RESEARCH ARTICLE

Prevalence of neurogenic pulmonary edema among patients who died from head injury – a retrospective chart review

[version 1; peer review: 1 approved, 1 not approved]

Erasmus E. Okello¹, Janat Tumukunde¹, Patience Atumanya¹ , Sam Kalungi², Alex Muhindo², Arthur Kwizera¹

¹Department of Anesthesia, College of Health Sciences, Makerere University, Kampala, 7062, Uganda

²Mulago National Referral and Teaching Hospital, Kampala, 7051, Uganda

V1 First published: 18 May 2018, 7:611
<https://doi.org/10.12688/f1000research.13750.1>

Latest published: 18 May 2018, 7:611
<https://doi.org/10.12688/f1000research.13750.1>

Abstract

Background: Neurogenic pulmonary edema is a less recognized complication of head injuries and is seldom considered in management protocols in most centers. We therefore conducted a study to determine the prevalence of Neurogenic Pulmonary Edema among patients who died from head injury at Mulago National Referral Hospital, Uganda.

Methods: An observational study conducted from the 1st June to 31st August 2013, with ethical approval. We consecutively enrolled patients who died of head injuries in the hospital. Demographic data, duration of illness, severity of illness, and patient management instituted were gathered from patient medical files. Autopsy results of the brain, lungs, heart, liver and kidneys performed within 24 hours after death were reviewed.

Results: Twenty-six patients who died from head injury were enrolled in this study over the study period. Only one patient had preexisting hypertension and obesity while the rest had no known premorbid medical history. Intracranial abnormalities including raised intracranial pressure had been detected by CT scan in 18/26 of the patients while others had a normal scan (1/26) or did not have a scan done (7/26). Features of pulmonary edema were detected in 76.9% (20/26) of the bodies on gross lung examination. Pulmonary edema was bilateral in 85% of the bodies. Congestion was also noted in the liver, heart and kidneys.

Conclusions: Pulmonary edema is highly prevalent in head injury patients and needs to be critically recognized early in the formulation of a management plan, as it contributes to morbidity and secondary brain injury through respiratory embarrassment.

Keywords

head injury, neurogenic pulmonary edema

Open Peer Review

Approval Status

	1	2
version 1
18 May 2018	view	view

1. **Mabrouk Bahloul** , Centre Hospitalier Universitaire Habib Bourguiba, Sfax, Tunisia
2. **Roger P. Simon**, Morehouse School of Medicine, Atlanta, USA

Any reports and responses or comments on the article can be found at the end of the article.

Corresponding author: Patience Atumanya (atumanyap@gmail.com)

Author roles: **Okello EE:** Conceptualization, Data Curation, Formal Analysis, Investigation, Methodology, Project Administration, Resources, Visualization, Writing – Original Draft Preparation, Writing – Review & Editing; **Tumukunde J:** Data Curation, Investigation, Methodology, Writing – Original Draft Preparation, Writing – Review & Editing; **Atumanya P:** Writing – Original Draft Preparation, Writing – Review & Editing; **Kalungi S:** Investigation, Methodology, Supervision; **Muhindo A:** Investigation, Methodology, Supervision; **Kwizera A:** Methodology, Supervision, Writing – Review & Editing

Competing interests: No competing interests were disclosed.

Grant information: The author(s) declared that no grants were involved in supporting this work.

Copyright: © 2018 Okello EE *et al.* This is an open access article distributed under the terms of the [Creative Commons Attribution License](#), which permits unrestricted use, distribution, and reproduction in any medium, provided the original work is properly cited. Data associated with the article are available under the terms of the [Creative Commons Zero "No rights reserved" data waiver](#) (CC0 1.0 Public domain dedication).

