Management of neurotrauma during COVID-19: a single centre experience and lessons for the future

Manivannan S[1], Sharouf F[2], Mayo I[2], Albaqer H[2], Mehrez M[2], Jaber H[3], Nicholls Z[3], Woodward BO[3], Watkins WJ[4], Zaben M[2]

Affiliations

1. Department of Neurosurgery, Southampton General Hospital, Southampton, UK
2. Department of Neurosurgery, University Hospital of Wales, Cardiff, UK
3. Department of Radiology, University Hospital of Wales, Cardiff, UK
4. Department of Infection & Immunity, College of Biomedical & Life Sciences, Cardiff University, Cardiff, UK

Disclosure Statement

The authors report no conflict of interest.

Ethics

This study follows the principles of the Declaration of Helsinki.

Data Availability

Available on request to corresponding author.

Corresponding Author

Dr. Malik Zaben

Neuroscience and Mental Health Research Institute (NMHRI),

School of Medicine,

Cardiff University

Room 4FT 80E, 4th Floor, University Hospital Wales,

Heath Park

Cardiff

CF14 4XN

Tel: 02920743861

Abstract

Introduction

Traumatic brain injury (TBI) is amongst the leading causes of morbidity and mortality worldwide. The unprecedented emergence of COVID-19 has mandated neurosurgeons to limit viral spread and spare hospital resources whilst trying to adapt management plans for TBI. We aimed to characterize how this affects decision-making on TBI management and drive strategies to cope with future expected waves.

Methods

Retrospective TBI data collection from a single tertiary referral unit was performed between: 01/04/2019 - 30/06/2019 ('Pre-Epidemic') and 01/04/2020 - 30/06/20 ('Epidemic'). Demographics, mechanism of injury, TBI severity, radiological findings, alcohol/anticoagulants/antiplatelets use, and management decisions were extracted.

Results

646 TBI referrals were received in 'Pre-Epidemic' (N=317) and 'Epidemic' (N=280) groups. There was reduction in RTA-associated TBI (14.8 vs 9.3%; p=0.04) and increase in patients on anticoagulants (14.2 vs 23.6%; p=0.003) in the 'Epidemic' group. Despite similarities between other TBI-associated variables, a significantly greater proportion of patients were managed conservatively in local referring units without neurosurgical services (39.1 vs 56.8%; p<0.0001), predominantly constituted by mild TBI.

Conclusion

Despite COVID-19 public health measures, the burden of TBI remains eminent. Increases in local TBI management warrant vigilance from primary healthcare services to meet post-TBI needs in the community.

Keywords- COVID-19, traumatic brain injury, neurosurgery

Introduction

Since the identification of COVID-19 (Coronavirus identified in 2019) in the Hubei Province of China in December 2019, it has emerged as a global pandemic with devastating figures of infections and deaths in the scale of millions worldwide [1]. Aside from the direct effects of COVID-19, which range from being asymptomatic to experiencing life-threatening respiratory distress [2], public health measures to prevent further transmission of the virus have limited patient mobility between hospitals and caused significant disruptions to healthcare services around the world. Furthermore, redeployment of healthcare staff to Emergency Medicine and Intensive Care departments, incorporation of COVID-19 status into clinical decision-making, and requirements for self-isolation of healthcare staff have significantly impacted healthcare provision.

Since the implementation of UK national lockdown measures on 23 March 2020, the general public were advised to limit all non-essential travel and work from home where possible. Given that these are unprecedented measures, there is increasing interest in the effects of lockdown on healthcare provision. This is essential in order to: (i) address potentially unanticipated complications of lockdown if it is required again in the event of subsequent 'waves'; (ii) anticipate the longer term ramifications of reduced accessibility of healthcare services during lockdown, which is becoming increasingly recognised in the context of cancer diagnosis [3]; and (iii) ensure adequate allocation of healthcare staff and resources to respond to non-COVID-19 related ailments.

Traumatic brain injury (TBI) is currently amongst the leading causes of mortality and morbidity worldwide, necessitating time-critical management in the acute phase and adequate rehabilitation and community support in the longer term [4]. Poor recognition of the insidious, chronic neuropsychological deficits associated with even milder forms of TBI have resulted in its depiction as a 'silent epidemic'. Since the implementation of lockdown, several studies have examined shifts in the incidence, presentation, and management of orthopedic trauma; with current evidence indicating a decrease in volume of trauma [5-7][8][9][10][11][12]. However, the effects of lockdown on the presentation and management of TBI remains unexplored. Therefore, in this single centre retrospective study,

we examined our experience with TBI referrals during the pre- and post-lockdown period at a tertiary neurosurgical unit.

Methods

Study Design

Retrospective cohort study to examine TBI referrals during a three-month COVID period and an equivalent period prior to the emergence of COVID.

Patient Sampling

Retrospective data collection was performed by searching our local neurosurgical database at the University Hospital of Wales (UHW). UHW provides a tertiary Neurosurgery service for Southern Wales/ Southwest England.

Study Period

The following time periods were examined: 01/04/2019 - 30/06/2019 ('Pre-Epidemic') and 01/04/2020 - 30/06/20 ('Epidemic').

