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Managing Traumatic Brain Injury During the Coronavirus Disease 2019 Pandemic—A Case-Matched Controlled Analysis of Immediate Outcomes

Intekhab Alam¹, Kanwaljeet Garg¹, Amol Raheja¹, Vivek Tandon¹, Ravi Sharma¹, Manmohan Singh¹, Gyaninder Pal Singh², Shashwat Mishra¹, Pankaj Kumar Singh¹, Deepak Agrawal¹, Kapil Dev Soni³, Ashish Suri¹, Poodipedi Sarat Chandra¹, Shashank Sharad Kale¹

■ **OBJECTIVE:** The primary objective of this study was to evaluate the outcome of patients with traumatic brain injury (TBI) during the coronavirus disease 2019 (COVID-19) pandemic and to compare their outcome with case-matched controls from the prepandemic phase.

■ **METHODS:** This is a retrospective case-control study in which all patients with TBI admitted during COVID-19 pandemic phase (Arm A) from March 24, 2020 to November 30, 2020 were matched with age and Glasgow Coma Scale score—matched controls from the patients admitted before March 2020 (Arm B).

■ **RESULTS:** The total number of patients matched in each arm was 118. The length of hospital stay (8 days vs. 5 days; $P < 0.001$), transit time from emergency room to operation room (150 minutes vs. 97 minutes; $P = 0.271$), anesthesia induction time (75 minutes vs. 45 minutes; $P = 0.002$), and operative duration (275 minutes vs. 180 minutes; $P = 0.002$) were longer in arm A. Although the incidence of fever and pneumonia was significantly higher in arm A than in arm B (50% vs. 26.3%, $P < 0.001$ and 27.1% vs. 1.7%, $P < 0.001$, respectively), outcome (Glasgow Outcome Scale—Extended) and mortality (18.6% vs. 14.4% respectively; $P = 0.42$) were similar in both the groups.

■ **CONCLUSIONS:** The outcome of the patients managed for TBI during the COVID-19 pandemic was similar to matched

patients with TBI managed at our center before the onset of the COVID-19 pandemic. This finding suggests that the guidelines followed during the COVID-19 pandemic were effective in dealing with patients with TBI. This model can serve as a guide for any future pandemic waves for effective management of patients with TBI without compromising their outcome.

INTRODUCTION

The first case of coronavirus disease 2019 (COVID-19) was reported from Wuhan, China on December 31, 2019.¹ Rapid spread of this highly contagious disease led to unprecedented challenges in health care delivery worldwide. COVID-19 has also disrupted the care of patients with traumatic brain injury (TBI), as it has affected the other specialties in neurosurgery. The clinical decision-making process in patients with TBI with COVID-19—positive status is further complicated by overlapping clinical, radiologic, and biochemical profiles. Concomitant increases levels of serum inflammatory markers, neurogenic pulmonary edema, and ventilatory support often required in patients with obtunded TBI are some of the cardinal features seen in patients with head injury, which can mimic observations seen in severe COVID-19 infection. Many studies have highlighted this aspect.²

Key words

- COVID-19
- Outcome
- Traumatic brain injury

Abbreviations and Acronyms

- COVID-19:** Coronavirus disease 2019
- EDH:** Extradural hematoma
- GCS:** Glasgow Coma Scale
- GOS-E:** Glasgow Outcome Scale—Extended
- NCCT:** Noncontrast computed tomography
- PPE:** Personal protective equipment
- SDH:** Subdural hematoma
- TBI:** Traumatic brain injury

From the ¹Department of Neurosurgery, ²Department of Neuroanaesthesiology and Critical Care, and ³Critical and Intensive Care, JPN Apex Trauma Centre, All India Institute of Medical Sciences, New Delhi, India

To whom correspondence should be addressed: Vivek Tandon, M.B.B.S., M.S., M.Ch. [E-mail: drtandonvivek@gmail.com]

Intekhab Alam and Kanwaljeet Garg are co—first authors.

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To control the COVID-19 pandemic in India, a nationwide lockdown was enforced on March 24, 2020. During the nationwide lockdown, it was quickly realized that the patients with TBI and the treating neurosurgeons encountered unique challenges. We undertook this retrospective case-control study, in which patients with TBI treated during the first wave of the pandemic, when a vaccine was not available, were compared with matched (age, radiologic diagnosis and Glasgow Coma Scale [GCS] score equivalent) controls with TBI who were treated before the onset of the COVID-19 pandemic and nationwide lockdown at our tertiary-care referral center. The objective of the study was to understand the impact of COVID-19 on the treatment and outcomes of patients with TBI and ascertain the factors predicting outcome. We have also formulated guidelines for the management of patients with TBI based on our experience and pertinent studies from the literature. These guidelines may be useful in the future, if there is a resurgence in the number of COVID-19 cases. Although there has been an abundance of articles describing the perceptions of neurosurgeons and guidelines to manage patients with TBI during the COVID-19 pandemic, few articles have compared the outcomes of patients with TBI managed during the COVID-19 pandemic with those managed before the onset of the COVID-19 pandemic.³⁻⁵ The data in this article present the results of a test of the guidelines followed at our center during the pandemic.

METHODS

Study Design

This retrospective case-control study included patients with TBI managed at a tertiary-care referral center dedicated to trauma care in northern India with a large catchment area. Patients in arm A (cases) included patients with TBI admitted between March 24, 2020 and November 30, 2020 (during the first wave of the COVID-19 pandemic), whereas arm B (controls) included patients with TBI managed before December 31, 2019. The study was conducted after obtaining the required ethical clearance (IEC PG-257/24.06.2020).

The following inclusion and exclusion criteria were used to select patients for our study: all consecutively managed patients with TBI after the onset of COVID-19 pandemic from 24th March 24 to November 30, 2020 were included (arm A). Patients with incomplete records, those who had follow-up <6 months, concomitant spinal injury, previous surgery, pregnancy, or previous head injury were excluded.

Matched Controls

Arm B consisted of case-matched patients with TBI (controls), who were managed at our center for TBI before December 31, 2019. Matching was performed in a 1:1 ratio for age, GCS score, and radiologic diagnosis. For matching of age, the exact number in years was matched in patients in both arm A and arm B. For patients aged <18 years, exact matching of age in years was performed. Similarly exact matching for GCS (eye/verbal/motor) scores was performed for patients in both arms. For matching of radiologic diagnosis, patients with TBI were categorized based on the most pertinent finding on noncontrast computed tomography (NCCT) head and matched (e.g., subdural hematoma [SDH] with SDH, extradural hematoma [EDH] with EDH).

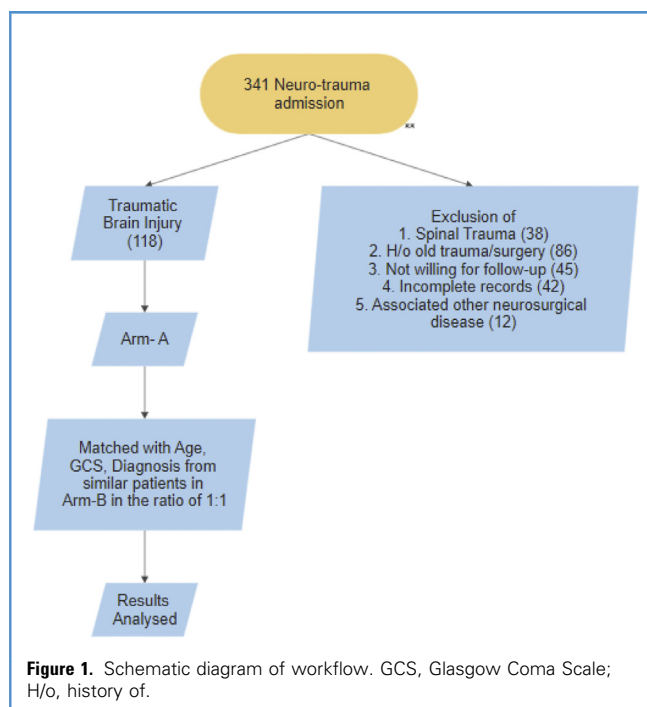


Figure 1. Schematic diagram of workflow. GCS, Glasgow Coma Scale; H/o, history of.

Outcome Measures

The primary outcome measure was the Glasgow Outcome Scale–Extended (GOS-E) of patients with TBI at discharge. To understand the impact of COVID-19 on patients with TBI, we compared the data of COVID-19–positive patients with TBI (all COVID-19–positive patients were positive on reverse transcription polymerase chain reaction) with other patients with TBI admitted during the same duration. Also, the patients with TBI in arm A were subgrouped into the early phase of the pandemic (i.e., March 24–July 31, 2020) and the late phase of the pandemic (i.e., August 1–November 30, 2020) and their outcomes assessed.