How to cite this article: Okello EE, Tumukunde J, Atumanya P *et al.* **Prevalence of neurogenic pulmonary edema among patients who died from head injury – a retrospective chart review [version 1; peer review: 1 approved, 1 not approved]** F1000Research 2018, 7:611 <https://doi.org/10.12688/f1000research.13750.1>

First published: 18 May 2018, 7:611 <https://doi.org/10.12688/f1000research.13750.1>

Introduction

Neurogenic pulmonary edema (NPE) is an age-old clinical syndrome characterized by the acute onset of pulmonary edema following a significant central nervous system (CNS) insult¹. NPE can occur after virtually any form of injury of the CNS, and is a potential early contributor to pulmonary dysfunction in patients with head injuries². A myriad of CNS events, including spinal cord injury, subarachnoid hemorrhage, traumatic brain injury (TBI), intracranial hemorrhage, status epilepticus, meningitis, and subdural hemorrhage, have been associated with this syndrome^{3–6}.

The exact mechanism is unknown as it is believed to be multi-pronged and data is sparse. The connection between CNS injury and hemodynamic dysfunction was first described by Harvey Williams Cushing in 1903¹. This was followed by reports of cases in which acute pulmonary edema developed after CNS insult resultant from status epilepticus^{1,7} and isolated head bullet wounds³. The etiology is thought to be a surge of catecholamines following the head injury that results in cardiopulmonary dysfunction^{8,9}. Several cardiovascular events are likely to result from this stimulation resulting in capillary leak and eventual pulmonary edema¹. Bahloul *et al.* identified features of left ventricular myocardial dysfunction in an echocardiographic study performed on previously healthy traumatic brain injury patients presenting with neurogenic pulmonary edema⁵.

TBI is one of the world's major causes of mortality and morbidity, particularly in the developing world, where motor vehicle and cyclist crashes are largely due to human error and poor roads^{10–13}. With increasing industrialization of the developing world, there is a proportional increase in motorized trauma. Uganda is currently ranked second in the world in road traffic accidents after Ethiopia¹⁴. These in a country with a limited health budget, mean resources are stretched to the limit by the burden of care required by trauma patients. TBI forms the majority of trauma cases occurring, either in isolation or as part of multiple trauma^{14,15}.

The neurosurgery Unit of Mulago NRH admits at least ten critically ill patients per day, while the intensive care unit (ICU) can only admit a maximum of four patients. The national critical care bed capacity is significantly limited for the enormous population in need¹⁶. An in-hospital mortality of 25% following severe TBI was reported in a retrospective study in Mulago NRH¹³ while Kwizera *et al.* found an ICU mortality rate of 45.3% from head injury nationally. Mortality was commonly due to hemorrhagic shock, respiratory failure and sepsis¹. The majority of survivors are left with gross disabilities while out-of-hospital mortality post-discharge remains largely unknown¹⁶.

Awareness of NPE may lead to early intervention in brain-injured patients. *However*, although NPE was identified over 100 years ago, it is still underappreciated in the clinical arena. Its sporadic and relatively unpredictable nature, and a lack of etiologic-specific diagnostic markers and treatment modalities, may in part be responsible for its poor recognition at the bedside¹.

Worse still, there is very little data on the subject. Current data estimate the prevalence of NPE following severe brain insults, like trauma, stroke, status epilepticus etc., to be about 50%¹⁷, rising up to 92% in fatal subarachnoid hemorrhage¹⁸, being directly related to duration since insult⁴. Most data were, however, based on reviews of hospital records and case studies.

In this study, we determined the prevalence of neurogenic pulmonary edema through postmortem studies of head injured patients and sought to establish its relationship to the different patterns of organ dysfunction in head injured patients. This study also indirectly assessed quality of care of neurosurgery patients in the hospital. There are no published data on a similar study to the best of our knowledge.

Methods

Study design

This was an observational study carried out in Mulago National Referral and Teaching Hospital, Uganda, involving patients who died from head injury. We consecutively enrolled subjects into the study upon death over two months (1st June to 31st August 2013). Medical records were reviewed and data on patient demographics and progressive medical/surgical management collected. Particularly, data about diagnosis and diagnostic procedures, medication, fluid administration, ICU admission, mechanical ventilation, and surgical procedures carried out.