Inclusion criteria/ Data extraction

All adult patients (age > 16 years) with a primary diagnosis of TBI were included. The following data was extracted: patient demographics, mechanism of injury, alcohol use, anticoagulant/ antiplatelet use, Glasgow Coma Score (GCS) on presentation, radiological findings, and management strategy. GCS was used to stratify severity of TBI into mild (GCS 13-15) and moderate-severe (GCS <13) categories. Management strategy was divided into the following categories: no input required (no formal clinical advice nor patient transfer required), local management, transfer to Neurosurgical unit.

Statistical Analysis

Statistical analysis was performed using R Version 3.6.0 and figures generated using Prism software (GraphPad Software Inc. Version 8.0.1, San Diego, CA, USA). Pearson's Chi-Square tests were used to compare relevant variables between both time periods. The Mann-Whitney U test was used to compare age. Two-way ANOVA was used to examine the

relationship between number of referrals received and the month of referral during both periods. $P < 0.05$ were considered statistically significant across all analyses. Univariate and multivariate models were performed using IBM SPSS Statistics. Outcome was dichotomised as 'no input/ local management' and 'transfer to Neurosurgical unit'. Association between the time period and outcome was tested with the Pearson's Chi-Square test. Association between injury-associated variables and outcome were examined in the two time periods separately using the Pearson's Chi-Square test. Next, a multivariable model was created for Pre-Epidemic and Epidemic groups to identify any differences in influencing factors for the decision to transfer. Variables fulfilling the following criteria were eligible for multivariable modelling: (i) $p < 0.20$ on univariate analysis in Pre-Epidemic and/ or Epidemic groups (including both significant and near-significant results); (ii) individual cell counts of at least 3 in variables with two categories. The preliminary multivariable model was then refined by removing variables that did not demonstrate $p < 0.20$ in Pre-Epidemic and/ or Epidemic groups (see **Supplementary Material 1**).

Ethical Approval: This service survey was approved by Neuroscience Directorate Clinical Audit Lead at UHW.

Results

Patient Cohort

A total of 597 TBI referrals were made across both time periods, with an approximately even split between Pre-Epidemic (N=317; 53.1%) and Epidemic (N=280; 46.9%) groups (**Table 1**). Proportion of TBI referrals per month did not differ significantly between both groups ($p = 0.058$). There were no significant differences in baseline characteristics between both groups with respect to age (65 ± 22 years vs 67 ± 22 years; $p = 0.118$) or gender (62.1 vs 57.1% male; $p = 0.214$).

Falls were the most common mechanism of injury in both groups, followed by road traffic accidents (RTA) and assault. Whilst proportions of mechanism of injury did not change significantly between Pre-Epidemic and eEpideemic groups overall (p = 0.161), there was a significant reduction in the proportion of RTA associated TBI (14.8 vs 9.3%; p = 0.02) (**Figure 1**). There was a significant difference between severity of TBI between both groups (p=0.016), with a greater proportion of mild TBI (79.2 vs 85.9%) and smaller proportion of moderate/ severe TBI (12.3 vs 7.9%) referrals.

Contributing Factors/ Imaging

Other contributing factors including alcohol abuse, anticoagulants, and antiplatelets were also examined (**Figure 2**). There was a significantly greater proportion of patients on anticoagulants in the COVID group (14.2 vs 23.6%; p = 0.003), whilst antiplatelet use was very similar between both groups (15.8 vs 15.7%; p = 0.984). Indications for anticoagulants included atrial fibrillation and history of recurrent thrombosis. Indications for antiplatelets included previous cerebrovascular accident (CVA), cardiac stents, or primary prevention for ischaemic heart disease. Although a decrease in alcohol-associated TBI was demonstrated, this did not reach statistical significance (16.7 vs 12.9%; p = 0.186). Radiological findings included skull fractures, extradural haematoma (EDH), subdural haematoma (SDH), subarachnoid haemorrhage (SAH), contusions, and intraparenchymal (IPH) or intraventricular (IVH) haemorrhage. The most common radiological findings in both groups were SDH, and traumatic SAH. There was no significant difference between both groups with respect to intracranial bleeds. However, there were significantly more patients with skull fractures (23.0 vs 30.4%, p = 0.043) and multiple pathological findings (24.9 vs 37.5%, p <0.001) on imaging during the COVID period (**Figure 2**).

Management

Management decisions were classified into the following: no neurosurgical input required, local conservative management, and transfer for monitoring/ neurosurgical intervention. Despite general similarities in the TBI-associated variables, there was a significant difference in management decisions between both groups (p<0.001) (**Figure 3A-B**). In particular, a

significantly greater proportion of patients were managed conservatively in local referring units (39.1 vs 56.8%; p <0.001) and smaller proportion of patients were deemed as not requiring neurosurgical input (52.1 vs 37.9%; p < 0.001). A smaller proportion of patients were transferred (8.8 vs 5.4%; p = 0.12) but this did not reach statistical significance. Given the finding of a greater proportion of locally managed patients, the severity of TBI in this group was examined (**Figure 3C**). A greater number of mild TBI referrals were advised for local management (108 vs 144 patients) during the epidemic, whilst local management advice for moderate/ severe TBI (16 vs 15 patients) remained largely unchanged between Pre-Epidemic and Epidemic periods (**Figure 3D**).