Data Retrieval and Statistical Analysis

The computed patient database of our hospital was used to retrieve demographic, clinical, management, and outcome data of the selected cases. Statistical analysis was performed using SPSS version 26 (IBM Corp., Armonk, New York, USA) and R language version 4.0.3 (R Foundation for Statistical Computing, Vienna, Austria). Categorical data are expressed as a percentage, whereas continuous data are expressed as mean with standard deviation. Categorical data were analyzed using the χ^2 test or Fisher exact test, wherever indicated. Continuous data were tested using the Student t test or analysis of variance if the data met the condition of normality for these tests; otherwise, nonparametric counterparts were used. Multivariate logistic regression analysis was run to ascertain factors predicting outcome.

RESULTS

A total of 341 patients were managed with a diagnosis of traumatic craniospinal injuries at our center during the study period. This number was significantly lower compared with the number of

Table 1. Comparison of Demographics, Clinical Features, and Management of Patients with Traumatic Brain Injury in Arm A and Arm B

	Arm A	Arm B	P Value
Age (years), mean (standard deviation)	31.79 (20.09)	32.11 (20.23)	0.354
Male	32.40 (18.15)	32.20 (19.41)	
Female	29.62 (26.16)	31.63 (24.67)	
Total participants			
Male	92 (78)	99 (83.9)	0.310
Female	26 (22)	19 (16.1)	
Mode of injury			
Road traffic accident	56 (47.5)	66 (55.9)	0.140
Fall from height	52 (44.1)	39 (33.1)	
Assault	8 (6.8)	5 (4.2)	
Others	2 (1.7)	8 (6.8)	
Place of injury			
Delhi National Capital Region	74 (62.7)	70 (59.3)	0.229
Others	44 (37.3)	48 (40.7)	
COVID status			
Negative	89 (75.4)		
Positive	29 (24.6)		
Comorbidities			
Diabetes mellitus	40 (33.9)	32 (27.1)	0.186
Hypertension	20 (16.9)	16 (13.6)	0.481
Diagnosis			
Contusion	42 (35.6)	42 (35.6)	
DAI	4 (3.4)	4 (3.4)	
Extradural hematoma	18 (15.3)	18 (15.3)	
Cranial fracture	9 (7.6)	9 (7.6)	
Intracranial hemorrhage	2 (1.7)	2 (1.7)	
Infarcts	1 (0.8)	1 (0.8)	
Intraventricular hemorrhage	1 (0.8)	1 (0.8)	
Pneumocephalus	1 (0.8)	1 (0.8)	
Subarachnoid hemorrhage	8 (6.8)	8 (6.8)	
Subdural hematoma	32 (27.1)	32 (27.1)	
Computed tomography findings			
Midline shift	39 (33.1)	40 (33.9)	1.000
Closed basal cistern	5 (4.2)	3 (2.5)	0.727
Continues			

Table 1. Continued

	Arm A	Arm B	P Value
Effaced sulci and gyri	34 (28.8)	34 (28.8)	1.000
Size of hematoma (mL), median (IQR)	40.4 (60)	48.4 (55)	0.187
Management			
Conservative	87 (73.7)	78 (66.1)	0.188
Surgical	31 (26.2)	40 (33.9)	
ICP measurement	7 (5.9)	8 (6.8)	1.000
Increased ICP	3 (2.5)	1 (0.8)	1.000
Antiedema	81 (68.6)	79 (66.9)	0.839
Barbiturates	4 (3.4)	4 (3.4)	1.000
Hypothermia	2 (1.7)	0 (0)	0.500
Time to shift patients to operating room from emergency room (minutes), median (IQR)	150.0 (465)	97.5 (244)	0.271
Time from induction to incision (minutes), median (IQR)	75.0 (49)	45.0 (30)	0.002*
Time from incision to closure (minutes), median (IQR)	275.0 (520)	180.0 (70)	0.002*
Blood loss (mL), median (IQR)	400.0 (513)	500.0 (600)	0.228
Length of hospital stay (days), median (IQR)	8.0 (11)	5.0 (5)	<0.001*
March 24–July 31, 2020 (N = 67)	9.0 (11)	5.0 (5)	<0.001*
August 1–November 30, 2020 (N = 51)	6.0 (9)	5.0 (7)	0.120
GCS score on admission			
3–8	40 (33.9)	40 (33.9)	
9–12	14 (11.9)	14 (11.9)	
13–15	64 (54.2)	64 (54.2)	
GCS score on discharge			
3–8	27 (22.9)	19 (16.1)	0.095
9–12	11 (9.3)	13 (11)	
13–15	80 (67.8)	86 (72.9)	
Glasgow Outcome Scale—Extended score			
1	22 (18.6)	21 (17.8)	0.557
2	0 (0)	0 (0)	
3	6 (5.1)	2 (1.7)	
Values are number (%) except where indicated otherwise. IQR, interquartile range; ICP, intracranial pressure; GCS, Glasgow Coma Scale; DAI, diffuse axonal injury; LAMS, left against medical advice. *Significant at the level of $P < 0.05$.			
			Continues

Table 1. Continued

	Arm A	Arm B	P Value
4	9 (7.6)	6 (5.1)	
5	2 (1.7)	4 (3.4)	
6	1 (0.8)	4 (3.4)	
7	7 (5.9)	11 (9.3)	
8	71 (60.2)	70 (59.3)	
Final outcome			
Discharge	94 (79.7)	100 (84.7)	0.423
Death	22 (18.6)	17 (14.4)	
LAMA	2 (1.7)	1 (0.8)	
Complications			
Fever	59 (50)	31 (26.3)	<0.001*
Meningitis	12 (10.2)	8 (6.8)	0.481
Ventilator-associated pneumonia	7 (5.9)	7 (5.9)	1.000
Pneumonia	32 (27.1)	2 (1.7)	<0.001*
Surgical site infection	6 (5.1)	4 (3.4)	0.754
Pressure sores	7 (5.9)	7 (5.9)	1.000
Others	1 0.8	—	

Values are number (%) except where indicated otherwise.
IQR, interquartile range; ICP, intracranial pressure; GCS, Glasgow Coma Scale; DAI, diffuse axonal injury; LAMS, left against medical advice.
*Significant at the level of $P < 0.05$.

patients with craniocspinal trauma managed at our center during the same period in 2018 ($n = 1302$) and 2019 ($n = 1246$). A total of 118 patients met the inclusion criteria and were included in arm A of our study (Figure 1). A similar number of matched controls ($n = 118$) were selected as per the methodology described earlier and were included in arm B. The patients in both arms were comparable in terms of gender, mode of injury, place of injury, and comorbidities ($P > 0.05$) (Table 1).

Comparison of All Patients (Irrespective of their COVID-19 Status) in Arm A and B

The mean age of the patients in arm A and B was 31.8 ± 20.1 years and 32.1 ± 20.2 years ($P = 0.354$), respectively (Table 1). Road traffic accidents (high-velocity trauma) were the predominant mode of injury in both arms. There were 29 COVID-19-positive patients (24.6%) in arm A. The median GCS score was 14 (range, 12) in both groups. Of the patients, 33.9% had a severe head injury, 54.2% had a minor head injury, and 11.9% had a moderate head injury in arm A, and the numbers were similar in the matched arm B. Contusion (35.6%) was the most common radiologic diagnosis in both arms. Thirty-one patients (26.2%) required surgical intervention in arm A, whereas 40 patients (33.9%) required surgical intervention in arm B ($P = 0.188$). All patients with acute SDH and patients with intracerebral bleed, requiring surgical intervention, underwent traditional unilateral decompressive

craniectomy with hematoma evacuation and lax duraplasty. Patients with EDH underwent hematoma evacuation. Patients with contusion underwent unilateral frontoparietotemporal decompressive craniectomy and lax duroplasty.

The median time taken to shift patients from the emergency room to the operating room was more in arm A compared with arm B (150.0 minutes vs. 97.5 minutes; $P = 0.271$). The median time required from induction to incision during operation as well as the total operative time of patients with TBI was significantly longer in arm A than in arm B (75.0 minutes vs. 45 minutes, $P = 0.002$ and 275.0 minutes vs. 180.0 minutes, $P = 0.002$, respectively). The median length of hospital stay of patients with TBI in arm A was significantly longer than in arm B (8.0 days vs. 5.0 days; $P < 0.001$) (Figure 2).

The median GOS-E score at discharge was similar in both the arms (GOS-E 8 in arm A vs. GOS-E 8 in arm B; $P = 0.557$) as was the mortality (18.6% in arm A vs. 14.4% in arm B; $P = 0.423$). Median GCS score at the time of discharge was 15 in both the arms ($P = 0.095$). The incidence of fever and pneumonia was statistically significantly higher in the patients in arm A compared with those in arm B (50% vs. 26.3%, $P < 0.001$ and 27.1% vs. 1.7%, $P < 0.001$, respectively). The mortality of patients with severe TBI was 40% ($n = 16$) and 30% ($n = 12$) in arm A and B, respectively ($P = 0.238$).