Protocol

Consent to enroll patients was gathered from relatives upon death between June and August, 2013. We recruited all patients who died from TBI and excluded patients with documented cardiac dysfunction, chronic renal or hepatic dysfunction. A medical record review was performed to collect pertinent information on demographic, diagnosis (clinical, radiological, laboratory), duration of injury (from time of injury to time of death), patient management (length of hospital stay, nursing care, fluid management, medications, surgical interventions, ICU admission, mechanical ventilation) up to time of death. Medications sought for included steroids, antibiotics, diuretics, vasopressors, and anticonvulsants.

Postmortem studies were performed by a pathologist (KS) within 24 hours of death. Full physical examination of the bodies was done, and notable abnormalities documented. Features of edema were sought during the examination of the heart, lungs, brain and kidneys. Edema was defined by tissue congestion with interstitial fluid on gross examination. A calibrated beam balance was used to weigh the brain, lungs, kidneys and heart. Organ weights were compared to standardized normal ranges based on the European guidelines¹⁹.

Data analysis

Basic descriptive statistics were used to analyze demographic data and other study variables. Data were analysed in STATA 10.0. Logistic regression analysis was used to determine the association between different variables with presence of NPE. P-values <0.05 were considered statistically significant (Table 3). Data are presented as modes and means unless otherwise indicated.

Results

During the study period, twenty-six patients were enrolled in this study. No patient had a premorbid diagnosis of renal, liver or lung disease. Only one patient had preexisting hypertension and obesity but with no documented cardiac disease. No drug or transfusion reactions were noted during the patients' treatment. Only one patient (3.9%) had aspiration pneumonia. Intracranial abnormalities including raised intracranial pressure had been detected by brain Computed Tomography (CT) scan in 18/26 of the patients. One patient's brain CT scan showed no acute intracranial pathology while 26.9% (7/26) of patients did not have a brain CT scan performed (Table 1). Autopsy showed features consistent with pulmonary edema in 76.9% of patients, being bilateral in 85% of these. All the 15% in whom edema was unilateral had involvement of the right lung (Table 2).

Brain CT findings included intracranial edema and hemorrhage in 69.2%. 14 (53.9%) of patients had concomitant brain contusions while only one did not reveal any radiological features of intracranial pathology. Only three (11.5%) patients had had chest x-rays performed which revealed features consistent with bilateral airspace disease (Table 1). All patients admitted to ICU received invasive artificial ventilation. Average daily total fluid input was 2 liters with an average overall measured fluid balance (total IV and oral fluid input minus outputs from drains (urine, GI) (Table 1) of +560 mL at time of death. No transfusion reactions were recorded. None of the patients required instrumentation of the chest wall. Five patients (30.8%) had received orthopedic surgical care, two (7.7%) had received surgical toilet for soft tissue injuries while an additional two patients had undergone exploratory laparotomy for blunt abdominal trauma (ruptured spleen and ruptured liver, respectively) (Table 1).

Features of pulmonary edema were noted in 76.9% of patients. 85% of these showed evidence of pulmonary edema bilaterally. Additional injuries noted at autopsy included liver and splenic contusion in one patient each, musculoskeletal injuries (degloving injuries (7.7%), long bone fractures (30.8%). There was no evidence of spinal trauma at autopsy (Table 2). Organs from one patient aged 9 years were not weighted against the European standard to which organ weights were referenced.

Dataset 1. Extracted medical data from patients with neurogenic pulmonary edema following head injury

<http://dx.doi.org/10.5256/f1000research.13750.d202806>

Discussion

The true incidence of NPE after acute head injury is difficult to estimate because much of the information comes from small autopsy series or isolated case reports. In this postmortem study, we found prevalence of neurogenic pulmonary edema of 76.9%. In an autopsy and in-patient database study, Rogers *et al.* found a prevalence of neurogenic pulmonary edema of

Table 1. Baseline characteristics.

