outcomes in traumatic brain injury, there is a dearth of studies assessing Mean Arterial Pressure (MAP) in non traumatic injury, particularly in the paediatric age group.

**Aim:** To examine the association between MAP and outcomes in children with acute non traumatic neurological illnesses in the Paediatric Intensive Care Unit (PICU), focusing on mortality and length of PICU stay.

**Materials and Methods:** This prospective cohort study was conducted at Gandhi Medical College, Bhopal, Madhya Pradesh, India from September 2021 to August 2022. A total of 249 children aged between 1 to 14 years with acute non traumatic neurological illnesses were included, and their mean blood pressure was

recorded. Associated co-morbidities (severe anaemia, respiratory failure, sepsis, and acute kidney injury), mean length of hospital stay, and outcome were also assessed. Categorical variables were analysed using either the Chi-squared ( $\chi^2$ ) test or Fisher's exact test, while continuous variables were assessed using the Analysis of Variance (ANOVA) test for mean length of stay.

**Results:** Out of the 249 subjects, 157 (63.1%) were male, and 143 (57.4%) belonged to the age group of 1-5 years. Among them, 36 (14.5%) experienced hypotension, and 17 (6.8%) had hypertension during their PICU stay, while 196 (78.7%) had normal blood pressure. Abnormal MAP was significantly associated with a higher mortality rate among the study subjects (p-value <0.001), and the mean length of PICU stay was significantly longer (p-value <0.001) in study subjects with abnormal MAP.

**Conclusion:** Both high and low MAP were significantly associated with higher mortality and longer duration of stay in children with acute non traumatic neurological illnesses.

**Keywords:** Acute kidney injury, Blood pressure, Brain injury, Length of stay, Paediatrics

## INTRODUCTION

Acute non traumatic neurological illnesses refer to any brain insult that affects its structure or function, resulting in impairments of behaviour (encephalopathy), cognition, and communication. These conditions do not include brain injuries caused by trauma or congenital anomalies [1,2]. Examples of non traumatic neurological illnesses include acute encephalitis syndrome, meningitis, paediatric stroke, metabolic encephalopathy, and other related disorders [2]. While much attention has been given to traumatic brain injuries, however, its important to recognise the negative and long-term consequences of non traumatic brain injuries as well [3]. Patients in the PICU with neurological injuries have been found to have higher mortality rates, long-term morbidity, and longer hospital stays [4].

The MAP is the average arterial pressure during one cardiac cycle and is considered a better indicator of perfusion to vital organs compared to Systolic Blood Pressure (SBP). MAP is influenced by both cardiac output and systemic vascular resistance [5]. Auto-regulation of regional perfusion helps protect critical organs such as the brain and kidney from systemic hypotension, but below a certain threshold MAP, tissue perfusion becomes dependent on arterial pressure [6]. MAP is particularly useful in guiding treatment for patients with sepsis and septic shock [6]. Optimising and maintaining MAP, as well as avoiding systemic hypotension, are critical in the first 5 to 7 days after acute brain injury to reduce secondary ischemic damage [7].

Physiological targets such as SBP, Diastolic Blood Pressure (DBP), and cerebral perfusion pressure remain problematic in the paediatric population due to developmental variations in these parameters [4]. Abnormal blood pressure is common among critically ill patients. Therefore, there is a need to evaluate the effects of mean blood pressure on neurological conditions to prevent the associated mortality and morbidity. The role of MAP in critically ill patients and its impact on outcomes also remain unclear. Hence, this study was conducted to examine the association between MAP and outcomes in children with acute non traumatic neurological illnesses in the PICU, specifically in terms of mortality and length of PICU stay.

## MATERIALS AND METHODS

This prospective cohort study was conducted at Gandhi Medical College, Bhopal, Madhya Pradesh, India over a period of 12 months from September 2021 to August 2022. The study was approved by the Institutional Ethical Committee (IEC) of Gandhi Medical College, Bhopal (Letter no. 27166/MC/IEC/2021; Dated: 25/08/2021).

**Inclusion criteria:** Children aged between 1-14 years who were admitted to the PICU with a diagnosis of acute non traumatic neurological illness (like acute encephalitis syndrome, paediatric stroke, meningitis, and hepatic encephalopathy) were included in the study.

**Exclusion criteria:** Children with a history of trauma or any chronic illness (like chronic liver/kidney disease, cerebral palsy, etc.) were excluded from the study.