Comparison of COVID-19-Positive Patients with Matched Controls

The demography of COVID-19-positive patients with TBI, including mode of injury, place of injury and comorbidities in arm A was like that of their matched controls in arm B. The median time needed for induction during operation and the total operative time was significantly longer in the COVID-19-positive patients with TBI in arm A compared with their matched controls in arm B (60 minutes vs. 27.7 minutes, $P = 0.032$ and 300 minutes vs. 130 minutes, $P = 0.016$, respectively) (Table 2). The median length of hospital stays of COVID-19-positive patients with TBI in arm A was significantly longer than that of their matched controls in arm B (12 days vs. 4 days; $P < 0.001$). The incidence of fever and pneumonia was higher in arm A than in arm B (65.5% vs. 24.1%, $P = 0.002$ and 96.6% vs. 6.9%, $P < 0.001$, respectively). The median GOS-E score at discharge in arm A and arm B was 7 and 8, respectively ($P = 0.113$), with the median GCS score at discharge of 15 in both the groups ($P = 0.141$). The mortality in COVID-19-positive patients in arm A was 27.6% and in arm B was 17.2% ($P = 0.375$).

Comparison of COVID-19-Positive Patients with COVID-19-Negative Patients in Arm A

COVID-19-positive patients in arm A were comparable to COVID-19-negative patients with respect to gender, mode of injury, place of injury, and comorbidities. COVID-19-positive patients with TBI were comparatively older than the COVID-19-negative patients in arm A (39.9 ± 18.0 years vs. 29.2 ± 20.1 years; $P = 0.012$). Time to shift patients with TBI to operating rooms, time for induction, total operative time, and final patient outcome were similar in the COVID-19-positive patients and COVID-19-negative patients in arm A (Table 3). However, COVID-19-positive patients had a longer duration of hospital stay than did COVID-19-negative patients (12 days vs. 7 days; $P = 0.001$).

Algorithm for management of TBI patients during COVID pandemic

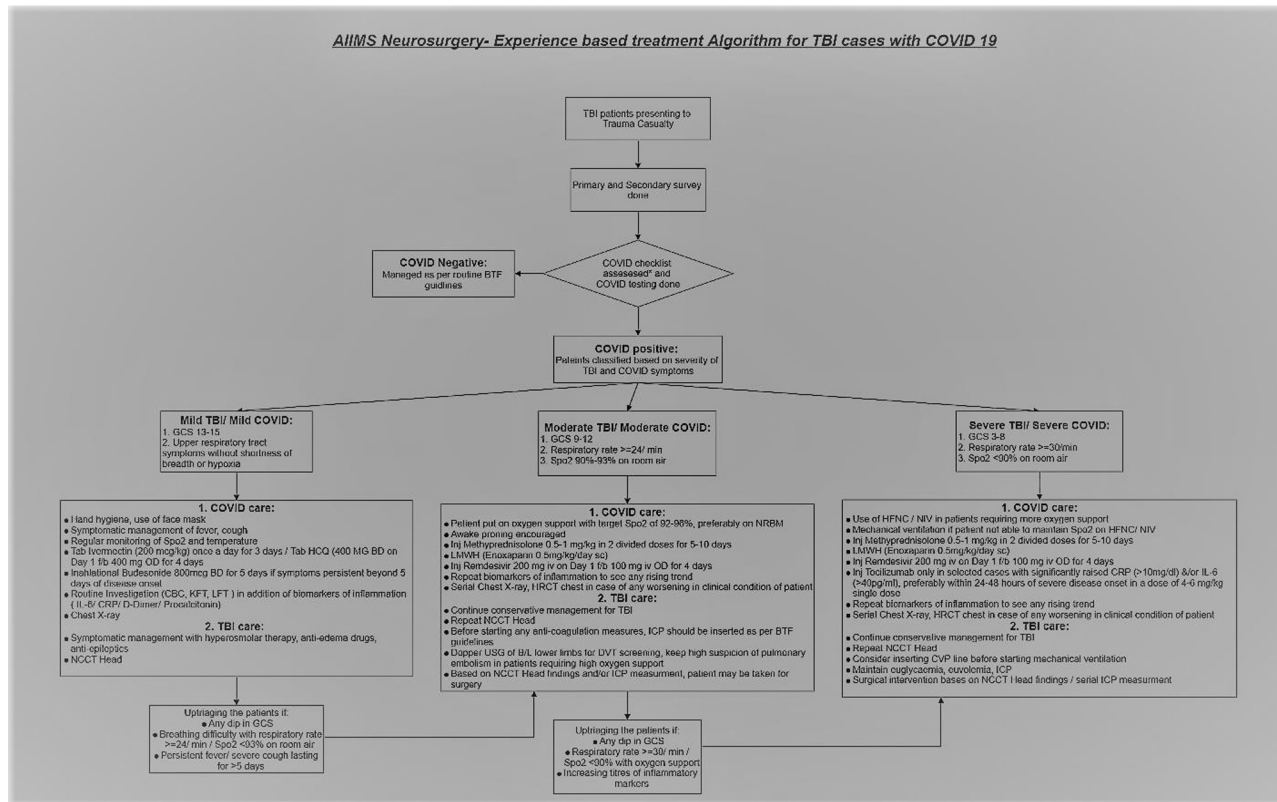


Figure 2. Algorithm for management of patients with traumatic brain injury during COVID pandemic. B/L, bilateral; BTF, Brain Trauma Foundation; CBC, complete blood count; CRP, C-reactive protein; CVP, central venous pressure; DVT, deep vein thrombosis; GCS, Glasgow Coma Scale; HCQ, hydroxychloroquine; HFNC, high flow nasal cannula; HRCT,

high-resolution computed tomography; ICP, intracranial pressure; IL-8, interleukin-8; KFT, kidney function tests; LFT, liver function tests; LMWH, low-molecular-weight heparin; NCCT, noncontrast computed tomography; NIV, noninvasive ventilation; NRBM, non-rebreather mask; TBI, traumatic brain injury; USG, ultraaonography.

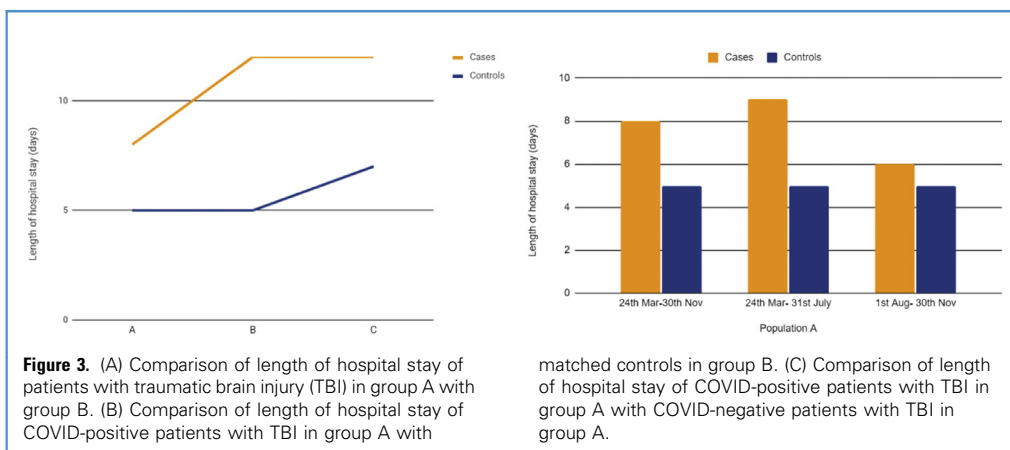


Figure 3. (A) Comparison of length of hospital stay of patients with traumatic brain injury (TBI) in group A with group B. (B) Comparison of length of hospital stay of COVID-positive patients with TBI in group A with COVID-negative patients with TBI in group A with

matched controls in group B. (C) Comparison of length of hospital stay of COVID-positive patients with TBI in group A with COVID-negative patients with TBI in group A.