Multivariate Analysis

Given the difference in management strategies between Pre-Epidemic and Epidemic periods, univariate and multivariate analyses were performed to identify any differences in influencing factors. Only complete cases were included, resulting in 288 patients in the Pre-Epidemic and 259 patients in the Epidemic groups. There was a 46.1% decrease in the proportion of patients that were transferred during the epidemic (8.9 vs 4.8%; p = 0.053) (**Supplementary Material 1**). Univariate analysis revealed a significant association between management decision and the following variables in both groups: age, mechanism of injury, GCS motor score, severity of TBI, and skull fracture (**Table 2** & **Supplementary Material 1**). Gender, anticoagulation, and polytrauma were only significantly associated with management decision during the Pre-Epidemic period, while the presence of an extra-axial bleed was significantly associated with management decision during the Epidemic period. On multivariate analysis (**Table 3**), the following variables demonstrated a significant effect on odds of transfer in the pre-Epidemic group: age (OR 0.94, CI 0.92 – 0.97, p <0.001), GCS motor score (OR 0.03, CI 0.01 – 0.10, p <0.001), and intra-axial bleeding (OR 3.55, CI 1.06 – 11.85, p = 0.04). In the Epidemic group, GCS motor score (OR 0.33, CI 0.07 – 1.58, p = 0.17) and intra-axial bleeding (OR 3.16, CI 0.63 – 15.86, p = 0.16) both demonstrated similar effects to the Pre-Epidemic group, though they did not reach statistical significance. Within the Epidemic group, the following variables demonstrated a significant effect on odds of transfer: age (OR 0.93, CI 0.90 – 0.97, p <0.001) and extra-axial bleeding (OR 6.29, CI 1.35 – 29.36, p = 0.02). Extra-axial bleeding (OR 2.10, CI 0.67 – 6.60, p = 0.20) was also associated

with increased odds of transfer in the Pre-Epidemic group, though this did not reach statistical significance.

Discussion

Our results demonstrate that there have been no significant differences in the incidence, demographics, mechanism of injury, or traumatic pathology in patients with TBI between pre- and post-lockdown periods in our single centre. Despite consistency in TBI referrals, however, there has been a significant shift in clinical decision making, with a larger proportion of patients being managed locally. Whilst the underlying cause for this shift is likely multifactorial, including a greater proportion of mild TBI referrals, general concern regarding COVID-19 status is likely to be a major contributing factor. In the event of recurrent lockdowns in response to 'future wave(s)', this change in decision-making must be reviewed in order to ensure that adequate specialist care is provided without COVID-19 bias. Univariable and multivariable analyses were also performed to identify any difference in factors influencing decision-making between the two time periods. In general, factors eligible for inclusion in the multivariable model showed similar effects on odds of transfer in both time periods. However, statistical significance was not consistent, making reliable interpretation difficult. This is likely due to the sample size and relatively small counts within individual categories. In sum, although we identified a shift towards local management and reduced transfer of patients with TBI to a tertiary neurosurgical unit, the influence of injury-associated factors on management decision have not changed drastically between Pre-Epidemic and Epidemic groups.

Recent studies have evaluated changes in the incidence of orthopaedic trauma pre- and post-lockdown in the UK. One multi-centre study compared a two-week period during lockdown with a matching period in the previous year, and demonstrated an approximately 50% decrease in both the presentation and admission of adult trauma cases [5]. In addition, differences in mechanisms of injury were also demonstrated, such as an increase in falls and decrease in RTC. Similarly, a single-center study, performed in Ireland, demonstrated a 40% reduction in the volume of trauma when comparing a one-month period during lockdown

with the previous year [6]. This was also in keeping with findings from a Level 1 Trauma Center in London, demonstrating a 50% decrease in acute trauma referrals across the same time periods [7]. When comparing matching time periods between Pre-Epidemic and Epidemic groups, we demonstrated a 26.7% drop in TBI referrals in April, but this was not the case in subsequent months. Over a longer time period of 3 months, we demonstrate that volume of TBI referrals were not significantly reduced over matching time periods with only an 11.1% decrease overall. Therefore, previous findings of reduced volume of trauma referrals during brief snapshots of the earlier phase of lockdown may reflect public adherence to lockdown rules or reluctance to access healthcare due to fears of contracting COVID-19. Although proportions of mechanism of injury did not change significantly between our sampling periods, a significant decrease in RTA-associated TBI referrals was observed, in keeping with previous studies and reduced used of motor vehicles during lockdown. Essentially, differences between studies of trauma referrals may be explained by: (i) regional variations within the UK; (ii) duration of sampling periods; and (iii) differences in the nature of injury required to sustain brain injury, in comparison to bone and soft tissue injury.

National bodies within the UK, including the Society of British Neurological Surgeons (SBNS) and Royal College of Surgeons (RCS), have issued general guidance regarding the management of neurotrauma during the current pandemic [13, 14]. Whilst TBI is listed as a pathology requiring time critical transfer in the event of unsuccessful conservative management, there is little information with respect to longer term follow up of patients managed conservatively in local non-neurosurgical units. Indeed, the SBNS guidelines have recommended “postponing long-term follow-up patients until the crisis has passed” and emphasised the avoidance of unnecessary transfers. Given the current global crisis and requirement for aggressive prioritisation of healthcare services, this approach is arguably inevitable. However, the unknown future duration of the COVID-19 pandemic and imminent threat of ‘future wave(s)’ emphasise the fact that longer-term follow-up must remain in the list of priorities to avoid indefinite delays associated with an unpredictable timeline. The importance of early rehabilitation has been demonstrated relatively recently, with the successful development of Head Injury teams providing continuity of care from the hospital to the community for patients with TBI [15, 16]. Flexibility and adaptation of this multi-

