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Base deficit correlates with mortality in pediatric abusive head trauma

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Abstract

Background/purpose: Children suffering from abusive head trauma (AHT) have worse outcomes compared to non-AHT, but the reasons for this are unclear. We hypothesized that delayed medical care associated with AHT causes prolonged pre-hospital hypotension and hypoxia as measured by admission base deficit (BD), and that this would correlate with outcome.

Methods: We performed a 10-year retrospective chart review of children admitted for AHT at two academic level-I trauma centers. Statistics were performed using Student's t test, chi-square analysis, and multivariate logistic regression, and considered significant at $p < 0.05$.

Results: Four-hundred twelve children with AHT were identified, and admission BD was drawn for 148/412 (36%) children, including 104 survivors and 44 non-survivors. Non-survivors had significantly higher BD compared to survivors (12.6 ± 1.6 versus 5.3 ± 0.6, $p < 0.001$). Non-survivors were more likely to be intubated pre-hospital and get cardiopulmonary resuscitation (CPR) ($p < 0.001$). Mortality increased with rising BD, according to CPR status. There was no difference in patterns of brain injury between survivors and non-survivors ($p > 0.05$).

Conclusions: BD correlates with mortality in children suffering severe AHT. Non-survivors are also more likely to be intubated pre-hospital and require CPR, with no difference in pattern of brain injury, suggesting that secondary injury is a major determinant of outcome in severe AHT.

Abusive head trauma (AHT), shaken baby or shaken infant syndrome, inflicted traumatic brain injury, and non-accidental head injury all refer to intentional head injury of infants and young children [1]. In 2009, the American Academy of Pediatrics adopted AHT as the official term for this type of injury to streamline discussion on the topic and to prevent practitioners from excluding patients from this group who were not shaken [2]. The prevalence of AHT is difficult to determine owing to lack of recognition and misdiagnosis

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as unintentional head trauma, but is estimated to be 17:100,000 person-years [3]. In children <24 months of age, it has been suggested that more than 50% of traumatic brain injuries requiring hospitalization are secondary to AHT [3]. These children tend to be younger, have distinctive patterns of injury, worse functional outcomes, and higher mortality compared with patients suffering from non-AHT [3–7]. The reason for the differences in mortality and functional outcome in children with AHT compared to non-AHT remains elusive and cannot be explained solely by differences in injury severity score (ISS), intracranial pressure (ICP), or Glasgow Coma Scale (GCS) [4,6].

Base deficit (BD) is a rapidly and widely available serum laboratory marker of systemic acidosis that increases with hypoxemia and/or shock. In the trauma setting, BD correlates with blood transfusion requirement, risk of multi-organ failure, and mortality in adult patients, including adults with traumatic brain injury (TBI) [8–10]. Similarly, in pediatric trauma patients, BD correlates with blood transfusion requirement, duration of mechanical ventilation, infectious complications, and mortality [11,12]. Differences between AHT and non-AHT are not always easy to discern; it seems, however, that children suffering AHT are more apt to suffer delays in definitive care. For example, children with non-AHT are more likely to arrive at an ED while asymptomatic and with a witnessed injury, whereas children with AHT more often are brought to the ED because of symptoms without any given history of trauma [4]. In adults suffering TBI, hypotension and hypoxia are independently associated with worse functional outcomes and higher mortality [10,13,14]. For children with TBI, even brief episodes of hypoxia and hypotension increase mortality markedly [15–18]. In the setting of severe AHT, delays in seeking emergent medical care can result in prolonged periods of hypoxia and hypotension, which in turn can lead to increased anaerobic metabolism, elevated serum lactic acidosis, and greater BD. We hypothesized that children with fatal AHT would have increased serum BD, and that higher levels of BD would correlate with worse functional outcomes in survivors.

1. Methods

A retrospective chart review was performed of children ages 0–24 months who were admitted for AHT at two academic level-I trauma centers from January 2002–January 2012. The Child Protection Teams at both institutions determined presence of AHT. Medical records were evaluated for patient demographics, injuries, laboratory studies, and treatment information, including initial BD drawn within three hours of arrival, as well as the first recorded GCS on the day of presentation. We also examined need for cardiopulmonary resuscitation (CPR) and intubation within the first 24 hours. Continuous numerical data are reported as mean ± standard error of the mean, and comparisons were made by Student's t test. Categorical data comparisons were made by Pearson's chi-square analysis with a single degree of freedom. Data were further analyzed by using multivariate logistic regression to determine which variables were independently predictive of death. Functional outcome scores for survivors were calculated using the King's Outcome Scale for Childhood Head Injury (KOSCHI) [19]. All statistical tests were considered to be significant at a two-sided $p < 0.05$, and were reported as <0.001 when values were lower. Analyses were performed using SAS, version 9.3 (Cary, NC).