Table 2. Comparison of Demographics, Clinical Features, and Management of COVID-19–Positive Patients with Traumatic Brain Injury in Arm A with Arm B

	Arm A	Arm B	P Value
Age (years), mean (standard deviation)	39.86 (18.01)	40.10 (17.45)	0.638
Male	39.00 (15.58)	40.12 (40.00)	
Female	45.25 (32.22)	18.28 (9.16)	
Total participants			
Male	25 (86.2)	26 (89.7)	1.000
Female	4 (13.8)	3 (10.3)	
Mode of injury			
Road traffic accident	17 (58.6)	19 (65.5)	0.776
Fall from height	8 (27.6)	4 (13.8)	
Assault	3 (10.3)	4 (13.8)	
Others	1 (3.4)	2 (6.9)	
Place of injury			
Delhi National Capital Region	20 (68.9)	16 (55.2)	0.113
Others	9 (31.1)	13 (44.8)	
Comorbidities			
Diabetes mellitus	14 (48.3)	8 (27.6)	0.109
Hypertension	8 (27.6)	5 (17.2)	0.453
Diagnosis			
Contusion	9 (31.0)	9 (31.0)	
DAI	2 (6.9)	2 (6.9)	
Extradural hematoma	4 (13.8)	4 (13.8)	
Cranial fracture	1 (3.4)	1 (3.4)	
Intraventricular hemorrhage	1 (3.4)	1 (3.4)	
Subarachnoid hemorrhage	3 (10.3)	3 (10.3)	
Subdural hematoma	9 (31.0)	9 (31.0)	
Computed tomography findings			
Midline shift	9 (31.0)	7 (24.1)	0.687
Closed basal cistern	1 (3.4)	- -	1.000
Effaced sulci and gyri	9 (31.0)	7 (24.1)	0.754
Size of hematoma (mL), median (IQR)	36.8 (52)	39.7 (35)	0.527
Management			
Conservative	22 (75.9)	21 (72.4)	0.068
Surgical	7 (24.1)	8 (27.6)	
Time to shift patients to operating room from emergency room (minutes), median (IQR)	660.0 (—)	180.0 (—)	0.400
Continues			

Table 2. Continued

	Arm A	Arm B	P Value
Time from induction to incision (minutes), median (IQR)	60.0 (60)	27.5 (38)	0.032*
Time from incision to closure (minutes), median (IQR)	300.0 (105)	130.0 (66)	0.016*
Blood loss (mL), median (IQR)	500.0 (613)	750.0 (550)	1.000
Length of hospital stay (days), median (IQR)	12.0 (12)	5.0 (4)	<0.001*
GCS score on admission			
3–8	10 (34.5)	10 (34.5)	
9–12	4 (13.8)	4 (13.8)	
13–15	15 (51.7)	15 (51.7)	
GCS score on discharge			
3–8	10 (34.5)	5 (17.2)	0.141
9–12	2 (6.9)	5 (17.2)	
13–15	17 (58.6)	19 (65.5)	
Glasgow Outcome Scale—Extended score			
1	1 (27.6)	5 (17.2)	0.113
2	—	—	
3	3 (10.3)	—	
4	2 (6.9)	4 (13.8)	
5	—	1 (3.4)	
6	—	—	
7	2 (6.9)	2 (6.9)	
8	14 (48.3)	17 (58.6)	
Final outcome			
Discharge	21 (72.4)	24 (82.8)	0.375
Death	8 (27.6)	5 (17.2)	
Complications			
Fever	19 (65.5)	7 (24.1)	0.002*
Meningitis	5 (17.2)	1 (3.4)	0.125
Ventilator-associated pneumonia	3 (10.3)	2 (6.9)	1.000
Pneumonia	28 (96.6)	2 (6.9)	<0.001*
Surgical site infection	1 (3.4)	1 (3.4)	1.000
Pressure sores	3 (10.3)	1 (3.4)	0.500
Others			
Values are number (%) except where indicated otherwise. IQR, interquartile range; ICP, intracranial pressure; GCS, Glasgow Coma Scale; DAI, diffuse axonal injury. *Significant at the level of $P < 0.05$.			

Table 3. Comparison of Demographics, Clinical Features, and Management of COVID-19–Positive Patients with Traumatic Brain Injury with COVID-19–Negative Patients with Traumatic Brain Injury in Arm A

	Positive Cases (Arm A)	Negative Cases (Arm A)	P Value
Age (years), mean (standard deviation)	39.86 (18.01)	29.16 (20.13)	0.012*
Male	39.00 (15.58)	29.94 (18.53)	
Female	45.25 (32.22)	26.77 (24.73)	
Total participants			
Male	25 (86.2)	67 (75.3)	0.218
Female	4 (13.8)	22 (24.7)	
Mode of injury			
Road traffic accident	17 (58.6)	39 (43.8)	0.381
Fall from height	8 (27.6)	44 (49.4)	
Assault	3 (10.3)	5 (5.6)	
Others	1 (3.4)	1 (1.1)	
Place of injury			
Delhi National Capital Region	20 (68.9)	54 (60.7)	0.449
Others	9 (31.1)	35 (39.3)	
Comorbidities			
Diabetes mellitus	14 (48.3)	26 (29.2)	0.060
Hypertension	8 (27.6)	12 (13.5)	0.092
Diagnosis			
Contusion	9 (31.0)	33 (37.1)	
DAI	2 (6.9)	2 (2.2)	
Extradural hematoma	4 (13.8)	14 (15.7)	
Cranial fracture	1 (3.4)	8 (9.0)	
Intracranial hemorrhage	—	2 (2.2)	
Infarcts	—	1 (1.1)	
Intraventricular hemorrhage	1 (3.4)	—	
Pneumocephalus	—	1 (1.1)	
Subarachnoid hemorrhage	3 (10.3)	5 (5.6)	
Subdural hematoma	9 (31.0)	23 (25.8)	
Computed tomography findings			
Midline shift	10 (4.2)	29 (12.2)	0.027*
Closed basal cistern	1 (0.4)	4 (1.7)	
Effaced sulci and gyri	8 (3.4)	25 (10.5)	1.000
Size of hematoma (mL), median (IQR)	40.4 (56)	40.6 (60)	0.693
Management			
Conservative	22 (75.9)	65 (73.0)	0.500
Surgical	7 (24.1)	24 (27.0)	
Time to shift patients to operating room from emergency room (minutes), median (IQR)	660.0 (—)	140.0 (251)	0.300
Values are number (%) except where indicated otherwise. IQR, interquartile range; ICP, intracranial pressure; GCS, Glasgow Coma Scale; DAI, diffuse axonal injury; LAMA, left against medical advice. *Significant at the level of $P < 0.05$.			
			Continues

Table 3. Continued

	Positive Cases (Arm A)	Negative Cases (Arm A)	P Value
Time from induction to incision (minutes), median (IQR)	60.0 (60)	75.0 (45)	0.705
Time from incision to closure (minutes), median (IQR)	300.0 (105)	260.0 (138)	0.374
Blood loss (mL), median (IQR)	500.0 (613)	325.0 (513)	0.100
Length of hospital stay (days), median (IQR)	12.0 (12)	7.0 (9)	0.001*
GCS score on admission			
3–8	10 (34.5)	30 (33.7)	0.818
9–12	4 (13.8)	10 (11.2)	
13–15	15 (51.7)	49 (55.1)	
GCS score on discharge			
3–8	10 (34.5)	17 (19.1)	0.159
9–12	2 (6.9)	9 (10.1)	
13–15	17 (58.6)	63 (70.8)	
Glasgow Outcome Scale—Extended score			
1	8 (27.6)	14 (15.7)	0.087
2	—	—	
3	3 (10.3)	3 (3.4)	
4	2 (6.9)	7 (7.9)	
5	—	2 (2.2)	
6	—	1 (1.1)	
7	2 (6.9)	5 (5.6)	
8	14 (48.3)	57 (64.0)	
Final outcome			
Discharge	21 (72.4)	73 (82.0)	0.299
Death	8 (27.6)	14 (15.7)	
LAMA		2 (2.2)	
Complications			
Fever	19 (65.5)	40 (44.9)	0.05*
Meningitis	5 (17.2)	7 (7.9)	0.165
Ventilator-associated pneumonia	3 (10.3)	4 (4.5)	0.361
Pneumonia	28 (96.6)	4 (4.5)	<0.001*
Surgical site infection	1 (3.4)	5 (5.6)	1.000
Pressure sores	3 (10.3)	4 (4.5)	0.361
Others	—	1 (1.1)	

Values are number (%) except where indicated otherwise.
 IQR, interquartile range; ICP, intracranial pressure; GCS, Glasgow Coma Scale; DAI, diffuse axonal injury; LAMA, left against medical advice.
 *Significant at the level of $P < 0.05$.