disciplinary approach is vital to respond to the anticipated demands of patients in the upcoming future. As shown in our study, a larger proportion of patients are being managed locally in non-neurosurgical units in order to minimise risk of COVID-19 spread between hospitals. This raises significant concerns regarding whether these patients are followed up adequately, given the risk of neuro-psychological impairment. Indeed, there is increasing recognition of cognitive deficits in even milder forms of TBI, with recent estimates indicating that up to half of individuals that sustained mild TBI may suffer long term cognitive impairment [17]. In a similar fashion to concerns that diagnostic delays in oncology investigations may result in an increase in avoidable deaths in the future [3], primary healthcare services must remain vigilant to the needs of patients with TBI within the community. Further studies are required to elucidate whether this shift in decision making is reflected across neurosurgical units globally. Future strategies must be developed to ensure that risks of COVID-19 posed to the public are effectively balanced against optimal management of the TBI community. Another key finding included a greater proportion of TBI referrals involving anticoagulant use. Holding anticoagulants for several weeks following TBI is common practice in the absence of other absolute contra-indications but will require adequate follow up in the community to ensure that medications are re-commenced appropriately. With increasingly overstretched primary healthcare services, it is vital that underlying cardiovascular co-morbidities are also addressed. Whilst beyond the scope of this study, the development of risk stratification scoring systems to guide effective and safe management of TBI under current circumstances is paramount, and should therefore be the focus of future multi-centre larger studies.

Limitations/ Future Directions

The conclusions of this study are limited by its retrospective nature. We are currently in the process of prospective data collection to compare changes in TBI referrals and management during subsequent waves. Further studies are required to elucidate the longer term outcomes of patients managed in local units to identify whether their needs are being met in the community. Systems flagging up patients discharged from local units to primary healthcare services following TBI are essential to allow communication with Head Injury teams.

Conclusion

Despite the implementation of extensive public health measures during the COVID-19 pandemic, the burden of TBI remains a significant problem. Maintaining high quality care for these patients should be taken in consideration whilst we try to combat the spread of COVID-19 and conserve our resources. Our study demonstrated a significant shift in clinical decision making, with a greater proportion of patients being managed in local hospitals during the post-lockdown period. Whilst this may be understandable, as these patients may have not required immediate surgical intervention, those sustain even mild forms of TBI are increasingly recognised to suffer with neuropsychological deficits in the longer term. Therefore, it is vital that primary healthcare services remain alert to the potentially unmet needs of patients discharged to the community without specialist follow up.

Figure Legends

Figure 1. Mechanism of injury of TBI in Pre-Epidemic and Epidemic groups. (A) Illustration of proportions of different mechanisms of injury during both time periods; (B) Histograms of age of patients in Pre-Epidemic and Epidemic groups; (C) Significant decrease in proportion of RTA-associated TBI referrals was demonstrated in the Epidemic group (*Chi Square test*, $p < 0.039$*).

Figure 2. Associated features of TBI in Pre-Epidemic and Epidemic groups. (A) TBI referrals across equivalent time periods (no significant difference on *Chi Square test*); (B) Significant increase in percentage of referrals involving anticoagulant use during the Epidemic period (*Chi Square test*, $p = 0.003$**); (C) No significant differences with respect to intracranial bleed, but significant differences were demonstrated with respect to patients with skull fractures (*Chi Square test*, $p = 0.043$*) and multiple findings (*Chi Square test*, $p < 0.001$***) on imaging.

Figure 3. Management decisions regarding TBI referrals in Pre-Epidemic and Epidemic groups. (A) Illustration of proportions of different management decisions during both time

periods, with an increase in local management; (B) Significant increase in advice given for local management (*Chi Square test*, p<0.001***); (C) Subgroup analysis of locally managed patients revealed a higher number of patients with mild TBI.

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Table 1. Summary of data extraction from 'Pre-Epidemic' and 'Epidemic' groups, and statistical comparisons.

	Pre-Epidemic (N=317) N (%)	Epidemic (N=280) N (%)	Difference N (%)	p-value
Demographic				
Age (Mean ± SD)	65 ± 22 years	67 ± 22 years	+ 2 years	0.118^
Male	197 (62.1)	160 (57.1)	-37 (18.8)	0.214
Female	120 (37.9)	120 (42.9)	±0 (0)	
Month				
April	115 (36.3)	83 (29.6)	-32 (27.8)	0.058
May	91 (28.7)	105 (37.5)	+14 (15.4)	
June	111 (35.0)	92 (32.9)	-19 (17.1)	
Mechanism				
Fall	201 (63.4)	196 (70.0)	-5 (2.5)	0.089
RTA	47 (14.8)	26 (9.3)	-21 (44.7)	0.039*
Assault	20 (6.3)	14 (5.0)	-6 (30.0)	0.491
Other	49 (15.5)	43 (15.4)	-6 (12.2)	0.973
Overall	-	-	-	0.161
Injury				
Isolated TBI	271 (85.5)	225 (80.4)	-46 (17.0)	0.095
Polytrauma	46 (14.5)	55 (19.6)	+9 (19.6)	
Contributing Factors				
Alcohol	53 (16.7)	36 (12.9)	-17 (32.1)	0.186
Antiplatelet use	50 (15.8)	44 (15.7)	-6 (12)	0.984
Anticoagulant use	45 (14.2)	66 (23.6)	+21 (46.7)	0.003**
Severity of TBI				
Mild	271 (79.2)	261 (85.9)	-10 (3.7)	0.016*
Moderate/ Severe	42 (12.3)	24 (7.9)	-18 (42.9)	
Radiology				
Intracranial bleed	267 (84.2)	241 (86.0)	-26 (9.7)	0.528
SAH	105 (33.1)	110 (39.3)	+5 (4.8)	-
SDH	126 (39.7)	139 (49.6)	+13 (10.3)	-
EDH	10 (3.2)	12 (4.3)	+2 (20.0)	-
Contusion	82 (25.9)	74 (26.4)	-8 (9.8)	-
IPH/ IVH	27 (8.5)	22 (7.9)	-5 (18.5)	-
Fracture	73 (23.0)	85 (30.4)	+12 (16.4)	0.043*
Multiple findings	79 (24.9)	105 (37.5)	+26 (32.9)	<0.001***
Management				
No neurosurgical input required	165 (52.1)	106 (37.9)	-59 (35.8)	<0.001***
Local conservative management	124 (39.1)	159 (56.8)	+35 (28.2)	<0.001***
Transfer	28 (8.8)	15 (5.4)	-13 (46.4)	0.101
Overall	-	-	-	<0.001***