**Sample size:** All consecutive 249 patients presenting with acute non traumatic neurological illnesses within the study duration were enrolled in the study.

**Data collection:** Demographic data, including age, gender, and primary diagnosis, were collected upon admission to the PICU. Informed consent was obtained from the parents/guardians of the children, and a detailed history was taken from the mother/caregiver. MAP measurements were recorded at admission and every six hours until the first 48 hours of PICU stay. MAP was calculated using the formula:  $MAP = DBP + 1/3 * (SBP - DBP)$  [8].

MAP readings were recorded as "Normal" (MAP between the 5<sup>th</sup> and 90<sup>th</sup> centile for age and height), "High MAP" (MAP above the 90<sup>th</sup> centile for age and height), and "Low MAP" (MAP below the 5<sup>th</sup> centile for age and height) [8].

Blood pressure was measured using a multiparameter monitor (Schiller Truscope 2 Multi-parameter patient monitor) with appropriate blood pressure cuffs based on the age and weight of the patient [9]. World Health Organisation (WHO) standards and IAP growth charts were used for the categorisation of growth parameters [10].

Data on associated co-morbidities such as severe anaemia (according to WHO criteria) [11], respiratory failure (defined as the presence and persistence of respiratory acidosis,  $SpO_2 < 90\%$  or arterial oxygen tension less than 60 mmHg, and arterial carbon dioxide tension greater than 45 mmHg, tachypnoea, or increased work of breathing) [12], sepsis, and acute kidney injury (KDIGO staging of acute kidney injury) [13] were also collected during the patient's PICU stay. The PICU outcome was categorised as either "Discharged" (discharged home or to an inpatient or outpatient rehabilitation service) or "Death" (in-hospital death).

## STATISTICAL ANALYSIS

Demographic variables were reported as counts and percentages or mean  $\pm$  Standard Deviation (SD). A descriptive analysis was performed to obtain the general characteristics of the study population. Categorical variables were analysed using either the Chi-squared ( $\chi^2$ ) test or Fisher's exact test. Continuous variables were assessed using the ANOVA test for mean length of stay. A p-value  $< 0.05$  was considered statistically significant. The data analysis was conducted using Statistical Package for Social Sciences (SPSS) software version 25.0.

## RESULTS

In the present study, a total of 249 subjects were analysed. Out of the total 249 subjects, 157 (63.1%) were males and 92 (36.9%) were females. Among the subjects, 143 (57.4%) belonged to the age group of 1-5 years, 77 (30.9%) were aged 5-10 years, and 29 (11.7%) were older than 10 years. Age, gender, underweight for age, stunted growth, and severe anaemia were not significantly associated with outcomes (p-value=0.739, 0.576, 0.067, 0.531, and 0.352, respectively) [Table/Fig-1].

Variables	Mortality (n=28) n (%)	Discharged (n=221) n (%)	Total n (%)	p-value
<b>Sex</b>				
Male	19 (67.9)	138 (62.4)	157 (63.1)	0.576
Female	9 (32.1)	83 (37.6)	92 (36.9)	
<b>Age (years)</b>				
1-5	17 (60.7)	126 (57)	143 (57.4)	0.739
>5-10	7 (25)	70 (31.7)	77 (30.9)	
>10-14	4 (14.3)	25 (11.3)	29 (11.7)	
<b>Growth parameters</b>				
<b>Weight for age</b>				
Underweight for age	8 (28.6)	33 (14.9)	41 (16.5)	0.067
Normal	20 (71.4)	188 (85.1)	208 (83.5)	
<b>Height for age</b>				
Stunted	1 (3.6)	15 (6.8)	16 (6.4)	0.531
Normal	27 (96.4)	206 (93.2)	233 (93.6)	

<b>Co-morbidities</b>				
Severe anaemia	4 (14.3)	12 (5.4)	16 (6.4)	0.352
Acute kidney injury	2 (7.1)	1 (0.5)	3 (1.2)	<0.001
Sepsis	2 (7.1)	8 (3.6)	10 (4.0)	<0.001
Respiratory failure	9 (32.1)	3 (1.4)	12 (4.8)	<0.001
<b>Neurological illness</b>				
Acute encephalitis syndrome	24 (85.7)	79 (35.7)	103 (41.4)	<0.001
Acute flaccid paralysis	0	5 (2.3)	5 (2)	
Bacterial meningitis	2 (7.1)	11 (5)	13 (5.2)	
Hepatic encephalopathy	0	1 (0.5)	1 (0.4)	
Paediatric stroke syndrome	0	1 (0.5)	1 (0.4)	
Seizure	2 (7.1)	124 (56.1)	126 (50.6)	
<b>Blood pressure</b>				
Normotensive	4 (14.2)	192 (86.4)	196 (78.7)	<0.001
Hypertensive	10 (35.7)	7 (3.16)	17 (6.8)	
Hypotensive	14 (50)	22 (9.95)	36 (14.5)	