2. Results

A 10-year retrospective chart review revealed 412 children diagnosed with AHT, of which 359 survived to discharge, and 54 died (13% mortality). An admission BD was drawn for 148/412 (36%) children, including 104 of the survivors and 44 of the non-survivors. Further analysis in this study was limited to this group of 148 patients.

2.1. Demographics

Age, gender, and ethnicity were compared between survivors and non-survivors (Table 1). The average age was

Table 1 Demographic, intervention, injury, and laboratory comparison between survivors and non-survivors of abusive head trauma

	Survivors	Non-survivors	p-value
Age (days)	204	248	0.26
Gender			
Male	68%	32%	0.48
Female	74%	26%	0.48
Ethnicity			
Caucasian	68%	32%	0.54
African American	86%	14%	0.36
Hispanic	71%	29%	0.93
Other/Unknown	71%	29%	0.86
CPR	15%	66%	**<0.001**
Intubated	81%	100%	
Pre-hospital	8%	32%	**<0.001**
Initial GCS	7.8	3.9	**<0.001**
Max AIS Head	4.4	4.9	**<0.001**
Injury Severity Score	22.5	31.1	**<0.001**
Retinal hemorrhage	76%	95%	**0.02**
Hematocrit	29.9%	29.5%	0.68
Base deficit (mEq/L)	5.3	12.6	**<0.001**

Demographic, intervention, injury, and laboratory comparison between survivors and non-survivors of pediatric abusive head trauma with an admission base deficit. Values represent either the mean, or percentage of children in that subset. p-values are derived from Student's t test for numerical data or chi-square analysis for categorical data. Bold p-values meet the threshold for statistical significance.

219 days ± 17 days (range 6 days–730 days), with no statistical difference between survivors and non-survivors (p = 0.26). There was a male predominance, with 98/148 (66%) of all patients being male, including 31/44 (70%) of the non-survivors, which was not statistically different compared to females (p = 0.47). There were no statistically significant differences between the surviving and non-surviving groups for ethnicity: 65/148 (44%) were Caucasian, 41/148 (28%) were Hispanic, 7/148 (5%) were African American, and 35/148 (23%) were other/unknown.

2.2. Initial interventions

Interventions including CPR and intubation were compared between survivors and non-survivors (Table 1). A total of 45/148 (30%) patients received CPR. This included 16/104 (15%) survivors and 29/44 (66%) non-survivors. CPR was statistically more common among non-survivors (p < 0.001). The majority of patients, 128/148 (87%), required intubation. This included 44/44 (100%) non-survivors, 14/44 (32%) of which were intubated in a pre-hospital setting. This is compared to 84/104 survivors (81%) who required intubation, with only 8/104 (8%) intubated prior to arrival at the hospital. Pre-hospital intubation was statistically more common among non-survivors (p < 0.001).

2.3. Injuries

Types and degree of injury, including initial GCS, pattern of head injury, maximum abbreviated injury scale for the head (max AIS head), ISS, and retinal hemorrhage were compared between survivors and non-survivors (Table 1). The average initial GCS was 6.6 ± 0.4 for all children. Non-survivors had statistically lower initial GCS (3.9 ± 0.4, range 3–13) compared to survivors (7.8 ± 0.5, range 3–15) (p < 0.001). When evaluating head injuries, 139/148 (94%) children were diagnosed with a subdural hemorrhage, 33/148 (22%) were diagnosed with subarachnoid hemorrhage, 13/148 (9%) were diagnosed with intraparenchymal hemorrhage, 33/148 (22%) were diagnosed with a skull fracture, and 60/148 (41%) were diagnosed with some combination of the above injuries. Types of head injury did not differ between survivors and non-survivors (Table 2). The average max AIS head for all patients was 4.5 ± 0.1. The average max AIS head for survivors was 4.4 ± 0.1, which was statistically lower compared to non-survivors, who had an average max AIS head of 4.9 ± 0.1 (p < 0.001). The average ISS for all patients was 25.1 ± 0.7. For survivors, the average was 22.5 ± 0.6, which was statistically lower compared to non-survivors, who had an average ISS of 31.1 ± 1.3 (p < 0.001). Retinal hemorrhage was present in 113/139 (81%) of patients, and was more common among non-survivors, as seen in 35/37 (95%) of these children, compared to 78/102 (76%) survivors (p = 0.02). Retinal hemorrhage was not assessed in 9 patients.