Abbreviations/ superscripts- EDH- extradural haematoma, IPH- intraparenchymal haemorrhage, IVH- intraventricular haemorrhage, RTA- road traffic accident, SAH- subarachnoid haemorrhage, SDH- subdural haematoma, TBI- traumatic brain injury. Pearson's Chi-Square tests used for all comparisons except for age (^Mann-Whitney U test); *$p<0.05$, **$p<0.01$, ***$p<0.001$.

Table 2. Univariable analysis examining the association between injury-associated variables and management decisions during 'Pre-Epidemic' and 'Epidemic' periods.

		Pre-Epidemic						Epidemic					
		Local/ No Input		Transfer		Total	P-value	Local/ No Input		Transfer		Total	P-value
		N	%	N	%	N		N	%	N	%	N	
Sex	Female	115	95.8%	5	4.2%	175	<0.05	112	95.7%	5	4.3%	117	0.734
	Male	173	88.3%	23	11.7%	56	-	147	94.8%	8	5.2%	155	-
Mechanism of injury	Fall	194	96.5%	7	3.5%	260	<0.001	187	96.9%	6	3.1%	193	0.015
	RTA	32	69.6%	14	30.4%	46	-	21	91.3%	2	8.7%	23	-
	Assault	17	85.0%	3	15.0%	20	-	11	78.6%	3	21.4%	14	-
	Other	45	91.8%	4	8.2%	49	-	40	95.2%	2	4.8%	42	-
Alcohol	No	242	92.0%	21	8.0%	263	0.222	225	95.3%	11	4.7%	236	0.815
	Yes	46	86.8%	7	13.2%	53	-	34	94.4%	2	5.6%	36	-
Anti-platelets	No	240	90.2%	26	9.8%	266	0.187	217	94.3%	13	5.7%	230	0.114
	Yes	48	96.0%	2	4.0%	50	-	42	100.0 %	0	0.0%	42	-
Anti-coagulants	No	243	89.7%	28	10.3%	271	<0.05	199	94.8%	11	5.2%	210	0.514
	Yes	45	100.0 %	0	0.0%	45	-	60	96.8%	2	3.2%	62	-
Polytrauma	No	252	93.0%	19	7.0%	271	<0.01	206	94.5%	12	5.5%	218	0.260
	Yes	36	80.0%	9	20.0%	45	-	53	98.1%	1	1.9%	54	-
Severity of TBI	Mild/ Moderate	34	60.7%	22	39.3%	56	<0.001	21	87.5%	3	12.5%	24	0.063
	Severe	254	97.7%	6	2.3%	260	-	238	96.0%	10	4.0%	248	-
GCS M-score	1-5	40	63.5%	23	36.5%	63	<0.001	20	83.3%	4	16.7%	24	<0.005
	6	248	98.0%	5	2.0%	253	-	239	96.4%	9	3.6%	248	-
Skull Fracture	No	229	94.2%	14	5.8%	243	<0.001	187	98.4%	3	1.6%	190	<0.001
	Yes	59	80.8%	14	19.2%	73	-	72	87.8%	10	12.2%	82	-
Extra-axial bleed	No	170	92.4%	14	7.6%	184	0.355	127	97.7%	3	2.3%	130	0.067
	Yes	118	89.4%	14	10.6%	132	-	132	93.0%	10	7.0%	142	-
Intra-axial bleed	No	132	93.6%	9	6.4%	141	0.164	115	97.5%	3	2.5%	118	0.130
	Yes	156	89.1%	19	10.9%	175	-	144	93.5%	10	6.5%	154	-

Abbreviations: GCS- Glasgow Coma Score, M-score- motor score, TBI- traumatic brain injury.
P-values represent significance on Pearson's Chi-Square test or Fisher's Exact test.

Table 3. Multivariable logistic regression models examining the influence of different injury-associated factors on management decisions during 'Pre-Epidemic' and 'Epidemic' periods.