Characteristics		N=26
Sex	Male	23 (88.46%)
	Female	3 (11.54%)
Age (Mean/SD) (Years)		26 (11)
Referrals		17 (65.38%)
Average Injury to Admission duration (days)		6
Average length of stay (days)		4
Diagnosis at admission	Closed head injury	16 (61.54%)
	Open head injury	10 (38.46%)
Level of care	ICU	7 (26.9%)
	Neurosurgical ward	19 (73.1%)
Brain CT Scan	Radiological abnormality	18 (69.2%)
	No radiological abnormality	1 (3.9%)
	Not performed	7 (26.9%)
Chest X-ray	Lung parenchymal pathology	3 (11.5%)
	X-ray not performed	23 (88.5%)
Diagnosis		
Respiratory	Pneumonia	5 (19.2%)
	Pulmonary edema	1 (3.8%)
	Lung contusion	1 (3.8%)
Non-respiratory in-hospital comorbidity		
	Sepsis	5 (19.2%)
	AKI	1 (3.9%)
	Undifferentiated Shock	3 (11.5%)
	Liver injury	1 (3.9%)
Treatment		
Fluid therapy	Crystalloid only	21 (80.8%)
	Crystalloid + Blood product	4 (15.4%)
	No fluid therapy	1 (3.8%)
Steroids	Administered	5 (19.2%)
	Not administered	21 (80.8%)
Antibiotics		25 (96.2%)
Diuresis	Mannitol only	1 (3.9%)
	Mannitol + Furosemide	14 (53.8%)
	No diuretics	11 (43.3%)
Neurosurgical Intervention		5 (19.2%)
Artificial ventilation		7 (26.9%)

CT: Computed tomography, ICU: Intensive care unit, AKI: Acute kidney injury

Table 2. Autopsy findings.

n=26			
	Organ Weight		Important Gross findings
Brain	Normal	19 (73%)	Skull fracture 20 (76.9%)
	Increased	6 (23.1%)	Hemorrhage 24 (92.3%)
	Not applicable	1(3.9%)	Edema 1 (3.9%)
Right lung	Normal	17 (61.5%)	Lung contusion 1 (3.8%)
	Increased	9 (34.6%)	Hemothorax 1 (3.8%)
Left lung	Normal	17 (61.5%)	Rib fracture 1 (3.8%)
	Increased	9 (34.6 %)	Lung edema 20 (76.9%)
	Not applicable	1 (3.9%)	
Heart	Normal	21 (80.8%)	Myocardial edema 1 (3.9%)
	Increased	4 (15.3%)	
	Not applicable	1 (3.9%)	
Left kidney	Normal	22 (84.9)	1 (3.9%) right kidney not applicable.
	Increased	3 (11.5%)	All others were of normal weight
	Not applicable	1 (3.9%)	

Standard normal organ weights at autopsy¹⁹:

- Brain Weight: Male: 1365–1450g; Female: 1250–1275g
- Lung Weight: Left: 420–600g; Right: 480–680g
- Heart Weight: Male: 270–280g; Female: 250–280g
- Kidneys: Left: 150g; Right: 190g

Table 3. Univariate analysis of association between patient characteristics and interventions with pulmonary edema.

Characteristic		OR (95%CI)	p-value
Sex		1.14 (0.09-14.78)	0.92
Referral Status		1.91 (0.30-12.26)	0.50
ICU Admission		3.50 (0.35-35.37)	0.29
Artificial Ventilation		3.50 (0.35-35.37)	0.29
Neurosurgical Intervention		2 (0.17-22.95)	0.58
Diuretics	Diuretic therapy	1.57 (0.29-8.42)	0.60
	No diuretic therapy	0.60 (0.11-3.30)	0.29
Fluids	None	Reference	
	Crystalloids	1.7	
	Blood	1.94	
CT Diagnosis	None pathology	Reference	
	CHI	1.95 (0.32-12.1)	0.47
	OHI	1	
Steroids		2.00 (0.19-21.43)	0.56

CT: Computed Tomography; CHI: Closed head injury; OHI: Open head injury

32% in patients dying within the first 24 hours and up to 50% in 96 hours².

Pulmonary dysfunction after acute brain injury is a common but poorly understood phenomenon. In classic medical literature, the causes of pulmonary dysfunction in patients with head injury include pneumonia, aspiration, and pulmonary embolus, while NPE is seldom recognized. NPE is a form of pulmonary edema that develops rapidly after a cerebral injury²⁰. It has been described in trauma patients as parenchymal edema, hemorrhage, and congestion without evidence of chest trauma in patients with isolated head injury^{18,21}.