Table 2 Patterns of head injury in survivors and non-survivors of abusive head trauma.

	Survivors	Non-survivors	p-value
Subdural hemorrhage	96%	89%	0.08
Subarachnoid hemorrhage	18%	32%	0.07
Intraparenchymal hemorrhage	11%	5%	0.23
Skull fracture	20%	25%	0.52
Combination of injuries	38%	48%	0.24

Patterns of head injuries in survivors and non-survivors of pediatric abusive head trauma with an admission BD. Numbers are presented as percentage of total number of children in each group. P-values are derived from chi-square analysis.

Of these 9 children, 7 did not survive to discharge and 1 went to hospice.

2.4. Laboratory values

Laboratory values including admission hematocrit and BD were compared between survivors and non-survivors (Table 1). The average admission hematocrit for all children was 29.8 ± 0.5%. There was no difference between survivors and non-survivors (29.9 ± 0.6% versus 29.5 ± 0.9%, p = 0.68). The average BD for all patients was 7.5 ± 0.7 mEq/L. Survivors had an average BD of 5.3 ± 0.6 mEq/L (range −3.0 to 28.5), whereas non-survivors had an average BD of 12.6 ± 1.6 mEq/L (range 3.0–32.4), which was statistically higher (p < 0.001). Percent mortality increased with rising BD in a step-wise fashion (Fig. 1). This was statistically significant overall (p < 0.001), for the <5 versus 6–12 mEq/L group (p < 0.001), and the 12–18 versus >18 mEq/L group (p = 0.03). Multivariate logistic

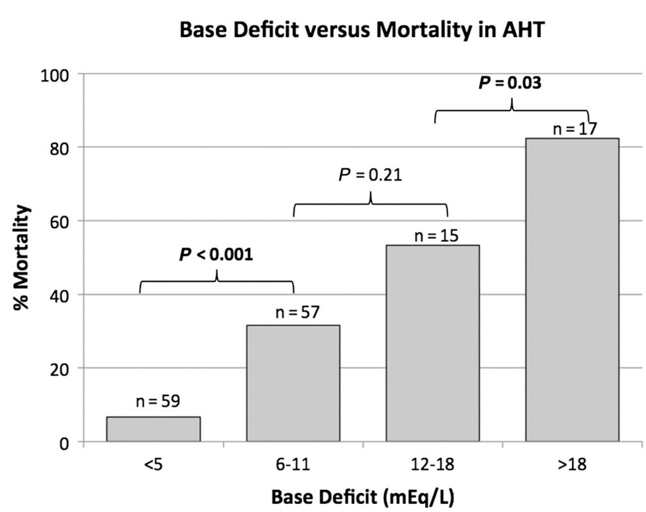

Fig. 1 Percent mortality increases with rising BD in a step-wise fashion. The number of subjects in each BD group is represented at the top of each bar. p-values are derived from chi-square analysis comparing groups. Bold p-values meet the threshold for significance.

regression demonstrated that BD, ISS, and CPR were all independently associated with mortality in our cohort, whereas age and hematocrit were not associated. For every 3 mEq/L increase in BD the risk of dying increased 0.66 fold. For every 10-unit increase in ISS the risk of dying increased 4.9 fold. If CPR was initiated, the risk of dying increased 3.5 fold (Table 3). The ROC area under the curve for BD was 0.90, indicating that it was highly predictive of death. Logistic regression was used to create a graph of the probability of mortality in relation to BD and the need for CPR, with an ISS of 25 (Fig. 2). The BD LD_{50} for a child suffering severe AHT who did not receive CPR was 18.0, whereas it decreased to 10.7 for a child who did receive CPR.