**[Table/Fig-1]:** Baseline demographic variables.

Chi-squared test was used

Among the 249 subjects, 36 (14.5%) had low MAP, 17 (6.8%) had high MAP, and 196 (78.7%) had normal MAP at any point during their PICU stay. The incidence of mortality among the subjects was 28 (11.2%). There was a significant association between abnormal MAP (low or high MAP) and mortality at various time points during the PICU stay (p-value  $< 0.001$ ) [Table/Fig-2].

MAP		Outcome n (%)		Total n (%)	p-value
		Death (28)	Discharged (221)		
Admission	High	9 (32.1)	9 (4.1)	18 (7.2)	<0.001
	Low	15 (53.6)	21 (9.5)	36 (14.5)	
	Normal	4 (14.3)	191 (86.4)	195 (78.3)	
6 hours	High	8 (28.5)	9 (4.0)	17 (6.8)	<0.001
	Low	15 (53.6)	21 (9.5)	36 (14.5)	
	Normal	5 (17.9)	193 (86.4)	196 (78.7)	
12 hours	High	8 (28.5)	9 (4.0)	17 (6.8)	<0.001
	Low	15 (53.6)	21 (9.5)	36 (14.5)	
	Normal	5 (17.9)	191 (86.4)	196 (78.7)	
18 hours	High	8 (28.5)	9 (4.0)	17 (6.8)	<0.001
	Low	15 (53.6)	19 (8.6)	34 (13.7)	
	Normal	5 (17.9)	193 (87.3)	198 (79.5)	
24 hours	High	8 (28.6)	9 (4.0)	17 (6.8)	<0.001
	Low	14 (50)	18 (8.1)	32 (12.9)	
	Normal	6 (21.4)	194 (87.8)	200 (80.3)	
30 hours	High	8 (28.6)	9 (4.0)	17 (6.8)	<0.001
	Low	14 (50)	12 (5.4)	26 (10.5)	
	Normal	6 (21.4)	200 (90.5)	206 (82.7)	
36 hours	High	8 (28.6)	8 (3.6)	16 (6.4)	<0.001
	Low	14 (50)	10 (4.5)	24 (9.6)	
	Normal	6 (21.4)	203 (91.9)	209 (84)	
42 hours	High	8 (28.6)	7 (3.2)	15 (6)	<0.001
	Low	14 (50)	9 (4.0)	23 (9.2)	
	Normal	6 (21.4)	205 (92.8)	211 (84.8)	
48 hours	High	8 (28.6)	7 (3.2)	15 (6)	<0.001
	Low	14 (50)	9 (4.0)	23 (9.2)	
	Normal	6 (21.4)	205 (92.8)	211 (84.8)	

**[Table/Fig-2]:** Association of outcome with Mean Arterial Pressure (MAP).

Chi-squared test was used

The mean  $\pm$  SD length of PICU stay was significantly higher among subjects with low MAP ( $9.80 \pm 5.333$  days) and high MAP

(9.55±3.484 days) compared to subjects with normal MAP (4.89±1.678 days) with a p-value <0.001 [Table/Fig-3].

Parameters	N	Mean±SD length of stay (days)	p-value	
SBP	High	17	9.60±3.569	<0.001
	Low	36	9.68±5.376	
	Normal	196	4.91±1.687	
DBP	High	17	9.64±3.569	<0.001
	Low	36	9.80±5.333	
	Normal	196	4.90±1.689	
MAP	High	18	9.55±3.484	<0.001
	Low	36	9.80±5.333	
	Normal	195	4.89±1.678	

**[Table/Fig-3]:** Comparison of length of PICU stay between subjects with mean blood pressure, systolic blood pressure and diastolic blood pressure. ANOVA or independent sample t-test

On multivariate analysis, respiratory failure (p-value <0.001), Acute Kidney Injury (AKI) (p-value=0.002), and abnormal MAP (p-value <0.001) were found to be significantly associated with mortality [Table/Fig-4].

