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Editorial

Traumatic Brain Injuries: Comprehensive Management of Complex Clinical Scenarios

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The number of traumatic brain injuries (TBI) is on the rise worldwide, representing 30–40% of injury-related deaths in many countries [1, 2]. TBI is effectively a public health epidemic; this justifies the 6-fold increase in the number of studies published over the last decade [3]. As such, the impact of TBI on the global burden of disease (GBD) is substantial, according to the investigators of the GBD study who annually quantify health loss from all types of diseases and injuries with the aim of improving health systems all over the world, and in the long term helps in reducing/eliminating disparities [1, 2, 4].

Due to groundbreaking mechanistic studies and randomized clinical trials (RCT) published in recent years (accounting for more than 380 new PubMed-indexed RCT on TBI since 2019), the approach to neurotrauma patients has remarkably evolved with an increase in the overall quality of acute care. One of the reasons for this improvement is certainly the care provided by a broad spectrum of multidisciplinary team (MDT) specialists, including prehospital and emergency department (ED) doctors and nurses, neuroradiologists, neurosurgeons, anesthetists, and intensive care physicians. Conceived and addressed to those professionals, this Special Issue has gathered insightful quantitative and qualitative studies on various aspects of the basic sciences, ethics and clinical practice of TBI, contributing to the existing body of literature, reinforcing data from recent trials and covering existing knowledge gaps. This editorial is meant to summarize the main findings from this collection and its overall achievements.

First of all, the greatest measure of this Special Issue's success can be measured by the outreach on authors from both high-income countries (HIC) and low- and middle-income countries (LMIC). In fact, the major contributors to this collection were authors from the United Kingdom and Turkey, heavily involved into academic research in the field of global neurotrauma, and authors from sub-Saharan African countries, such as Cameroon and Ethiopia, who shared their practical experience on the management of adult and pediatric patients with TBI in remote geographical locations. The number of contributions from LMIC, where the epidemiological distribution of TBI is the highest, represents indeed a particularly relevant factor because we know that mechanisms of injury, referral pathways, and access to tertiary centers are vastly different among continents, and the challenges faced for TBI management in LMIC are quite different from those of HIC [5]. Among the reasons for limited resources available in LMIC, and sources of concern for the global neurotrauma community, is the paucity of neurosurgical workforce requiring a remarkable task shifting and sharing practices [6]. This aspect has obviously an impact on hospitals preparedness, as recently shown in a collaborative study published by the NIHR Global Health Unit on Global Surgery [7]. Hence, the first-hand experience from LMIC contributors was obviously deemed extremely valuable and welcomed by our Editorial Board in the context of this Special Issue.

Above all, one aspect that was underscored in this collection reflects the organizational heterogeneity across

centers dealing with high volumes of trauma referrals. This emerged quite well in the observational cross-sectional study from Bedry and Tadele [8], which provided data on the clinical profile and outcome of childhood TBI at a tertiary hospital in Southern Ethiopia where head injuries contribute to 7.4% of pediatric visits in the local EDs. Of note, their clinical series indicated that road traffic accidents (RTA) and falls represent the most common causes of TBI in LMIC, as recently confirmed by Dewan et al. who estimated that the proportion of TBIs resulting from RTA in Africa and Southeast Asia is up to 56% of the total cases of head injuries registered in those continents [9]. Besides the organizational challenges, both articles explored critical aspects allowing clinicians to prognosticate outcome: both concluded that prolonged hospital stay and poor outcome correlate with comorbid illness, loss of consciousness at presentation, increased ICP sign, severity of head injury, presence of seizures, hypotension, and hyperglycemia on presentation.

While early hyperglycemia mentioned in their list of risk factors is a known predictor of mortality and correlates with mechanisms of secondary injury, as previously shown by European studies conducted in the acute phase by Prisco et al. [10] and in the subacute phase by TRACK-TBI investigators [11], other serum, plasma, and cerebrospinal fluid (CSF) markers of inflammatory reaction have also emerged in recent times [12–15]. Some useful biomarkers were extensively discussed in this Special Issue: for instance, the narrative review from Erenler and Baydin [16] indicates that IL-33 has emerged, among multiple plasma biomarkers, as the one mostly implicated in cellular crosstalk and responsible for multiorgans impairment. IL-33 is in fact a powerful endogenous alarm signal (alarmin) meant to alert various types of immune cells to trauma, and the study from Erenler and Baydin allowed revisiting data from experimental preclinical models of TBI [17, 18] and case-control studies [19, 20] on TBI patients, concluding the great potential role of IL-33 as an early indicator of secondary injury.