2.5. Functional outcomes

Functional outcome of surviving children was assessed by determining the KOSCHI score [19] at discharge and at most recent follow-up. The average length of stay of survivors was 24 ± 3 days. The average length of follow-up was 2.9 ± 0.27 years, with 62/96 (65%) surviving children having follow-up >1 year after discharge (range 6 days–9.9 years, median 2.2 years). Functional outcome was compared to BD (Fig. 3). Few children (10/29, 34%) with a BD ≥12 survived, and only one of these children progressed to good recovery. No child with a BD >18 progressed to good recovery. While lower BD trended towards improved functional outcome, this was not statistically significant. Surviving children who had CPR after AHT were more likely to have severe functional deficits at follow-up, whereas those not receiving CPR were more likely to have moderate functional deficits (p = 0.05).

3. Discussion

We found that an elevated BD on admission correlates with the risk of mortality in AHT. Non-survivors of AHT were more likely to undergo CPR and pre-hospital intubation. These differences could not be explained by the patterns or types of brain injury and suggest that these patients may have sustained secondary brain injury owing to shock, which can be estimated from the degree of BD. For every 5 mEq/L increase in BD the risk of mortality doubled, and the need for CPR increased mortality by nearly four-fold. However, we found that by limiting our study to patients with an admission BD, we were also limiting our study to children with severe AHT, as evidenced by the average ISS of 25.1 ± 0.7 and average AIS head of 4.5 ± 0.1 for all children in our cohort. A blood gas is more likely to be drawn in a patient with respiratory distress, need for mechanical ventilation, or that otherwise appears more ill. Of the 411 children initially identified, 263 (64%) did not have an admission BD on record. Therefore, our conclusions should only be applied to patients who require a BD for clinical decision-making. Had a BD been available for all patients, this correlation with outcome may have changed, but given our understanding of traumatic brain injury and secondary brain injury, it is plausible that BD is a robust predictor of death in AHT. Survival often is not in question in less severely injured children who are less likely to have an admission BD. Therefore, we believe our findings are relevant specifically only for patients in which a clinician would question survival at admission.

It has been demonstrated that injury severity, ICP, and GCS are important predictors of death in non-AHT [17]. Oluigbo and colleagues found in a study of children with AHT versus non-AHT requiring decompressive craniotomy that the odds of death in the AHT group were increased 12-fold, and that this difference could not be explained by other measures of injury including ISS, ICP or GCS [6]. They questioned if secondary injury owing to hypoxia and/or hypotension could have contributed to the discrepancy in survival. Cerebral edema was not examined in this study, but is more common in children diagnosed with AHT, is a predictor of mortality, and correlates with poor functional outcome in survivors of AHT [4,20–22]. Cerebral edema can occur as a secondary insult owing to hypoxia and hypotension that develops over time after TBI [23,24]. These

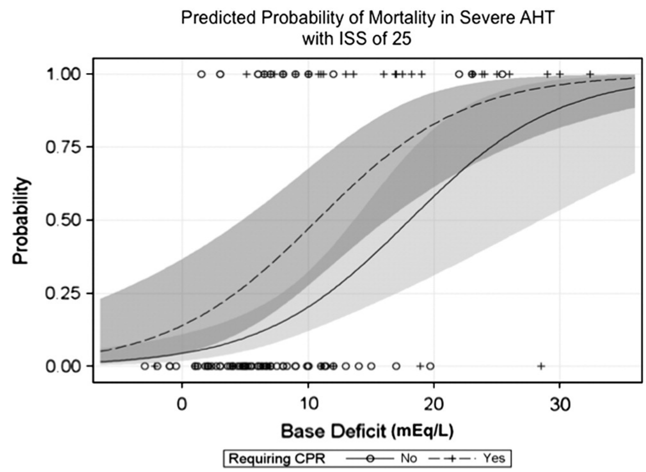

Fig. 2 Predictive probability of mortality based on admission BD and CPR status, with set ISS of 25.

Table 3 Odds ratio estimates for predictors of death in abusive head trauma.

	Odds ratio	95% CI	p-value
Base deficit by 1-unit	1.185	1.089–1.289	<0.001
Base deficit by 3-units	1.663	1.292–2.141	<0.001
Injury severity score by 1-unit	1.172	1.076–1.276	<0.001
Injury severity score by 10-units	4.87	2.071–11.462	<0.001
Cardiopulmonary resuscitation, yes vs. no	3.482	1.219–9.947	0.02

Odds ratio estimates for predictors of death in pediatric abusive head trauma. The odds of death increase by the amount that the point estimate is over equality (equality = 1). CI = Confidence interval.