Variables	Death	Discharge	Total	Odds ratio	95% CI	p-value
Respiratory failure	9 (75)	3 (25)	12 (100)	3.679	1.380-9.910	<0.001
Acute kidney injury	2 (66.7)	1 (33.3)	3 (100)	2.683	0.541-13.300	0.002
Sepsis	2 (20)	8 (80)	10 (100)	1.114	0.815-1.524	0.371
MAP (low/high)	23 (43.4)	30 (56.6)	53 (100)	17.011	6.791-42.613	<0.001
Systolic blood pressure (low/high)	23 (43.4)	30 (56.6)	53 (100)	17.011	6.791-42.613	<0.001
Diastolic blood pressure (low/high)	23 (43.4)	30 (56.6)	53 (100)	17.011	6.791-42.613	<0.001

**[Table/Fig-4]:** Multivariate analysis of the individual risk factors for outcome-multivariate logistic regression analysis.

## DISCUSSION

Acute non traumatic neurological illnesses pose a significant health problem in children, leading to considerable morbidity and mortality. Prompt diagnosis and identification of patients with such illnesses are crucial for early management, which can help reduce morbidity and mortality rates.

In present study, the most common age group presenting with acute non traumatic neurological illnesses was 1 to 5 years. However, no statistically significant association between age and mortality was found. Similar findings were reported by Shah R et al., who studied 50 comatose children and found the majority (n=24, 48%) in the 1 to 5-year age group, with an insignificant difference in mortality rate [14]. This could be attributed to the high-risk of infection in this age group. In present study, the mortality rate in children with acute non traumatic neurological illness was 11.2%, consistent with the findings of a study by Duyu M et al., where they reported an 8.2% mortality rate among 146 patients with non traumatic neurological illnesses [15].

The incidence of low MAP in present study was 14.5%, while high MAP was observed in 6.8% of the patients. Risk factors significantly associated with mortality were abnormal MAP, acute kidney injury, and respiratory failure. Subjects with abnormal MAP had a significantly longer mean length of stay in the PICU. Similarly, Fouad H et al., conducted a study on 100 paediatric non traumatic coma cases and reported that hypotension at admission was significantly associated with mortality. Abnormal respiratory pattern/apnoea also correlated

significantly with mortality. Logistic regression analysis revealed that abnormal respiratory pattern after 48 hours of admission was an independent significant predictor of mortality [16].

Likewise, Shah R et al., reported a significant correlation between abnormal blood pressure and mortality at admission (p-value=0.005), 24 hours (p-value=0.001), and 48 hours after admission. Abnormal heart rate (p-value=0.004) and abnormal neurological examination (p-value=0.001) were also significant predictors of death at 24 and 48 hours of admission. However, none of these factors were found to be significantly associated with mortality on logistic regression analysis [14].

In present study, 14.5% of patients were having low MAP and 6.8% were having high MAP, 78.7% were having normal MAP. Similarly a study performed by Saied HZ et al., on non traumatic coma in children reported that on admission, 61% of the patients were normotensive, 18% were hypotensive, and 20% were hypertensive. Also, there was a significant relationship between the outcome and the blood pressure (p-value <0.04). There was a high mortality of 38% in patients with hypotension and 34% in patients with hypertension [17]. Ahmed S et al., also reported that hypotension was significantly associated with mortality with a p-value of 0.002 [18].

Ahmad I et al., reported a mortality rate of 33.9% and identified several factors significantly associated with mortality both at admission and after 48 hours, including age ≤3, poor pulse volume, hypotension, abnormal respiratory pattern, and abnormal neurological examination [19]. Comparing the mean length of stay, present study found that children with low mean blood pressure had a longer duration of stay. Similarly, Ibekwe RC et al., reported that paediatric patients with non traumatic neurological illnesses and hypotension had a prolonged duration of stay [20].

Overall, present study and previous research highlight the importance of early recognition and management of acute non traumatic neurological illnesses in children. Factors such as age, blood pressure, respiratory pattern, and neurological examination play a role in predicting mortality and influencing the length of hospital stay.

## Limitation(s)

One limitation of this study was that the mean blood pressure could only be recorded every six hours due to manpower limitations.