	Pre-Epidemic					Epidemic				
	Beta	SE	P-value	OR	CI	Beta	SE	P-value	OR	CI
Age	-0.06	0.01	<0.001	0.94	0.92 – 0.97	-0.07	0.02	<0.001	0.93	0.90 – 0.97
GCS M-score 6 (vs <6)	-3.49	0.61	<0.001	0.03	0.01 – 0.10	-1.11	0.80	0.166	0.33	0.07 – 1.58
Skull fracture	0.76	0.53	0.153	2.14	0.75 - 6.07	0.96	0.76	0.204	2.62	0.59 – 11.57
Extra-axial bleed	0.74	0.58	0.204	2.10	0.67 – 6.60	1.84	0.79	0.019	6.29	1.35 – 29.36
Intra-axial bleed	1.27	0.61	0.039	3.55	1.06 – 11.85	1.15	0.82	0.161	3.16	0.63 – 15.86

Abbreviations: CI- confidence interval, GCS- Glasgow Coma Score, M-score- motor score, OR- odds ratio, SE- standard error.

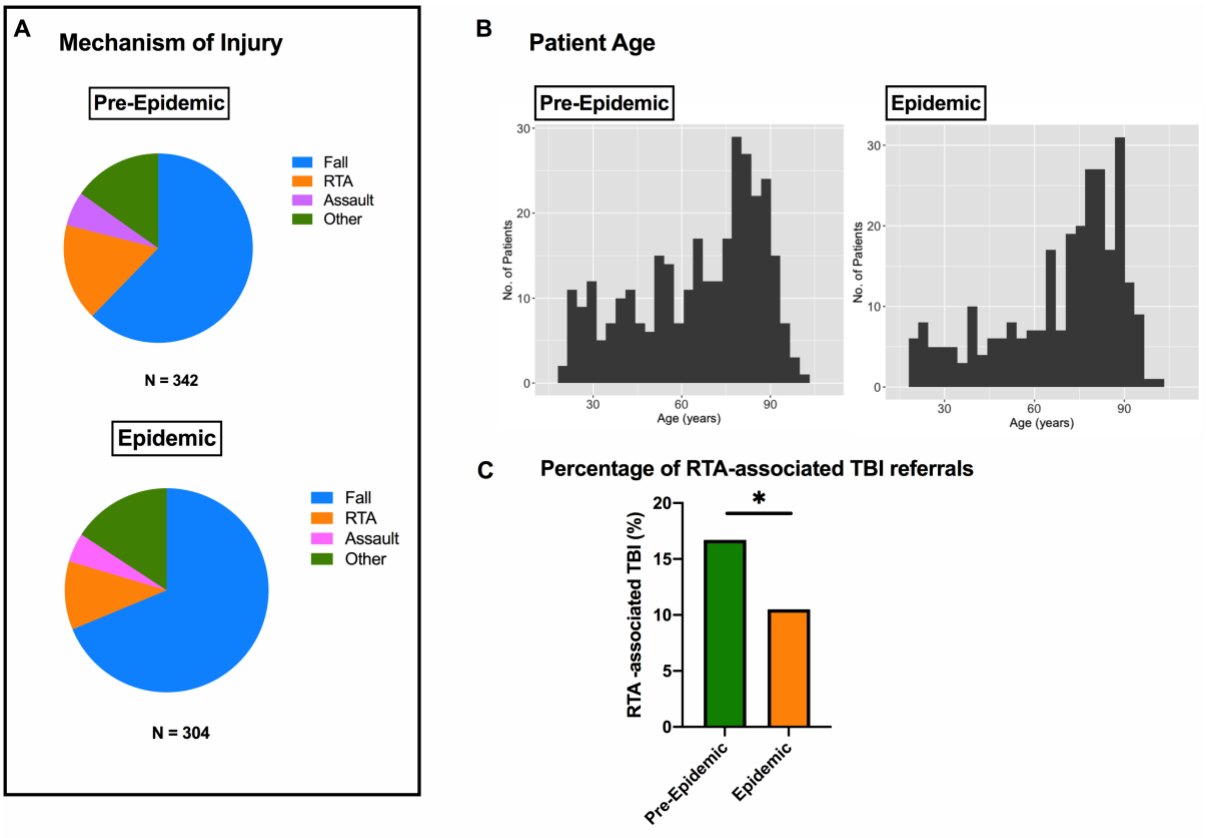

Figure 1. Mechanism of injury of TBI in Pre-Epidemic and Epidemic groups. (A) Illustration of proportions of different mechanisms of injury during both time periods; (B) Histograms of age of patients in Pre-Epidemic and Epidemic groups; (C) Significant decrease in proportion of RTA-associated TBI referrals was demonstrated in the Epidemic group (*Chi Square test*, $p < 0.039$*).