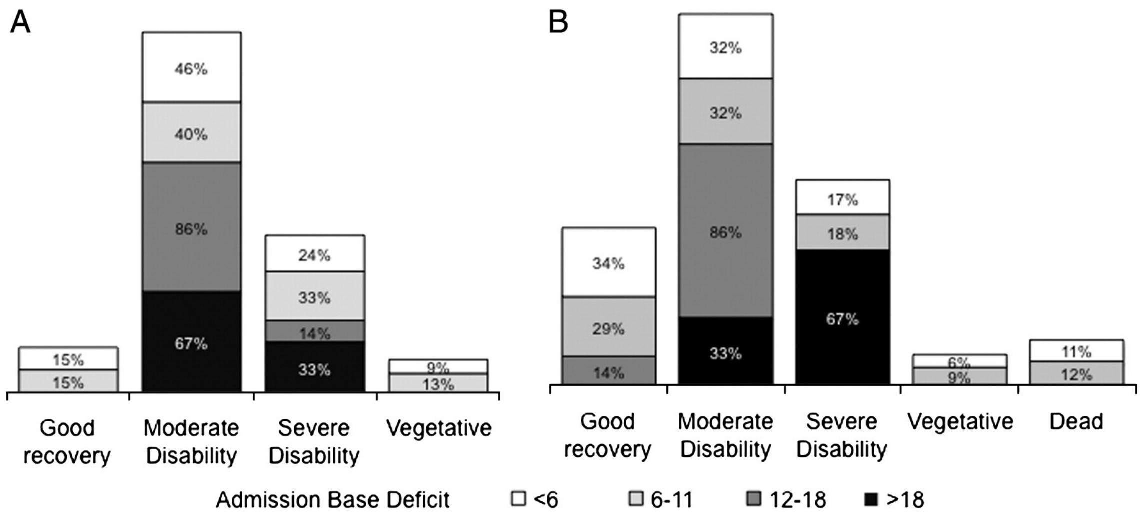

Fig. 3 A. Functional outcome at discharge. B. Functional outcome at follow-up. Outcome is based on KOSCHI scoring. Percentage represents proportion of children with similar admission BD.

findings support the idea that the increased morbidity and mortality in AHT, especially in the severely injured, are not solely related to the primary brain injury, but instead are significantly influenced by delays in definitive medical care with resultant secondary brain injury. A similar phenomenon is seen in adults who must be extricated from the vehicle after suffering a TBI in a motor vehicle crash [10]. It has previously been reported that sub-dural hemorrhage is more common in non-survivors of AHT compared with survivors [22]. In our study, however, nearly all children, survivors (96%) and non-survivors (89%) alike, were diagnosed with sub-dural hemorrhage. This difference may be owing to the inherent selection bias in our study created by limiting our evaluation to children with an admission BD.

We were unable to find a statistically significant relationship between BD and functional outcome among those children who survived to discharge. This is likely owing to the correction of BD with resuscitation in survivors, since it is the failure to clear BD that appears predictive of outcome in trauma. One series showed that all surviving children who suffered a traumatic injury cleared their BD within 24 hours [25]. Moreover, in our study, few children with a BD >12 survived. Of those children, only one progressed to good recovery while the others suffered moderate to severe functional deficits. No child with a BD >18 progressed to good recovery. Elevated levels of cytochrome C in cerebrospinal fluid have been correlated with the presence of AHT and poor outcome, but this requires ventricular access or a lumbar puncture to measure, neither of which are likely to be performed in the acute setting [26]. Similarly, neuron specific enolase has been shown to have diagnostic and prognostic significance; however it is less accessible than a BD, which can be measured in minutes with a blood gas [27,28]. In the absence of a readily available serum laboratory predictor of functional outcome, several clinical predictors of functional outcome have been described among survivors of pediatric AHT. Moderate to severe deficits post-injury have been associated with age >1 year, loss of consciousness on presentation, requirement for CPR, presence of seizures during the hospital course, need for neurosurgical intervention, longer ICU stay and number of ventilation days [4,21]. Our data corroborate that need for CPR is correlated with worse functional outcome.

In conclusion, we recommend that all children with suspected AHT who have a GCS <8 or who require intubation/CPR should have a BD drawn. The results offer early prognostic information when survival is in question. Moreover, an elevated BD can identify patients who may benefit from earlier goal directed therapies aimed at preventing secondary brain injury owing to hypoxia, hypotension, and/or cardiopulmonary instability. Future prospective studies are warranted to evaluate BD as a prognostic biomarker among children who suffer from AHT.

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