## CONCLUSION(S)

An abnormally low or high MAP is significantly associated with increased mortality and longer duration of hospital stay in children with acute non traumatic neurological illnesses. The presence of respiratory failure and acute kidney injury are also independently associated with higher mortality in these patients. A simple clinical tool like blood pressure measurement may be very useful in predicting and modifying outcomes, especially in low-resource countries. However, further studies on the association of MAP in children with acute non traumatic neurological illnesses are needed for a better understanding of the subject matter.

## REFERENCES

- [1] Ghai OP. Ghai Essential Paediatrics: Normal growth and its disorders. Ninth edition. Delhi-92 CSB publ: 2013. Pp. 7-37.
- [2] CARF international. CARF-CCAC standards manual 2015. Tucson, Arizona, USA.
- [3] Giustini A, Pistorini C, Pisoni C. Traumatic and nontraumatic brain injury. *Handb Clin Neurol*. 2013;110:401-09.
- [4] Kochanek PM, Carney N, Adelson PD. Guidelines for the acute medical management of severe traumatic brain injury in infants, children, and adolescents-second edition. *Paediatr Crit Care Med*. 2012;13(Suppl 1):S1-S82.
- [5] Berlin DA, Bakker J. Starling curves and central venous pressure. *Crit Care*. 2015;19(1):01-08.
- [6] Rhodes A, Evans LE, Alhazzani W. Surviving Sepsis Campaign: International Guidelines for management of sepsis and septic shock 2016. *Intensive Care Med*. 2017;43(3):304-77.
- [7] Grove MA. Mean arterial pressure in acute ischemic stroke study. The University of Tennessee Health Science Center. 2020. Paper 527.

- [8] Erickson SL, Killien EY, Wainwright M, Mills B, Vavilala MS. Mean arterial pressure and discharge outcomes in severe paediatric traumatic brain injury. *Neurocrit Care*. 2021;34(3):1017-25. <https://pubmed.ncbi.nlm.nih.gov/33108627/>.
- [9] Banker A, Bell C, Gupta-Malhotra M, Samuels J. Blood pressure percentile charts to identify high or low blood pressure in children. *BMC Paediatrics*. 2016;16(1):01-07.
- [10] Parekh BJ, Khadiolkar V. Pediatrician-friendly IAP growth charts for children aged 0-18 years. *Indian Pediatr*. 2020;57(11):997-98.
- [11] Hemoglobin concentrations for the diagnosis of anaemia and assessment of severity. Vitamin and mineral nutritional information system. Geneva, World Health Organization, 20211.
- [12] Friedman ML, Nitu ME. Acute respiratory failure in children. *Paediatr Ann*. 2018;47(7):e268-73.
- [13] Makris K, Spanou L. Acute kidney injury: Definition, pathophysiology and clinical phenotypes. *Clin Biochem Rev*. 2016;37(2):85-98.
- [14] Shah R, Mavaskar S, Seth R, Sakharkar S. Study of clinical profile, etiology and immediate outcome in non-traumatic coma in children. *Sch J App Med Sci*. 2016;4(6B):2012-19.
- [15] Duyu M, Altun ZK, Yildiz S. Nontraumatic coma in the paediatric intensive care unit: Etiology, clinical characteristics and outcome. *Turk J Med Sci*. 2021;51(1):214-23.
- [16] Fouad H, Haron M, Halawa EF, Nada M. Nontraumatic coma in a tertiary paediatric emergency department in Egypt: Etiology and outcome. *J Child Neurol*. 2011;26(2):136-41.
- [17] Saied HZ, Askar GA, El-Gheet AM. Outcome predictors of nontraumatic coma in children. *J Curr Med Res Pract*. 2022;7(3):253-57.
- [18] Ahmed S, Ejaz K, Shamim MS, Salim MA, Khan MU. Non-traumatic coma in paediatric patients: Etiology and predictors of outcome. *J Pak Med Assoc*. 2011;61(7):671-75.
- [19] Ahmad I, Ahmed K, Gattoo IA, Mir MY, Maqbool M, Baba AR. Non traumatic coma in children: A prospective observational study. *Int J Contemp Paediatr*. 2015;2(2):77-84.
- [20] Ibekwe RC, Ibekwe MU, Onwe EO, Nnebe-Agumadu UH, Ibe BC. Non-traumatic childhood coma in Ebonyi State University Teaching Hospital, Abakaliki, South Eastern Nigeria. *Niger. J Clin Pract*. 2011;14(1):43-46.

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