Comparison of Early Pandemic Outcomes with Later Pandemic Outcomes in Arm A

The patients with TBI in the early phase of the pandemic were comparable to those in the later part of the pandemic with respect

to age, gender, and the treatment that they received ($P > 0.05$). However, the median length of hospital stay of patients with TBI was significantly longer in the initial phase of the pandemic compared with the later phase (9 days vs. 6 days, $P = 0.023$)

Table 4. Comparison of Outcomes of Patients with Traumatic Brain Injury (Arm A) in Early Phase of Pandemic versus the Late Phase

	Early Phase	Late Phase	P Value
Age (years), mean (standard deviation)	30.75 (20.78)	27.73 (19.29)	0.521
Total participants			
Male	56 (83.6)	36 (70.6)	0.409
Female	11 (16.4)	15 (29.4)	
Management			
Conservative	49 (73.1)	38 (74.5)	1.000
Surgical	18 (26.9)	13 (25.5)	
Length of hospital stay (days), median (IQR)	9 (11)	6 (9)	0.023*
GCS score on admission			
3–8	23 (34.3)	17 (33.3)	0.282
9–12	12 (17.9)	2 (3.9)	
13–15	32 (47.8)	32 (62.7)	
GCS score on discharge			
3–8	17 (25.4)	10 (19.6)	0.124
9–12	9 (13.4)	2 (3.9)	
13–15	41 (61.2)	39 (76.5)	
Glasgow Outcome Scale—Extended score			
1	14 (20.9)	8 (15.7)	0.115
2	—	—	
3	4 (6.0)	2 (3.9)	
4	7 (10.4)	2 (3.9)	
5	2 (3.0)	—	
6	1 (1.5)	—	
7	3 (4.5)	4 (7.8)	
8	36 (53.7)	35 (68.6)	
Final outcome			
Discharge	52 (77.6)	42 (82.4)	0.096
Death	14 (20.9)	8 (15.7)	
LAMA	1 (1.5)	1 (2.0)	
Complications			
Fever	33 (49.3)	26 (51)	0.332
Meningitis	9 (13.4)	3 (5.9)	1.000
Ventilator-associated pneumonia	5 (7.5)	2 (3.9)	1.000
Continues			

Table 4. Continued

	Early Phase	Late Phase	P Value
Pneumonia	18 (26.9)	14 (27.5)	0.581
Surgical site infection	5 (7.5)	1 (2)	—
Pressure sores	5 (7.5)	2 (3.9)	1.000
Others	1 (1.5)	—	—
Values are number (%) except where indicated otherwise. IQR, interquartile range; ICP, intracranial pressure; GCS, Glasgow Coma Scale; LAMA, left against medical advice. *Significant at the level of $P < 0.05$.			

(Table 4). The GOS-E score at discharge, GCS score at discharge, and complications rate were similar during the early and the late phase of the pandemic ($P > 0.05$).

Predictors of Better Outcome

On univariate analysis, longer hospitalization; midline shift 5 mm; effaced sulci and gyri on NCCT head; larger size of hematoma (>40 mL); severe TBI; fever, meningitis and ventilator-associated pneumonia during hospital stay were significantly associated with poor outcome (GOS-E score ≤ 4) at the time of discharge. COVID-19 infection was not found to be an independent predictor of poor outcome on univariate analysis. On multivariate analysis, severe TBI and meningitis during hospital stay were found to be significant factors predicting poor outcome at discharge (Table 5).

DISCUSSION

The World Health Organization announced COVID-19 as a global pandemic on March 12, 2020 and many countries announced various measures including strict lockdowns to prevent transmission of the disease. At the peak of the pandemic in every country, health care facilities were overwhelmed because of the surge in COVID-19-positive cases. Medical facilities including intensive care unit beds and doctors were diverted to manage patients with COVID-19. Many international centers reported infrastructural changes during the COVID-19 pandemic to conform to new guidelines.^{4,6–8} Management protocols were devised in many parts of the world to manage emergency cases including TBI to ensure consistent and high-quality health care delivery to patients who did not have COVID-19.^{9–11} Safeguarding patients who did not have COVID-19 and health care workers from transmission of COVID-19 was a big challenge. The recommendations of our hospital infection control committee and other groups are summarized in Table 6. Stay-at-home orders or lockdowns were enforced to contain the spread of this novel infection, which resulted in decreased motor vehicular accidents. The decreased incidence of TBI, as appreciated at our center, has also been reported in the literature during the pandemic.¹⁷ However, unlike many studies reported in the literature, we did not find

Table 5. Factors Predicting Favorable Outcome of Patients with Traumatic Brain Injury at Discharge: Univariate and Multivariate Analysis

Parameter	Univariate Analysis		Multivariate Analysis	
	OR (95% CI)	P Value	OR (95% CI)	P Value
Younger age	1.7 (0.655–4.412)	0.27		
Female sex	2.240 (0.772–6.501)	0.14	7.20 (0.641–80.86)	0.110
Road traffic accident as mode of injury	0.58 (0.264–1.271)	0.17	0.324 (0.056–1.886)	0.210
Longer hospitalization	0.298 (0.131–0.677)	0.004	0.155 (0.012–1.944)	0.149
Pupillary reflex present	1.320 (0.500–3.489)	0.57		
Isolated head injury	1.593 (0.657–3.859)	0.30		
COVID positivity	0.454 (0.191–1.083)	0.75		
Diabetes mellitus	0.553 (0.247–1.238)	0.15	3.02 (0.387–23.53)	0.292
Hypertension	1.455 (0.486–4.355)	0.50		
Midline shift on computed tomography scan	0.260 (0.114–0.595)	0.001	1.01 (0.099–10.316)	0.992
Closed basal cisterns	0.0801 (0.009–0.712)	0.02	—	0.99
Effaced sulci and gyri	0.178 (0.0075–0.422)	<0.001	0.92 (0.107–7.918)	0.941
Larger hematoma	0.258 (0.102–0.654)	0.004	0.198 (0.018–2.139)	0.182
Severe traumatic brain injury	0.043 (0.016–0.119)	<0.001	0.028 (0.004–0.203)	<0.001
Type of management	0.595 (0.251–1.414)	0.24		
Intracranial pressure measured	0.162 (0.030–0.879)	0.035	0.039 (0.001–1.070)	0.055
Time to shift patients to operating rooms	0.833 (0.114–6.111)	0.86		
Time needed for induction before operation	0.682 (0.131–3.546)	0.65		
Total operative time	0.350 (0.065–1.895)	0.22		
Fever during hospital stay	0.199 (0.083–0.478)	<0.001	3.79 (0.266–53.98)	0.326
Pneumonia during hospital stay	0.566 (0.242–1.321)	0.19	0.63 (0.098–4.412)	0.63
Meningitis during hospital stay	0.120 (0.030–0.434)	0.002	0.038 (0.002–0.797)	0.04
Ventilator-associated pneumonia during hospital stay	0.065 (0.007–0.558)	0.013	0.21 (0.009–4.175)	0.33

OR, odds ratio; CI, confidence interval.

any significant change in the mode of TBI, with road traffic accidents remaining the biggest contributor in our cohort.

Triaging of Patients with TBI and COVID-19 Care

All patients with TBI coming to the emergency room of our hospital were screened for risk of COVID-19 with a “Checklist for COVID-19 suspicion” followed by cartridge-based nucleic acid amplification testing. Those patients who were negative for COVID-19 were managed as per the Brain Trauma Foundation guidelines. Patients with TBI who became positive for COVID-19 were shifted to COVID-19–designated facilities and were managed for COVID-19 apart from normal neurosurgical care. COVID-19–positive patients with TBI were categorized into 1) Mild COVID-19/mild TBI, 2) moderate COVID-19/moderate TBI, and 3)

Severe COVID-19/severe TBI based on GCS score at admission, blood oxygen saturation (SpO₂) on room air, and respiratory rate. In the initial phase of the pandemic, patients with mild COVID-19 were given hydroxychloroquine, ivermectin, tetracycline, zinc, and vitamin C, as per the guidelines of the national task force.^{18–21} However, with increasing evidence from the literature, we preferred only hydroxychloroquine or ivermectin for patients with mild COVID-19.²² However, the recent literature does not support the use of hydroxychloroquine and ivermectin as a prophylaxis in patients with COVID-19 and we have stopped their use in our clinical practice.^{23–25} Remdesivir and tocilizumab were reserved for patients with moderate to severe COVID-19, in whom the use of these drugs was indicated as per our protocol. Increasing evidence of the role of steroids in COVID-19 management led to the addition

Table 6. Recommendations by Various Groups for Management of Patients with Emergency Trauma During COVID-19 Pandemic