Together with contributions exploring prognostic factors and the role of biomarkers, this Special Issue includes more studies attempting to answer the demand for new pharmacological treatments. This was the case in the article written by Nguembu et al. [21] who explored the implication of paroxysmal sympathetic hyperactivity triggered by TBI, which could be effectively tackled by innovative neuroprotective strategies based on well-known, conventional drugs such as beta-blockers. Their scoping review suggests that beta-blockers diminish the effect of circulating catecholamines and attenuate the resting metabolism rate, which is markedly increased in patients with severe acute brain injury [22–29]. As such, their conclusions were that propranolol and labetalol should have a greater role in the acute management of TBI [30, 31]. Speaking of pharmacological strategies, another long-term retrospective study from Acar et al. [32] investigated the use of tranexamic acid (TXA) in blunt and penetrating TBI in the context of polytraumas. Their study design represented a pragmatic approach to the use of antifibrinolytic drugs in the treatment and prevention of major bleeding. Conducted between 2012 and 2020, the work from Acar et al. reached a conclusion about the safety of TXA in TBI (none of the 51 patients included had thrombotic complications nor died due to head injury), which is in keeping with the main findings from the CRASH 2 and the more recent CRASH 3 trials [33, 34]. Additionally, the article from Acar et al. offers a much needed confirmation in a civilian ED environment of the findings from the battlefield reported by Dixon et al. [35] and the results obtained within the constraints of the abovementioned RCT.

In terms of surgical strategies for TBI, with a specific focus for those developed in LMIC, Kanmounye [36] focused his attention to the rise of inflow cisternostomy, a more modern alternative to the 1940 ideas of outflow cisternostomy in the form of either ventriculocisternostomy and cystocisternostomy [37, 38]. Starting from the first description of such a surgical technique for the management of severe TBI, which dates back to the 2012 article by Dr. Cherian from Nepal [39], Kanmounye, who is also the founding President of the Association of Future African Neurosurgeons, provided an historical vignette of the evolution of such a technique in limited resource settings and offered a detailed argumentation for its rationale, limitations, and future challenges. That article highlighted that the use of cisternostomy in the surgical management of severe TBI certainly represents a revolutionary step, and we definitely agreed with the statement that the disruptive theory of CSF shift edema behind its conception has already contributed lessons to the entire neurotrauma community [40].

As mentioned in this Special Issue's call for papers new imaging tools, validated surgical strategies and optimized protocols for clinical follow-up, the early resuscitation, and management of difficult cases still represent a clinical, surgical, and ethical challenge most of the time. This is possibly the reason why one of the articles, which received most attention, earning double digits citations (the highest so far for this collection), was the contribution from Hasan et al. [41] revolving on public engagement as a tool to validate research questions and protocols in the management of TBI patients. Their qualitative study, consisting in a survey submitted to severe TBI survivors and their next of kin, helped identifying ways to direct future research into more accurate prognostic models and therapeutic options in the acute and subacute phases of TBI management. Furthermore, they explored the complex ethical aspects of dealing with sensitive issues revolving around TBI and the challenges faced in the aftermath of major trauma, not only by patients but also by clinicians and scientists.

Given the quality of the submissions received, it is no surprise that at time of writing this editorial, our Special Issue has gathered a cumulative number of 15,789 visualizations and a total of 8,111 downloads. Those results not only testify the valuable insights from both a scientific and teaching perspective offered by the authors who joined this endeavor but also the fulfillment of our initial goal of reaching out to and hopefully go beyond the vast scientific community of Emergency Medicine International.

Conflicts of Interest

The editors declare that they have no conflicts of interest regarding the publication of this Special Issue.

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References

[1] S. L. James, A. Theadom, R. G. Ellenbogen et al., "Global, regional, and national burden of traumatic brain injury and spinal cord injury, 1990-2016: a systematic analysis for the global burden of disease study 2016," *The Lancet Neurology*, vol. 18, no. 1, pp. 56–87, 2019.

[2] S. L. James, D. Abate, K. H. Abate et al., "Global, regional, and national incidence, prevalence, and years lived with disability for 354 diseases and injuries for 195 countries and territories, 1990-2017: a systematic analysis for the Global Burden of Disease Study 2017," *Lancet*, vol. 392, no. 10159, pp. 1789–1858, 2018.

[3] M. Ganau, A. Lavinio, and L. Prisco, "Delirium and agitation in traumatic brain injury patients: an update on pathological hypotheses and treatment options," *Minerva Anestesiologica*, vol. 84, no. 5, pp. 632–640, 2018.

[4] D. Clark, A. Joannides, A. O. Adeleye et al., "Casemix, management, and mortality of patients rreseceiving emergency neurosurgery for traumatic brain injury in the Global Neurotrauma Outcomes Study: a prospective observational cohort study," *The Lancet Neurology*, vol. 21, no. 5, pp. 438–449, 2022.