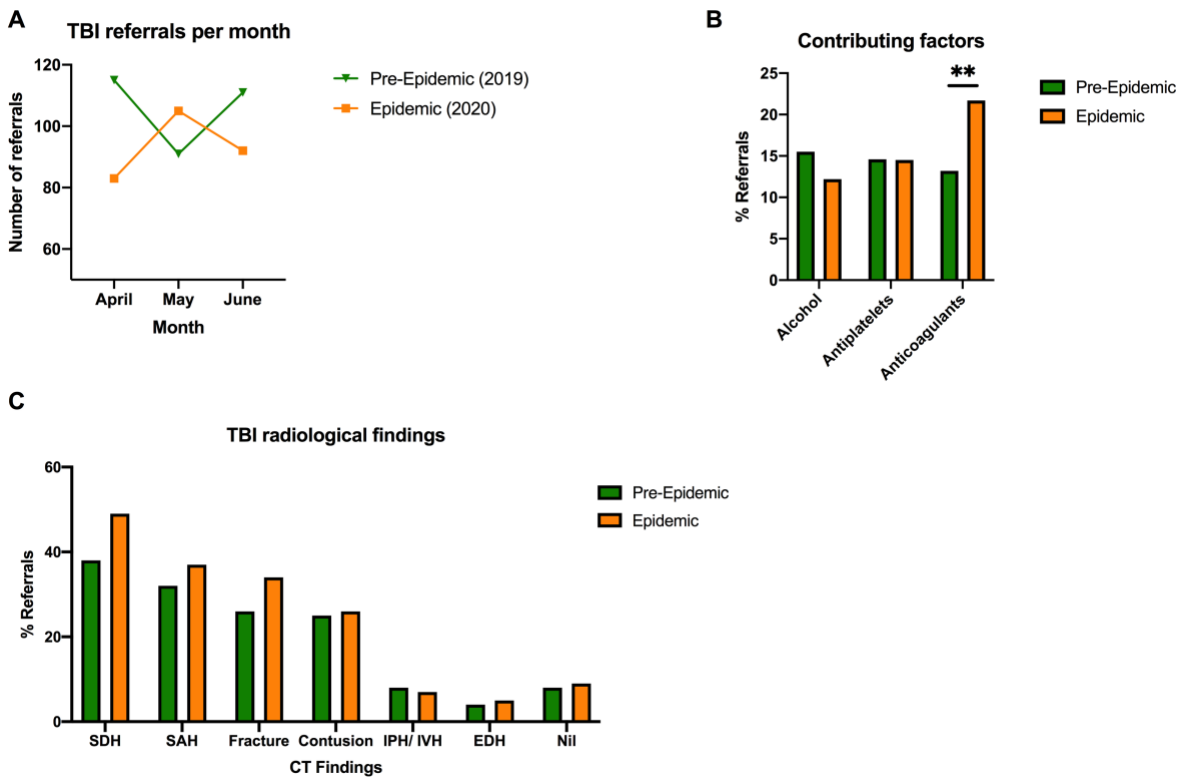

Figure 2. Associated features of TBI in Pre-Epidemic and Epidemic groups. (A) TBI referrals across equivalent time periods (no significant difference on *Chi Square test*); (B) Significant increase in percentage of referrals involving anticoagulant use during the Epidemic period (*Chi Square test*, p = 0.003**); (C) No significant differences with respect to intracranial bleed, but significant differences were demonstrated with respect to patients with skull fractures (*Chi Square test*, p = 0.043*) and multiple findings (*Chi Square test*, p <0.001***) on imaging.

Figure 3. Management decisions regarding TBI referrals in Pre-Epidemic and Epidemic groups. (A) Illustration of proportions of different management decisions during both time periods, with an increase in local management; (B) Significant increase in advice given for local management (*Chi Square test*, p<0.001***); (C) Subgroup analysis of locally managed patients revealed a higher number of patients with mild TBI.

Supplementary Material 1. Complete details of univariable and multivariable model analysis for assessing influence of injury-associated variables on management decision between 'Pre-Epidemic' and 'Epidemic' groups.

1. **Probability of transfer across 'Pre-Epidemic' and 'Epidemic' groups**

Outcome * Epidemic Crosstabulation

			Epidemic		
			Pre	Post	Total
Outcome	Local or No Input	Count	288	259	547
		% within Epidemic	91.1%	95.2%	93.0%
	Transfer	Count	28	13	41
		% within Epidemic	8.9%	4.8%	7.0%
Total		Count	316	272	588
		% within Epidemic	100.0%	100.0%	100.0%

Chi-Square Tests

	Value	df	Asymptotic Significance (2-sided)	Exact Sig. (2-sided)	Exact Sig. (1-sided)
Pearson Chi-Square	3.754[a]	1	.053		
Continuity Correction[b]	3.151	1	.076		
Likelihood Ratio	3.860	1	.049		
Fisher's Exact Test				.073	.037
Linear-by-Linear Association	3.747	1	.053		
N of Valid Cases	588				

a. 0 cells (0.0%) have expected count less than 5. The minimum expected count is 18.97.