In Uganda, over 20,000 road traffic crashes occur annually claiming many lives through multiple trauma, head injury being one of the leading causes of death^{14,15,22,23}. However, the incidence of NPE had not previously been established. In the study reported here, we included only patients with traumatic head injury who died after admission and treatment in the hospital. In addition, because of a shortage of resources, it was not possible to carry out several specialized tests on the patients before death.

Pulmonary edema was bilateral in most patients studied and was predominantly right sided in those with unilateral edema. This relates closely with the theory of a generalized pulmonary vascular disorder in head injured patients which is related to the severity of insult²⁴. The study by Rogers *et al.*, however, describes a predominantly right sided edema presentation². This difference could be related to the difference in severity of illness and quality of initial management instituted. Furthermore, our study applied an European standard to organ weight measurement which was validated in a different population and only gross lung examination was performed for evidence of pulmonary edema which could have contributed to disparity in measurements and findings.

Studies on the other organs showed no significant weight increases. In addition, no significant structural abnormalities indicative of preexisting chronic conditions could be found on anatomical examination of these organs. This correlates well with the definition of neurogenic pulmonary edema in which there is no other significant organ injury in a patient with severe brain injury^{1,24,25}. Edema was, however, seen in some dissections of the heart and kidneys that could be a result of multi-organ dysfunction as a result of critical illness. In addition, Bahloul *et al.* described myocardial dysfunction in neurogenic injury which could in part explain the pathophysiology of NPE⁵.

Severe TBI frequently presents with significant depression in level of consciousness compromising adaptive protective reflexes. Standard management for severe TBI patients includes ICU admission for intensive monitoring, interventions and supportive care such as invasive mechanical ventilation, among other therapies. Moreover permissive hypercapnia and tight control of blood carbon dioxide tension forms an integral part of neurocritical care^{26,27}. In our study however, only 26.9% of patients were managed in ICU. Consequently, only 26.9% of patients in this study had received mechanical ventilatory support despite

76.9% having potentially developed respiratory dysfunction due to pulmonary edema among other causes. This is partly explained by the shortage of ICU capacity nationally¹⁶ and underscores the pressing need for critical care services in the care of TBI patients.

Brain CT scan is a minimum diagnostic tool. In our study, 26.9% of patients never had a brain CT scan performed. This in addition to limited surgical capacity leads to delay and missed opportunities. As a result, the mortality of head injury patients is very high, resulting perhaps in complications such as neurogenic pulmonary edema. Absence of complete antemortem investigation of the patients before death for pulmonary edema plus associated conditions as well as the small sample size makes it difficult to deduce statistically significant causal relationships in our study. However, strong inferences can be derived from association between severity of brain injury (as shown by need for ICU admission, type of injury) with NPE.

Conclusion

We conclude that NPE occurs frequently in head injury patients. The process of edema formation begins early in the clinical course and is isolated to the lung. NPE thus needs to be critically recognized early in the formulation of a management plan. The contribution of NPE to mortality and morbidity in these patients cannot be deduced from this study, as a causal association between pulmonary edema and mortality was not studied.

Ethical approval and consent

Approval of the study protocol was obtained from Mulago National Referral and Teaching Hospital Ethics Board. Written informed consent to participate and publish patient records was obtained from relatives. Denial of consent was criteria for omission from the study. All authors vouch for the originality, completeness, accuracy of the data presented and for the fidelity of this report to the study protocol as detailed herein and copied to the Mulago National Referral and Teaching Hospital Ethics Board.

Data availability

Dataset 1: Extracted medical data from patients with neurogenic pulmonary edema following head injury [10.5256/f1000research.13750.d202806](https://doi.org/10.5256/f1000research.13750.d202806)²⁸

Competing interests

No competing interests were disclosed.

Grant information

The author(s) declared that no funding was involved in supporting this work.