[5] D. Dasic, L. Morgan, A. Panezai et al., "A scoping review on the challenges, improvement programs, and relevant output metrics for neurotrauma services in major trauma centers," *Surgical Neurology International*, vol. 13, p. 171, 2022.

[6] F. C. Robertson, I. N. Esene, A. G. Kolias et al., "Global perspectives on task shifting and task sharing in neurosurgery," *World Neurosurg X*, vol. 6, Article ID 100060, 2019.

[7] J. C. Glasbey, T. E. Abbott, A. Ademuyiwa et al., "Elective surgery system strengthening: development, measurement, and validation of the surgical preparedness index across 1632 hospitals in 119 countries," *Lancet*, vol. 400, no. 10363, pp. 1607–1617, 2022.

[8] T. Bedry and H. Tadele, "Pattern and outcome of pediatric traumatic brain injury at hawassa university comprehensive specialized hospital, southern Ethiopia: observational cross-sectional study," *Emergency Medicine International*, vol. 2020, Article ID 1965231, 9 pages, 2020.

[9] M. C. Dewan, A. Rattani, S. Gupta et al., "Estimating the global incidence of traumatic brain injury," *Journal of Neurosurgery*, vol. 130, no. 4, pp. 1080–1097, 2018.

[10] L. Prisco, F. Iscra, M. Ganau, and G. Berlot, "Early predictive factors on mortality in head injured patients: a retrospective analysis of 112 traumatic brain injured patients," *Journal of Neurosurgical Sciences*, vol. 56, no. 2, pp. 131–136, 2012.

[11] N. Temkin, J. Machamer, S. Dikmen et al., "Risk factors for high symptom burden three months after traumatic brain injury and implications for clinical trial design: a transforming research and clinical knowledge in traumatic brain injury study," *Journal of Neurotrauma*, vol. 39, no. 21-22, pp. 1524–1532, 2022.

[12] A. Petersen, M. Soderstrom, B. Saha, and P. Sharma, "Animal models of traumatic brain injury: a review of pathophysiology to biomarkers and treatments," *Experimental Brain Research*, vol. 239, no. 10, pp. 2939–2950, 2021.

[13] M. Hajiaghamemar, M. Seidi, R. A. Oeur, and S. S. Margulies, "Toward development of clinically translatable diagnostic and prognostic metrics of traumatic brain injury using animal models: a review and a look forward," *Experimental Neurology*, vol. 318, pp. 101–123, 2019.

[14] S. S. Shin, M. M. Hefti, V. M. Mazandi et al., "Plasma neurofilament light and glial fibrillary acidic protein levels over thirty days in a porcine model of traumatic brain injury," *Journal of Neurotrauma*, vol. 39, no. 13-14, pp. 935–943, 2022.

[15] T. N. Anderson, J. Hwang, M. Munar et al., "Blood-based biomarkers for prediction of intracranial hemorrhage and outcome in patients with moderate or severe traumatic brain injury," *Journal of Trauma and Acute Care Surgery*, vol. 89, no. 1, pp. 80–86, 2020.

[16] A. K. Erenler and A. Baydin, "Interleukin-33 (IL-33) as a diagnostic and prognostic factor in traumatic brain injury," *Emergency Medicine International*, vol. 2020, Article ID 1832345, 4 pages, 2020.

[17] F. Olde Heuvel, S. Holl, A. Chandrasekar et al., "STAT6 mediates the effect of ethanol on neuroinflammatory response in TBI," *Brain, Behavior, and Immunity*, vol. 81, pp. 228–246, 2019.

[18] S. P. Gadani, I. Smirnov, A. T. Smith, C. C. Overall, and J. Kipnis, "Characterization of meningeal type 2 innate lymphocytes and their response to CNS injury," *Journal of Experimental Medicine*, vol. 214, no. 2, pp. 285–296, 2017.

[19] Q. Du, J. F. Weng, L. F. Luo et al., "Serum ST2 as a potential prognostic biomarker for traumatic brain injury," *Clinica Chimica Acta*, vol. 487, pp. 145–152, 2018.

[20] G. Wicher, U. Wallenquist, Y. Lei et al., "Interleukin-33 promotes recruitment of microglia/macrophages in response to traumatic brain injury," *Journal of Neurotrauma*, vol. 34, no. 22, pp. 3173–3182, 2017.

[21] S. Nguembu, M. Meloni, G. Endalle et al., "Paroxysmal sympathetic hyperactivity in moderate-to-severe traumatic brain injury and the role of beta-blockers: a scoping review," *Emergency Medicine International*, vol. 2021, Article ID 5589239, 6 pages, 2021.

[22] J. H. Feibel, C. A. Baldwin, and R. J. Joynt, "Catecholamine-associated refractory hypertension following acute intracranial hemorrhage: control with propranolol," *Annals of Neurology*, vol. 9, no. 4, pp. 340–343, 1981.