Reference	Place	Recommendations
Rosyidi et al., 2021 ¹²	Mataram, Indonesia	<ul style="list-style-type: none"> Checklist for screening for COVID-19 (low risk, moderate risk, high risk) Protocol-based management based on an algorithm used in ER depending on the risk of having COVID-19 Different transfer routes for shifting of COVID-19 suspected and confirmed cases Negative-pressure ORs Minimum personnel in ORs Use of level 3 PPE in ORs
Randelli et al., 2020 ¹³	Milan, Italy	<ul style="list-style-type: none"> Restructuring resources and manpower Hub and spoke model of Zoia et al.,¹⁴ in which 2 referral centers were made as hubs for 24×7 referral for minor and nondeferrable elective surgeries. Formation of crisis unit for daily meetings and assessing the COVID-19 crisis in the country and formulation and implementation of guidelines for management of patients with trauma during such crises Specific ORs for operating confirmed or suspected patients Restricted access to hospitals including reduction of OPD services Conversion of general hospital wards to COVID-19–specific wards Physical distancing of at least 1 m from patients and use of PPEs
Qasim et al., 2020 ¹⁵	Philadelphia	<ul style="list-style-type: none"> Workforce planning and restructuring Weekly meeting among regional trauma program medical directors and trauma program managers for assessing the pandemic and taking necessary actions Limited personnel in ER and screening of patients in ER Negative-pressure ORs with limited personnel Designated area for donning and doffing of PPEs Limit the use of nonemergency blood transfusion and transfusion of rare blood types All academic activities through telemeetings
Britton et al., 2020 ¹⁶	Cambridge, United Kingdom	<ul style="list-style-type: none"> Increasing the workforce in critical care areas with the formation of intubation teams, proning teams, and tracheostomy surgical list Assessment forms to assess the health risk for individual health care workers and rotate them to various stations depending on their health risk Division of ORs into various zones: <ul style="list-style-type: none"> Zone 1, green (for donning of PPEs) Zone 2, amber (for scrubbing, no entry in this zone without PPEs) Zone 3, amber (anesthetic room, no entry in this zone without PPEs) Zone 4, red (the OR, only essential personnel allowed) Zone 5, amber to green (the exit room with no re-entry) Interdepartmental communication and peer support, daily meetings and conference calls for discussing the pandemic status and taking necessary action
AIIMS HICC/neurosurgery	AIIMS, New Delhi	<ul style="list-style-type: none"> Use of checklist for screening of high-risk suspects of COVID-19 Hub and spoke model of Zoia et al.,¹⁴ in which 2 designated centers, Jai Narayan Apex Trauma Centre and National Cancer Institute, Jhajjar, were made into COVID-19–designated facilities for management of COVID-19–positive patients Structured reorganization of workforce to COVID-19–designated facilities on a rotational basis Deferment of elective ORs and routine admissions Formulation of HICC guidelines for use of PPEs in different hospital settings Closure of physical OPD and use of telemedicine for patient follow-up

ER, emergency room; OR, operating room; PPE, personal protective equipment; AIIMS, All India Institute of Medical Sciences; HICC, Hospital Infection Control Committee; OPD, outdoor patient department.

of inhalational budesonide in the treatment protocol for patients with mild COVID-19 and injectable methylprednisolone for moderate and severe cases.²⁶ All COVID-19–positive patients with TBI were monitored serially with biomarkers of inflammation (interleukin 6, C-reactive protein, D-dimer, procalcitonin) as and when required. **Figure 3** shows the present management protocol for COVID-19–positive patients with TBI at our center. **Table 7**

shows the clinical and radiological details of the COVID-19 positive patients included in our study.

Changes Implemented to Manage Patients with TBI at our Center

As a result of closure of the trauma center, to avert acute shortage of beds, nearly one third of bed strength in the main neurosurgical center was dedicated for patients with neurotrauma. All

Table 7. Management and Outcome of COVID-19–Positive Patients at COVID-19 Facilities in Our Institute

Patient Number	Initial Glasgow Coma Scale Score	Injury	Preoperative Computed Tomography	Management	Chest Radiography	Outcome
1	E4V5M6	Assault	Multiple frontal contusions (right>left)	Right DC+ HITZC*	Normal	E4V5M6, GOS-E 8
2	E1VTM5	RTA	DAI	CM + HITZC	Unilateral pneumonitis	E4V5M6, GOS-E 7
3	E1V1M3	RTA	Right acute SDH with multiple contusions	Right DC + HITZC+R	Bilateral pneumonitis	GOS-E 1
4	E4V5M6	FFH	Left temporal contusion	CM + HITZC	Right upper zone opacity	E4V5M6, GOS-E 8
5	E4V4M6	RTA	Thin SAH left side	CM+ HITZC	Normal	E4V5M6, GOS-E 8
6	E4V5M6	RTA	Left acute on chronic SDH	CM + HITZC	Normal	E4V5M6, GOS-E 8
7	E4V5M6	FFH	Left acute SDH with EDH	Left DC + HITZC+ R+ O	Bilateral pneumonitis	GOS-E 1
8	E4V5M6	Assault	Right acute SDH	CM + HITZC	Unilateral pneumonitis	E4V5M6, GOS-E 8
9	E4V5M6	RTA	Right acute SDH	CM+ HITZC	Normal	E4V5M6, GOS-E 8
10	E1VTM5	RTA	DAI	CM + HITZC	Normal	E1VTM5, GOS-E 3
11	E4V5M6	RTA	Right parietal EDH	CM + HITZC	Normal	E4V5M6, GOS-E 8
12	E1VTM4	RTA	DAI with thin SAH	CM + HITZC	Right lower zone consolidation	E4VTM5, GOS-E 4
13	E1V1M4	Unknown	Left acute SDH	CM + HITZC	Bilateral pneumonitis	E4V5M6, GOS-E 8
14	E3V3M5	RTA	DAI with left frontal contusion	CM+ HITZC+ R+ O	Bilateral pneumonitis	E1V1M2, GOS-E 3
15	E4V5M6	RTA	DAI and diffuse SAH	CM + HITZC+ R	Right bronchiectasis	GOS-E 1
16	E4V5M6	RTA	Right frontal contusion and thin SDH	CM + HITZC	Right pneumonitis	E4V5M6, GOS-E 8
17	E4V5M6	Assault	Left temporal contusion	CM+ HITZC	Normal	E4V5M6, GOS-E 8
18	E1VTM5	RTA	Left frontal contusion	CM + HITZC	Unilateral pneumonitis	E4V5M6, GOS-E 7
19	E4V5M6	RTA	Left temporal contusion	CM + HITZC	Unilateral pneumonitis	E4V5M6, GOS-E 8
20	E3V2M6	Assault	Left temporal contusion	CM + HITZC+ R	Bilateral pneumonitis	GOS-E 1,
21	E4V5M6	Assault	Minor dot contusions with calvarial fracture	CM + HITZC	Normal	E4V5M6, GOS-E 8
22	E1VTM5	RTA	Large left parietal EDH with counter coupe contusions	Left EDH evacuation and DC+ HITZC+ R+ O	Bilateral pneumonitis	GOS-E 1
23	E4VTM6	FFH	Right frontal EDH and thin SDH	Right EDH evacuation and DC + HITZC+ R +O	Bilateral pneumonitis	GOS-E 1
24	E1VTM1	RTA	DAI, intraventricular bleed and SAH	CM + HITZC	Normal	GOS-E 1
25	E3V3M5	Assault	Left frontal SDH and contusions	Left EDH evacuation and DC + HITZC	Normal	E4VTM5, GOS-E 4
26	E1VTM4	Assault	Left acute SDH	Left DC + HITZC	Bilateral pneumonitis	E1VTM2, GOS-E 3
27	E4V5M6	RTA	Left SDH	CM+ HITZC	Bilateral pneumonitis	E4V5M6, GOS-E 8
28	E4V5M6	RTA	Right SDH	CM + HITZC	Pneumothorax	E4V5M6, GOS-E 8
29	E1VTM3	Assault	Right SDH, contusions and DAI	CM + HITZC+ R	Unilateral pneumonitis	GOS-E 1, died

DC, frontotemporoparietal decompressive craniectomy; *H, hydroxychloroquine 400 mg twice daily on day 1 followed by once daily for 1 week; I, ivermectin 12 mg daily for 5 days; T, Tetracycline 100 mg twice daily for 5 days; Z, zinc 50 mg daily for 14 days; C, vitamin C 500 mg for 14 days; GOS-E, Glasgow Outcome Scale—Extended; RTA, road traffic accident; R, remdesivir 200 mg on day 1 followed by 100 mg from day 2 to 5; CM, conservative management of TBI; SDH, subdural hematoma; FFH, fall from height (>3.04 m [10 feet]); O, tocilizumab 8 mg/kg (up to 800 mg) single intravenous injection, repeat dose after 12 hours if no improvement; EDH, extradural hematoma; E, eye response; V, verbal response; T, tracheostomized; M, motor response; DAI, diffuse axonal injury.