b. Computed only for a 2x2 table

2. Univariable analysis of injury-associated variables and effect on management decision

		Pre-Epidemic								Epidemic						
		Local or No Input		Transfer		Total		P		Local or No Input		Transfer		Total		P
		Count	Row N %	Count	Row N %	Count	Row N %			Count	Row N %	Count	Row N %	Count	Row N %	
Sex	Female	115	95.8%	5	4.2%	120	100.0%	<0.05		112	95.7%	5	4.3%	117	100.0%	0.734
	Male	173	88.3%	23	11.7%	196	100.0%			147	94.8%	8	5.2%	155	100.0%	
Cause	Fall	194	96.5%	7	3.5%	201	100.0%	<0.001		187	96.9%	6	3.1%	193	100.0%	0.015
	RTA	32	69.6%	14	30.4%	46	100.0%			21	91.3%	2	8.7%	23	100.0%	
	Assault	17	85.0%	3	15.0%	20	100.0%			11	78.6%	3	21.4%	14	100.0%	
	Other	45	91.8%	4	8.2%	49	100.0%			40	95.2%	2	4.8%	42	100.0%	
Alcohol	No	242	92.0%	21	8.0%	263	100.0%	0.222		225	95.3%	11	4.7%	236	100.0%	0.815
	Yes	46	86.8%	7	13.2%	53	100.0%			34	94.4%	2	5.6%	36	100.0%	
Antiplt	No	240	90.2%	26	9.8%	266	100.0%	0.187		217	94.3%	13	5.7%	230	100.0%	0.114
	Yes	48	96.0%	2	4.0%	50	100.0%			42	100.0%	0	0.0%	42	100.0%	
Anticoag	No	243	89.7%	28	10.3%	271	100.0%	<0.05		199	94.8%	11	5.2%	210	100.0%	0.514
	Yes	45	100.0%	0	0.0%	45	100.0%			60	96.8%	2	3.2%	62	100.0%	
PolyTrauma	No	252	93.0%	19	7.0%	271	100.0%	<0.01`		206	94.5%	12	5.5%	218	100.0%	0.260
	Yes	36	80.0%	9	20.0%	45	100.0%			53	98.1%	1	1.9%	54	100.0%	
M_Band	1-5	40	63.5%	23	36.5%	63	100.0%	<0.001		20	83.3%	4	16.7%	24	100.0%	<0.005
	6	248	98.0%	5	2.0%	253	100.0%			239	96.4%	9	3.6%	248	100.0%	
Fracture	No	229	94.2%	14	5.8%	243	100.0%	<0.001		187	98.4%	3	1.6%	190	100.0%	<0.001
	Yes	59	80.8%	14	19.2%	73	100.0%			72	87.8%	10	12.2%	82	100.0%	
Haematoma	No	170	92.4%	14	7.6%	184	100.0%	0.355		127	97.7%	3	2.3%	130	100.0%	0.067
	Yes	118	89.4%	14	10.6%	132	100.0%			132	93.0%	10	7.0%	142	100.0%	
Bleeding	No	132	93.6%	9	6.4%	141	100.0%	0.164		115	97.5%	3	2.5%	118	100.0%	0.130
	Yes	156	89.1%	19	10.9%	175	100.0%			144	93.5%	10	6.5%	154	100.0%	
GCS_Band	Mild/Moderate	34	60.7%	22	39.3%	56	100.0%	<0.001		21	87.5%	3	12.5%	24	100.0%	0.063
	Severe	254	97.7%	6	2.3%	260	100.0%			238	96.0%	10	4.0%	248	100.0%	

Age

Epidemic	Outcome	Mean	N	Std. Deviation	P
Pre	Local or No Input	66.66	288	21.353	<0.001
	Transfer	45.68	28	18.958	
	Total	64.80	316	21.952	
Post	Local or No Input	68.88	259	20.776	<0.001
	Transfer	38.85	13	19.052	
	Total	67.44	272	21.638	

3. Preliminary multivariable model (variables with p > 0.2 on univariable analysis and cell count < 3 with only two categories were excluded)

Pre-Epidemic					Epidemic			
	Wald Chi-Square	df	Sig.			Wald Chi-Square	df	Sig.
Age	4.591	1	0.032		Age	12.054	1	0.001
Sex	0.011	1	0.916		Sex	0.451	1	0.502
Cause	4.032	3	0.258		Cause	2.237	3	0.525

M_Band	4.158	1	0.041		M_Band	2.367	1	0.124
Fracture	3.740	1	0.053		Fracture	0.920	1	0.337
Haematoma	1.689	1	0.194		Haematoma	5.098	1	0.024
Bleeding	4.708	1	0.030		Bleeding	2.141	1	0.143
GCS_Band	2.201	1	0.138		GCS_Band	0.306	1	0.580

4. Refined multivariable model (variables with p > 0.2 in both 'Pre-Epidemic' and 'Epidemic' groups in preliminary model were excluded)

Overall

	Pre-Epidemic				Epidemic		
	Wald Chi-Square	df	Sig.		Wald Chi-Square	df	Sig.
Age	17.471	1	0.000		14.494	1	0.000
M_Band	32.922	1	0.000		1.922	1	0.166
Fracture	2.045	1	0.153		1.611	1	0.204
Haematoma	1.611	1	0.204		5.481	1	0.019
Bleeding	4.247	1	0.039		1.960	1	0.161

In Detail

	Pre-Epidemic						Epidemic					
	Beta	SE	Sig.	OR	OR CI Low	OR CI High	Beta	SE	Sig.	OR	OR CI Low	OR CI High
Age	-0.061	0.0145	0.000	0.941	0.915	0.968	-0.071	0.0186	0.000	0.931	0.898	0.966
M_Band=6	-3.486	0.6076	0.000	0.031	0.009	0.101	-1.111	0.8015	0.166	0.329	0.068	1.584
M_Band=1-5 ref	0			1			0			1		

Fracture= Yes	0.761	0.5320	0.153	2.140	0.754	6.071		0.962	0.7581	0.204	2.618	0.592	11.568
Fracture= No ref	0			1				0			1		
Haematoma= Yes	0.741	0.5841	0.204	2.099	0.668	6.595		1.840	0.7858	0.019	6.293	1.349	29.358
Haematoma= No ref	0			1				0			1		
Bleeding=Yes	1.267	0.6149	0.039	3.551	1.064	11.851		1.152	0.8225	0.161	3.163	0.631	15.859
Bleeding=No ref	0			1				0			1		