[23] R. L. Chioléro, E. Breitenstein, D. Thorin et al., "Effects of propranolol on resting metabolic rate after severe head injury," *Critical Care Medicine*, vol. 17, no. 4, pp. 328–334, 1989.

[24] S. Welle, R. G. Schwartz, and M. Statt, "Reduced metabolic rate during β-adrenergic blockade in humans," *Metabolism*, vol. 40, no. 6, pp. 619–622, 1991.

[25] L. Christin, E. Ravussin, C. Bogardus, and B. V. Howard, "The effect of propranolol on free fatty acid mobilization and resting metabolic rate," *Metabolism*, vol. 38, no. 5, pp. 439–444, 1989.

[26] J. A. Blackman, P. D. Patrick, M. L. Buck, and R. S. Rust, "Paroxysmal autonomic instability with dystonia after brain injury," *Archives of Neurology*, vol. 61, no. 3, pp. 321–328, 2004.

[27] D. Do, V. L. Sheen, and E. Bromfield, "Treatment of paroxysmal sympathetic storm with labetalol," *Journal of Neurology Neurosurgery and Psychiatry*, vol. 69, no. 6, pp. 832-833, 2000.

[28] M. van der Jagt and D. R. Miranda, "Beta-blockers in intensive care medicine: potential benefit in acute brain injury and acute respiratory distress syndrome," *Recent Patents on Cardiovascular Drug Discovery*, vol. 7, 2012.

[29] T. J. Schroeppel, J. P. Sharpe, L. J. Magnotti et al., "Traumatic brain injury and β-blockers: not all drugs are created equal," *Journal of Trauma and Acute Care Surgery*, vol. 76, no. 2, pp. 504–509, 2014.

[30] A. L. Diamond, R. C. Callison, J. Shokri, S. Cruz-Flores, and L. J. Kinsella, "Paroxysmal sympathetic storm," *Neurocritical Care*, vol. 2, no. 3, pp. 288–291, 2005.

[31] Y. Feng, X. Zheng, and Z. Fang, "Treatment progress of paroxysmal sympathetic hyperactivity after acquired brain injury," *Pediatric Neurosurgery*, vol. 50, no. 6, pp. 301–309, 2015.

[32] N. Acar, M. E. Canakci, and U. Bilge, "Early and ultraearly administration of tranexamic acid in traumatic brain injury: our 8-year-long clinical experience," *Emergency Medicine International*, vol. 2020, Article ID 6593172, 5 pages, 2020.

[33] H. Shakur, I. Roberts, R. Bautista et al., "Effects of tranexamic acid on death, vascular occlusive events, and blood transfusion in trauma patients with significant haemorrhage (CRASH-2): a randomised, placebo-controlled trial," *Lancet*, vol. 376, no. 9734, pp. 23–32, 2010.

[34] Crash-3 Trial Collaborators, "Effects of tranexamic acid on death, disability, vascular occlusive events and other morbidities in patients with acute traumatic brain injury (CRASH-3): a randomised, placebo-controlled trial," *Lancet*, vol. 394, no. 10210, pp. 1713–1723, 2019.

[35] A. L. Dixon, B. H. McCully, E. A. Rick et al., "Tranexamic acid administration in the field does not affect admission thromboelastography after traumatic brain injury," *Journal of Trauma and Acute Care Surgery*, vol. 89, no. 5, pp. 900–907, 2020.

[36] U. S. Kanmounye, "The rise of inflow cisternostomy in resource-limited settings: rationale, limitations, and future challenges," *Emergency Medicine International*, vol. 2021, Article ID 6630050, 4 pages, 2021.

[37] A. Torkildsen, "Ventriculo-cisternostomy: a post operative study," *Acta Chirurgica Scandinavica*, vol. 85, p. 254, 1941.

[38] P. K. Eide and T. Lundar, "Arne Torkildsen and the ventriculocisternal shunt: the first clinically successful shunt for hydrocephalus," *Journal of Neurosurgery*, vol. 124, no. 5, pp. 1421–1428, 2016.

[39] I. Cherian, "Basal cisternostomy-is it a panacea for traumatic brain swelling?" *Journal of College of Medical Sciences - Nepal*, vol. 8, no. 1, pp. 1–6, 2012.

[40] N. Goyal and P. Kumar, "Putting 'CSF-shift edema' hypothesis to test: comparing cisternal and parenchymal pressures after basal cisternostomy for head injury," *World Neurosurg*, vol. 148, pp. e252–e263, 2021.

[41] S. Hasan, A. Chari, M. Ganau, and C. Uff, "Defining new research questions and protocols in the field of traumatic brain injury through public engagement: preliminary results and review of the literature," *Emergency Medicine International*, vol. 2019, Article ID 9101235, 8 pages, 2019.