Acknowledgements

The authors of this study wish to convey their deep appreciation to the Intensive care, neurosurgical and pathology units of Mulago National Referral and Teaching Hospital for support and permission to access medical records and perform this research. Additionally, we would like to thank Mrs. Catherine Kwizera for the statistical work done in summarizing and analyzing data of this study.

References

1. Davison DL, Chawla LS, Selassie L, *et al.*: **Neurogenic pulmonary edema: Successful treatment with IV phentolamine.** *Chest.* 2012; **141**(3): 793–795.
[PubMed Abstract](#) | [Publisher Full Text](#)
2. Rogers FB, Shackford SR, Trevisani GT, *et al.*: **Neurogenic pulmonary edema in fatal and nonfatal head injuries.** *J Trauma.* 1995; **39**(5): 860–6; discussion 866–8.
[PubMed Abstract](#) | [Publisher Full Text](#)
3. Fontes RB, Aguiar PH, Zanetti MV, *et al.*: **Acute neurogenic pulmonary edema: Case reports and literature review.** *J Neurosurg Anesthesiol.* 2003; **15**(2): 144–150.
[PubMed Abstract](#) | [Publisher Full Text](#)
4. Kaufman HH, Timberlake G, Voelker J, *et al.*: **Medical complications of head injury.** *Med Clin North Am.* 1993; **77**(1): 43–60.
[PubMed Abstract](#) | [Publisher Full Text](#)
5. Bahloul M, Chaari AN, Kallel H, *et al.*: **Neurogenic pulmonary edema due to traumatic brain injury: evidence of cardiac dysfunction.** *Am J Crit Care.* 2006; **15**(5): 462–70.
[PubMed Abstract](#)
6. Martin AM Jr, Simmons RL, Heisterkamp CA 3rd: **Respiratory insufficiency in combat casualties. I. Pathologic changes in the lungs of patients dying of wounds.** *Ann Surg.* 1969; **170**(1): 30–38.
[PubMed Abstract](#) | [Free Full Text](#)
7. Colice GL: **Neurogenic pulmonary edema.** *Clin Chest Med.* 1985; **6**(3): 473–489.
[PubMed Abstract](#)
8. Grunsfeld A, Fletcher JJ, Nathan BR: **Cardiopulmonary complications of brain injury.** *Curr Neurol Neurosci Rep.* 2005; **5**(6): 488–493.
[PubMed Abstract](#) | [Publisher Full Text](#)
9. Zhao H, Lin G, Shi M, *et al.*: **The mechanism of neurogenic pulmonary edema in epilepsy.** *J Physiol Sci.* 2014; **64**(1): 65–72.
[PubMed Abstract](#) | [Publisher Full Text](#)
10. Helmy A, Vizcaychipi M, Gupta AK: **Traumatic brain injury: Intensive care management.** *Br J Anaesth.* 2007; **99**(1): 32–42.
[PubMed Abstract](#) | [Publisher Full Text](#)
11. Heegaard W, Biros M: **Traumatic Brain Injury.** *Emerg Med Clin North Am.* 2007; **25**(3): 655–678, viii.
[PubMed Abstract](#) | [Publisher Full Text](#)
12. Haddad SH, Arabi YM: **Critical care management of severe traumatic brain injury in adults.** *Scand J Trauma Resusc Emerg Med.* 2012; **20**: 12.
[PubMed Abstract](#) | [Publisher Full Text](#) | [Free Full Text](#)
13. Tran TM, Fuller AT, Kiryabwire J, *et al.*: **Distribution and characteristics of severe traumatic brain injury at mulago national referral hospital in Uganda.** *World Neurosurg.* 2015; **83**(3): 269–277.
[PubMed Abstract](#) | [Publisher Full Text](#)