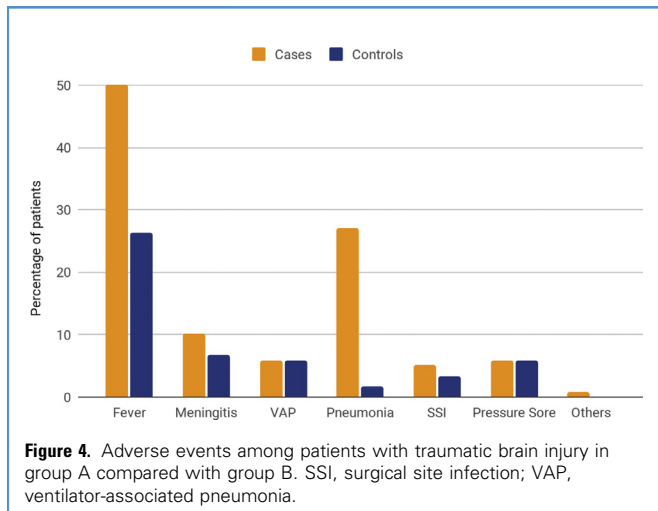


Figure 4. Adverse events among patients with traumatic brain injury in group A compared with group B. SSI, surgical site infection; VAP, ventilator-associated pneumonia.

semielective surgery such as surgery for brachial plexus injuries and cranioplasties was postponed. Testing and quarantine protocols were put in place for our department in sync with the hospital policies.²⁷ The logistic issues faced because of the new protocols gradually decreased, as is evident from the results shown in this study. The time needed to shift the patients from emergency department to operating room decreased in the second phase compared with phase 1.

Challenges in Managing COVID-19–Positive Patients

Longer Hospital Stay. We observed that the length of hospital stay of patients with TBI in arm A was significantly longer than in arm B. Moreover, the COVID-19–positive patients in arm A had statistically significantly longer length of hospital stay than their matched controls in arm B and COVID-19–negative patients in arm A. Thus, COVID-19 infection increased the morbidity in

patients with TBI by prolonging their hospital stay. One reason responsible for this situation might be the inability to send the admitted patients home from hospital because of nationwide lockdown impeding transport facilities. Longer hospital stay in the initial phase of the pandemic can also be attributed to initial skepticism of the treating team in discharging a COVID-19 patient with head injury, because the natural course of the disease was not well known. Moreover, relatives and patients during the complete lockdown phase encountered difficulties in arranging for the transport of the patient to far-flung areas. As the experience of our team increased, we were able to discharge patients earlier for care at home, and by September 2020, most lockdown restrictions had also been eased, which made travel across districts/states easier. This observation was supported by the subgroup analysis, which showed that the longer duration of hospital stay was mainly seen in the initial part of the pandemic.

Longer Time Taken for Shifting, Induction, and Surgery. The time needed for induction as well as the total operative time of patients with TBI in arm A was statistically significantly longer than those in arm B. Similar trends were seen when COVID-19–positive patients with TBI in arm A were compared with matched controls from arm B. However, no such difference was noted between the COVID-19–positive and COVID-19–negative patients in arm A. This difference can be attributed to the fact that, during the initial part of the pandemic, suspected or COVID-19–positive patients were operated on by surgeons donning full personal protective equipment (PPE), which decreased the dexterity and led to increased operative time. Moreover, to decrease aerosol generation in such cases, instead of pneumatic or electrical drills, surgeons preferred to use handheld burrs, which also increased the duration of the surgery.²⁸

Adverse Events and Outcome of Patients with TBI. During the hospital stay, patients in arm A had significantly higher chances of developing fever and pneumonia than did those in arm B (50% vs. 26.3% and 27.1% vs. 1.7%, respectively). Also, incidence of fever and pneumonia was significantly more in COVID-19–positive patients with TBI in arm A compared with matched controls in

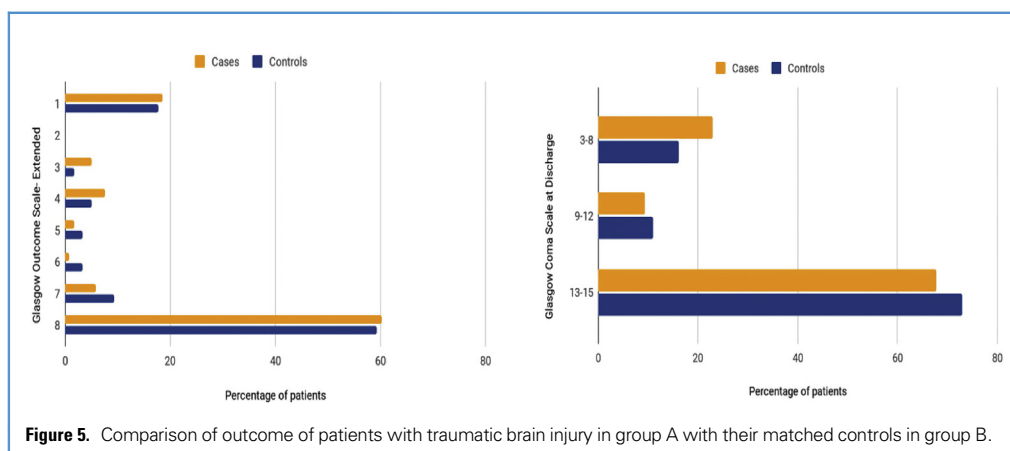
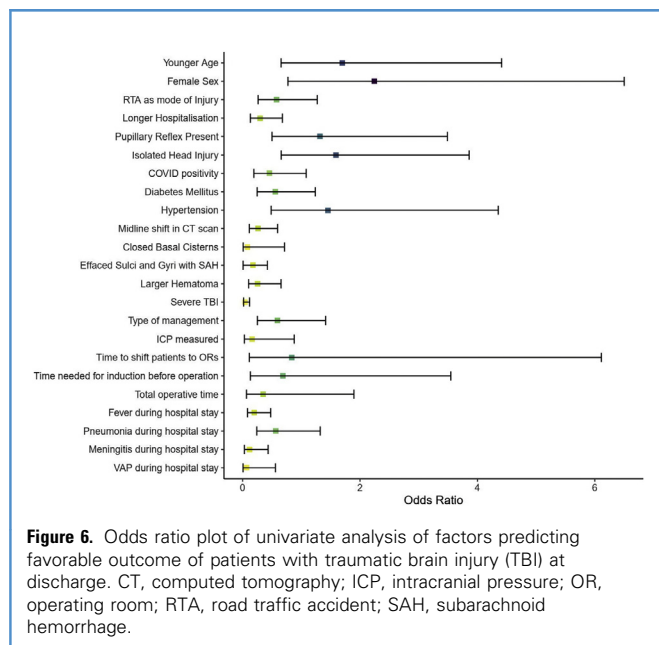


Figure 5. Comparison of outcome of patients with traumatic brain injury in group A with their matched controls in group B.



arm B and compared with COVID-19–negative patients in arm A. **Figure 4** shows the incidence of adverse events among patients with TBI in arm A compared with arm B.

This increased risk of fever/pneumonia in arm A could be because fewer residents than usual left to take care of patients who did not have COVID-19, because 30%–50% of residents were posted into COVID-19–designated areas. Moreover, sterility during surgery or the postoperative period is compromised when one is working after donning PPE. The increased chances of pneumonia in arm A might be related to the increased duration for which patients required ventilation in the postoperative period. Also, the COVID-19–positive patients with TBI had a higher incidence of fever and pneumonia than did COVID-19–negative patients in arm A, which can be explained by cytokine storms in COVID-19–positive patients.

The outcome of patients with TBI in arm A did not differ significantly compared with matched controls from arm B (**Figure 5**). The GOS-E and GCS scores at discharge of patients with TBI in arm A compared with arm B was similar ($P = -0.557$ and $P = -0.095$, respectively). Also, both arm A and arm B had similar death rates (18.6% vs. 14.4% respectively; $P = -0.423$).

Mortality, on the other hand, was similar in both the COVID-19–positive and COVID-19–negative patients in arm A (27.6% vs. 15.7%; $P = -0.299$). Also, the patients with TBI in the early pandemic phase did not have mortality significantly higher than that of those in the late pandemic phase (20.9% vs. 15.7%; $P = -0.096$).

Predictors of Outcome. The factors found to have significant effect on outcome (GOS-E), on univariate analysis, were longer hospitalization, midline shift >5 mm, effaced sulci and gyri on NCCT head, larger hematoma (40 mL), severe TBI (GCS score ≤ 8), fever,

pneumonia, meningitis, and ventilator-associated pneumonia during hospital stay. On multivariate analysis, severe TBI and meningitis during hospital stay were found to be statistically significant factors associated with poor outcome at discharge **Figure 6**. Thus, despite significant differences between arm A and their matched controls from arm B in length of hospital stay, duration in operating room, and incidence of fever and pneumonia, they fail to predict poor outcome in patients with TBI. Also, the COVID-19 positivity status did not predict an unfavorable outcome in patients with TBI (odds ratio, 0.454; confidence interval, 0.191–1.083; $P = -0.75$). All these findings suggest that the outcome of patients managed for emergency neurosurgical diseases during the COVID-19 pandemic were the same as for those managed before the COVID-19 pandemic.²⁹

Limitations

This is a retrospective study with limited patients with TBI being matched with their controls. A larger study is needed to evaluate the effect of COVID-19 on the outcome of patients with TBI. Also, with the availability of vaccines during the second wave in India, the role of COVID-19 in increasing morbidity among patients with TBI remains controversial. Further study is needed to evaluate such outcomes.

CONCLUSIONS

COVID-19 imposed several challenges to health care workers in managing patients with TBI during the pandemic. Guidelines for management of patients with TBI during the COVID-19 pandemic were formulated for our department. The outcome of the patients managed for TBI during the COVID-19 pandemic was similar to that of matched patients with TBI managed at our center before the onset of the COVID-19 pandemic despite the logistic problems leading to increased time required to shift patients from the emergency department to the operating room and increased duration of surgical intervention and length of hospital stay. This finding suggests that the guidelines followed during the COVID-19 pandemic were effective in dealing with patients with TBI. This model can serve as a guide for any future pandemic wave for effective management of patients with TBI without compromising their outcome.

CRedit AUTHORSHIP CONTRIBUTION STATEMENT

Intekhab Alam: Data retrieval, Formal analysis, Writing – original draft, Approved final manuscript. **Kanwaljeet Garg:** Formal analysis, Software, Writing – original draft, Approved final manuscript. **Amol Raheja:** Writing – original draft, Approved final manuscript. **Vivek Tandon:** Conceptualization, Writing – original draft, Approved final manuscript. **Ravi Sharma:** Writing – original draft, Approved final manuscript. **Manmohan Singh:** Writing – original draft, Approved final manuscript. **Gyaninder Pal Singh:** Writing – original draft, Approved final manuscript. **Shashwat Mishra:** Writing – original draft, Approved final manuscript. **Pankaj Kumar Singh:** Writing – original draft, Approved final manuscript. **Deepak Agarwal:** Writing – original draft, Approved final manuscript. **Kapil Dev Soni:** Writing – original draft, Approved final manuscript. **Ashish Suri:** Writing

— original draft, Approved final manuscript. **Poodipedi Sarat Chandra:** Writing — original draft, Approved final manuscript. **Shashank Sharad Kale:** Writing — original draft, Approved final manuscript.

REFERENCES

1. Archived: WHO Timeline - COVID-19. Available at: <https://www.who.int/news/item/27-04-2020-who-timeline-covid-19>. Accessed June 22, 2022.
2. Raheja A, Sinha S, Samson N, et al. Serum biomarkers as predictors of long-term outcome in severe traumatic brain injury: analysis from a randomized placebo-controlled phase II clinical trial. *J Neurosurg.* 2016;125:631-641.
3. Raheja A, Agarwal N, Mohapatra S, et al. Preparedness and guidelines for neurosurgery in the COVID-19 era: Indian perspective from a tertiary care referral hospital. *Neurosurg Focus.* 2020;49:E3.
4. Tan Y-T, Wang J-W, Zhao K, et al. Preliminary recommendations for surgical practice of neurosurgery department in the central epidemic area of 2019 coronavirus infection. *Curr Med Sci.* 2020; 40:281-284.
5. Deora H, Mishra S, Tripathi M, et al. Adapting neurosurgery practice during the COVID-19 pandemic in the Indian subcontinent. *World Neurosurg.* 2020;142:e396-e406.
6. Burke JF, Chan AK, Mummaneni V, et al. Letter: The coronavirus disease 2019 global pandemic: a neurosurgical treatment algorithm. *Neurosurgery.* 2020;87:E50-E56.
7. Giorgi PD, Villa F, Gallazzi E, et al. The management of emergency spinal surgery during the COVID-19 pandemic in Italy: a preliminary report. *Bone Jt J.* 2020;102-B:671-676.
8. Liaw J, Patel VA, Bann DV, et al. Letter: COVID-19 pandemic: safety precautions for stereotactic radiosurgery. *Neurosurgery.* 2020;87:E201-E202.
9. Germanò A, Raffa G, Angileri FF, Cardali SM, Tomasello F. Coronavirus disease 2019 (COVID-19) and neurosurgery: literature and neurosurgical societies recommendations update. *World Neurosurg.* 2020;139:e812-e817.
10. Tsermoulas G, Zisakis A, Flint G, Belli A. Challenges to neurosurgery during the coronavirus disease 2019 (COVID-19) pandemic. *World Neurosurg.* 2020;139:519-525.
11. Mahmud MR, Cheserem B, Esene IN, et al. The impact of COVID-19 on neurosurgical services in Africa. *World Neurosurg.* 2021;146:e747-e754.
12. Rosyidi RM, Wisnu Wardhana DP, Apriawan T, et al. Algorithm of traumatic brain injury management at Indonesia in the COVID 19 pandemic ERA. Retrospective cohort study. *Ann Med Surg (Lond).* 2021;62:98-103.
13. Randelli PS, Compagnoni R. Management of orthopaedic and traumatology patients during the Coronavirus disease (COVID-19) pandemic in northern Italy. *Knee Surg Sports Traumatol Arthrosc.* 2020;28:1683-1689.
14. Zoia C, Bongetta D, Veiceschi P, et al. Neurosurgery during the COVID-19 pandemic: update from Lombardy, northern Italy. *Acta Neurochir (Wien).* 2020;162:1221-1222.
15. Qasim Z, Sjöholm LO, Volgraf J, et al. Trauma center activity and surge response during the early phase of the COVID-19 pandemic—the Philadelphia story. *J Trauma Acute Care Surg.* 2020;89: 821-828.
16. Britton CR, Hayman G, Macfarlane C, et al. COVID-19 preparedness and response at a large UK major trauma operating theatres department. *J Perioper Pract.* 2020;30:210-220.
17. Figueroa JM, Boddu J, Kader M, et al. The effects of lockdown during the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) pandemic on neurotrauma-related hospital admissions. *World Neurosurg.* 2021;146:e1-e5.
18. Rathi S, Ish P, Kalantri A, Kalantri S. Hydroxychloroquine prophylaxis for COVID-19 contacts in India. *Lancet Infect Dis.* 2020;20:1118-1119.
19. Sodhi M, Etminan M. Therapeutic potential for tetracyclines in the treatment of COVID-19. *Pharmacother J Hum Pharmacol Drug Ther.* 2020;40: 487-488.
20. Name JJ, Souza ACR, Vasconcelos AR, Prado PS, Pereira CPM. Zinc, Vitamin D and vitamin C: perspectives for COVID-19 with a focus on physical tissue barrier integrity. *Front Nutr.* 2020;7: 606398.
21. Rajter JC, Sherman MS, Fatteh N, Vogel F, Sacks J, Rajter JJ. Use of ivermectin is associated with lower mortality in hospitalized patients with coronavirus disease 2019. *Chest.* 2021;159:85-92.
22. Stasi C, Fallani S, Voller F, Silvestri C. Treatment for COVID-19: an overview. *Eur J Pharmacol.* 2020; 889:173644.
23. López-Medina E, López P, Hurtado IC, et al. Effect of ivermectin on time to resolution of symptoms among adults with mild COVID-19: a randomized clinical trial. *JAMA.* 2021;325:1426-1435.
24. Motola D, Bonaldo G, Montanaro N. Safety profile of hydroxychloroquine used off-label for the treatment of patients with COVID-19: a descriptive study based on EudraVigilance data [e-pub ahead of print] *Fundam Clin Pharmacol.* 2022. <https://doi.org/10.1111/fcp.12797>, accessed June 22, 2022.
25. Fiolet T, Guihur A, Rebeaud ME, Mulot M, Peiffer-Smadja N, Mahamat-Saleh Y. Effect of hydroxychloroquine with or without azithromycin on the mortality of coronavirus disease 2019 (COVID-19) patients: a systematic review and meta-analysis. *Clin Microbiol Infect.* 2021;27:19-27.
26. Solinas C, Perra L, Aiello M, Migliori E, Petrosillo N. A critical evaluation of glucocorticoids in the management of severe COVID-19. *Cytokine Growth Factor Rev.* 2020;54:8-23.
27. Sharma R, Garg K, Katiyar V, et al. Analysis of neurosurgical cases before and during the coronavirus disease 2019 pandemic from a tertiary-care centre in India. *World Neurosurg.* 2021;152: e635-e644.
28. Givi B, Schiff BA, Chinn SB, et al. Safety recommendations for evaluation and surgery of the head and neck during the COVID-19 pandemic. *JAMA Otolaryngol Neck Surg.* 2020;146:579.
29. Grassner L, Petr O, Warner FM, et al. Trends and outcomes for non-elective neurosurgical procedures in Central Europe during the COVID-19 pandemic. *Sci Rep.* 2021;11:6171.

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