14. Hsia RY, Ozgediz D, Mutto M, *et al.*: **Epidemiology of injuries presenting to the national hospital in Kampala, Uganda: Implications for research and policy.** *Int J Emerg Med.* 2010; **3**(3): 165–172.
[PubMed Abstract](#) | [Publisher Full Text](#) | [Free Full Text](#)
15. Kobusingye O, Guwatudde D, Lett R: **Injury patterns in rural and urban Uganda.** *Inj Prev.* 2001; **7**(1): 46–50.
[PubMed Abstract](#) | [Publisher Full Text](#) | [Free Full Text](#)
16. Kwizera A, Dünser M, Nakibuuka J: **National intensive care unit bed capacity and ICU patient characteristics in a low income country.** *BMC Res Notes.* 2012; **5**: 475.
[PubMed Abstract](#) | [Publisher Full Text](#) | [Free Full Text](#)
17. Schievink WI, Wijdicks EF, Parisi JE, *et al.*: **Sudden death from aneurysmal subarachnoid hemorrhage.** *Neurology.* 1995; **45**(5): 871–4.
[PubMed Abstract](#) | [Publisher Full Text](#)
18. Ridenti FA: **Neurogenic pulmonary edema: a current literature review.** *Rev Bras Ter Intensiva.* 2012; **24**(1): 91–96.
[PubMed Abstract](#) | [Publisher Full Text](#)
19. De La Grandmaison GL, Clairand I, Durigon M: **Organ weight in 684 adult autopsies: new tables for a Caucasoid population.** *Forensic Sci Int.* 2001; **119**(2): 149–154.
[PubMed Abstract](#) | [Publisher Full Text](#)
20. Busl KM, Bleck TP: **Neurogenic Pulmonary Edema.** *Crit Care Med.* 2015; **43**(8): 1710–1715.
[PubMed Abstract](#) | [Publisher Full Text](#)
21. Simon RP: **Neurogenic pulmonary edema.** *Neurol Clin.* 1993; **11**(2): 309–323.
[PubMed Abstract](#)
22. Demyttenaere SV, Nansamba C, Nganwa A, *et al.*: **Injury in Kampala, Uganda: 6 years later.** *Can J Surg.* 2009; **52**(5): E146–50.
[PubMed Abstract](#) | [Free Full Text](#)
23. Jayaraman S, Ozgediz D, Miyamoto J, *et al.*: **Disparities in injury mortality between Uganda and the United States: comparative analysis of a neglected disease.** *World J Surg.* 2011; **35**(3): 505–511.
[PubMed Abstract](#) | [Publisher Full Text](#) | [Free Full Text](#)
24. Smith WS, Matthay MA: **Evidence for a hydrostatic mechanism in human neurogenic pulmonary edema.** *Chest.* 1997; **111**(5): 1326–1333.
[PubMed Abstract](#) | [Publisher Full Text](#)
25. Šedý J, Zicha J, Kuneš J, *et al.*: **Mechanisms of neurogenic pulmonary edema development.** *Physiol Res.* 2008; **57**(4): 499–506.
[PubMed Abstract](#)
26. Wijayatilake DS, Jigajinni SV, Sherren PB: **Traumatic brain injury: Physiological targets for clinical practice in the prehospital setting and on the Neuro-ICU.** *Curr Opin Anaesthesiol.* 2015; **28**(5): 517–524.
[PubMed Abstract](#) | [Publisher Full Text](#)
27. Wijayatilake DS, Shepherd SJ: **What's new in the management of traumatic brain injury on neuro ICU?** *Curr Opin Anaesthesiol.* 2014; **27**(5): 459–464.
[PubMed Abstract](#) | [Publisher Full Text](#)
28. Okello EE, Tumukunde J, Atumanya P, *et al.*: **Dataset 1 in: Prevalence of Neurogenic Pulmonary Edema among patients who died from Head Injury.** *F1000Research.* 2018.
[Data Source](#)

Open Peer Review

Current Peer Review Status:

Version 1

Reviewer Report 13 August 2018

<https://doi.org/10.5256/f1000research.14941.r36957>

© 2018 Simon R. This is an open access peer review report distributed under the terms of the [Creative Commons Attribution License](#), which permits unrestricted use, distribution, and reproduction in any medium, provided the original work is properly cited.

Roger P. Simon

Department of Medicine and Neurobiology, Morehouse School of Medicine, Atlanta, GA, USA

Okello et al provide observational data on the incidence of pulmonary edema at autopsy following death from head injury. Consecutive data, of organ weight, with in 24 hours of death, obtained over two months, in 26 patients are provided. Pulmonary edema was documented in 76.8% of patients; weight increase was not found in organs other than the lungs. The mean age was 26 making co morbid cardiovascular factors unlikely. This incidence is similar to that of Simmons (1969) report in fatal military head injuries (pulmonary edema found in 17 of 20 cases). The authors conclusion that neurogenic pulmonary edema begins early and is isolated to the lung adds incidence data to a fatal consequence of head injury about which the pathophysiology and therefore the treatment remains uncertain.

Is the work clearly and accurately presented and does it cite the current literature?

Yes

Is the study design appropriate and is the work technically sound?

Yes

Are sufficient details of methods and analysis provided to allow replication by others?

Yes

If applicable, is the statistical analysis and its interpretation appropriate?

Not applicable

Are all the source data underlying the results available to ensure full reproducibility?

No source data required

Are the conclusions drawn adequately supported by the results?

Yes

Competing Interests: No competing interests were disclosed.

I confirm that I have read this submission and believe that I have an appropriate level of expertise to confirm that it is of an acceptable scientific standard.

Reviewer Report 11 July 2018

<https://doi.org/10.5256/f1000research.14941.r35040>

© 2018 Bahloul M. This is an open access peer review report distributed under the terms of the [Creative Commons Attribution License](#), which permits unrestricted use, distribution, and reproduction in any medium, provided the original work is properly cited.

Mabrouk Bahloul

Service de Réanimation Médicale, Centre Hospitalier Universitaire Habib Bourguiba, Sfax, Tunisia

In patients with traumatic acute head injury, impaired pulmonary function is a common but poorly understood complication. NPE is a potential early contributor to the pulmonary dysfunction that occurs in patients with head injuries. Although NPE is a frequent complication of traumatic head injury, its occurrence in this specific condition is rarely described. In addition, despite clinical and experimental studies, the mechanisms leading to NPE are not fully understood. As consequence, studying the incidence of NPE after acute head injury is very interesting subject.

In this study, in this observational study carried out in Mulago National Referral and Teaching Hospital, Uganda, involving patients who died from head injury. Okello et al had consecutively enrolled subjects into the study upon death over two months (1st June to 31st August 2013) Medical records were reviewed and data on patient demographics and progressive medical/surgical management collected. Particularly, data about diagnosis and diagnostic procedures, medication, fluid administration, ICU admission, mechanical ventilation, and surgical procedures carried out. During the study period, twenty-six patients were enrolled in this study. Autopsy showed features consistent with pulmonary edema in 76.9% of patients, being bilateral in 85% of these. All the 15% in whom edema was unilateral had involvement of the right lung.

This study suffers from several limitations:

1. There is no hemodynamic exploration for all patients.
2. No electrocardiographic has been reported
3. How pulmonary contusion were excluded?
4. For patients with long bone fractures, how pulmonary fat embolism were excluded?
5. How other causes of pulmonary edema have been excluded: due to severe septic shock! cardiac arrhythmia?...
6. Brain CT scan were not performed in all patients

All these points represent a several limitations to understand the positive diagnosis and the mechanism of NPE.

Is the work clearly and accurately presented and does it cite the current literature?

Partly

Is the study design appropriate and is the work technically sound?

Partly

Are sufficient details of methods and analysis provided to allow replication by others?

Partly

If applicable, is the statistical analysis and its interpretation appropriate?

I cannot comment. A qualified statistician is required.

Are all the source data underlying the results available to ensure full reproducibility?

No

Are the conclusions drawn adequately supported by the results?

Partly

Competing Interests: No competing interests were disclosed.

I confirm that I have read this submission and believe that I have an appropriate level of expertise to state that I do not consider it to be of an acceptable scientific standard, for reasons outlined above.

The benefits of publishing with F1000Research:

- Your article is published within days, with no editorial bias
- You can publish traditional articles, null/negative results, case reports, data notes and more
- The peer review process is transparent and collaborative
- Your article is indexed in PubMed after passing peer review
- Dedicated customer support at every stage

For pre-submission enquiries, contact research@f1000.com

F1000Research