Since January 2020 Elsevier has created a COVID-19 resource centre with free information in English and Mandarin on the novel coronavirus COVID-19. The COVID-19 resource centre is hosted on Elsevier Connect, the company's public news and information website.

Epidemiological Pattern of Traumatic Brain Injury in the COVID-19 Pandemic: A Systematic Review and Meta-Analysis

Fachreza Aryo Damara[2], Galih Ricci Muchamad[3], Anton Anton[2], Alfya Nandika Ramdhani[2], Ivan Christian Channel[2], Ahmad Faried[1]

■ BACKGROUND: Although the incidence of traumatic brain injury (TBI) has decreased since the beginning of the coronavirus disease 2019 (COVID-19) pandemic and severe acute respiratory syndrome coronavirus 2 is still evolving, the number of TBI cases has still greatly increased in multiple countries. In the present systematic review and meta-analysis, we evaluated the epidemiological characteristics of patients with TBI before and during the COVID-19 pandemic.

■ METHODS: We conducted a systematic literature search of original studies, short reports, and research letters from databases on studies that contained data about the severity, mortality, presence of neurological deficits, radiological diagnosis, cause of injury, and type of management of TBI during a specified period within the pandemic compared with before the pandemic.

■ RESULTS: A total of 18,490 subjects from 13 studies were included in the present study. The results of the meta-analysis showed a higher TBI mortality rate during the COVID-19 pandemic in the low-to-middle income countries (odds ratio, 1.65; 95% confidence interval, 1.12–2.41; $P <$ 0.05; $I^2 = 40.8\%$; $P = 0.18$). The proportion of subdural hemorrhage was decreased, and the proportion of subarachnoid hemorrhage was increased in low- to middle-income and high-income countries, respectively. The proportion of assaults as the cause of TBI had increased during the pandemic (odds ratio, 1.40; 95% confidence interval, 1.06–1.86; $P = 0.02$; $I^2 = 20.8\%$; $P = 0.28$). We did not find any significant differences in the incidence of surgical intervention for TBI during the pandemic.

■ CONCLUSIONS: Our results have indicated that during the COVID-19 pandemic, the TBI mortality rate had increased in low- to middle-income countries. The rate of assault as the cause of TBI had also increased during the pandemic.

INTRODUCTION

Coronavirus disease 2019 (COVID-19), caused by SARS-CoV-2 (severe acute respiratory syndrome coronavirus 2) has infected millions of people worldwide. The rapid spread of the disease has also continued to burden healthcare providers by postponing necessary interventions for patients who require, not only elective procedures, but also emergency interventions.[1-3] Furthermore, the rapidly evolving nature of SARS-CoV-2 with distinct epidemiological features has required clinicians and stakeholders to adjust the healthcare and workflow settings to prevent COVID-19 complications.

During the COVID-19 outbreak, the incidence of neurological trauma has markedly declined as the practice of lockdowns, self-isolation, quarantine, and travel restrictions have been implemented.[4,5] Rigorous social distancing has been implemented that has shifted our standard methods of living. Many public places have been closed, workplaces have become remote, and people have only been seeking medical services if they had experienced an emergency.[6,7] Thus, the number of motor vehicle accidents, amount of public

Key words
- COVID-19
- Epidemiology
- Neurological trauma
- Traumatic brain injury

Abbreviations and Acronyms
CI: Confidence interval
COVID-19: Coronavirus disease 2019
HIC: High-income country
LMIC: Low- to middle-income country
OR: Odds ratio
PECO: Population, exposure, comparison, outcome
PRISMA: Preferred reporting items for systematic reviews and meta-analyses
PROSPERO: International Prospective Register of Systematic Reviews
RTA: Road traffic accident
SARS-CoV-2: Severe acute respiratory syndrome coronavirus 2

SAH: Subarachnoid hemorrhage
SDH: Subdural hematoma
TBI: Traumatic brain injury

mobility, and number of outdoor activities have decreased, attributing to the declining number of neurological trauma cases.

Despite the reduced number of trauma-related cases, some people have still experienced traumatic brain injury (TBI).[4] The altered behavior of the population could have significantly affected the epidemiological characteristics of neurological trauma cases, including TBI. Thus, we evaluated the severity of TBI, mortality, presence of neurological deficits, radiology diagnosis, cause of injury, and the type of management of TBI during versus before the pandemic.

METHODS

The present systematic review was reported in accordance with the PRISMA (preferred reporting items for systematic reviews and meta-analyses) guidelines.[8,9] A detailed protocol was registered in PROSPERO (International Prospective Register of Systematic Reviews; registry no. CRD42021251648).

Eligibility Criteria

The present study followed the design structure of PECO (population, exposure, comparison, outcome) to define the inclusion and exclusion criteria for exposure and outcomes.[10] The inclusion criteria were original research articles, letters, and short reports. The outcomes of interest was the severity of TBI, mortality, neurological deficits, radiology diagnosis, cause of injury, and type of management during the COVID-19 pandemic compared with before the pandemic. We excluded case reports, non—research letters, editorials, invited commentaries, reviews, abstract-only reports, and pre-print reports. No language restriction was applied in the present study.

Search Strategy and Study Selection

A systematic search of PubMed and the Cochrane Collaboration Central Register of Controlled Clinical Trials was performed from inception to December 20, 2021 by 2 of us (F.A.D. and A.F.) independently (Appendix). The following search terms were used: ("Brain Injuries, Traumatic"[MeSH] OR Traumatic Brain Injury OR "Brain Concussion"[MeSH] OR "Brain Injuries"[MeSH] OR Brain Injury OR "Accidents, Traffic"[MeSH]) AND (Pandemic OR COVID-19 OR "COVID-19"[MeSH]). We used the "related articles" feature and manually searched the reference lists of the included reports to expand the search and obtain additional studies. Duplicate results were removed after the initial search. We attempted to contact the authors of the reports for which the study data were incomplete or full-text reports were unavailable.

Data Extraction

Data extraction was conducted independently by 2 of us (F.A.D. and A.F.). The standardized form included author, year, study design, sample size, age, gender, control period, and pandemic period. Different perceptions in the extraction of the data and in the elimination of possible duplicates were resolved through discussion and consensus.

We used Newcastle-Ottawa scale to assess the quality of included studies.[11] The following aspects were evaluated for each study and cohort selection: the comparability of the cohort according to the design or analysis, the method of exposure, and the determination of the outcomes of interest. Discrepancies of perception were resolved by discussion.

Outcomes and Effect Measures

The primary outcome of the present study was the severity of TBI and mortality during the COVID-19 pandemic compared with before the pandemic. The pooled estimates are presented using the odds ratio (OR).

The secondary outcome was the presence of neurological deficits, radiology diagnosis, cause of injury, and type of management. The radiology diagnosis included epidural hematoma, subdural hematoma (SDH), subarachnoid hemorrhage (SAH), contusion, and skull fracture. The cause of injury included road traffic accidents (RTAs), high falls, low and mechanical falls, and assaults. The type of management was surgical versus nonsurgical management.

We also conducted a subset outcomes analysis according to the country's income level using the World Bank classification.[12] The countries in which the studies were conducted were divided into low- to middle-income countries (LMICs) and high-income countries (HICs). A minimum of 2 studies were required for the creation of a subset of outcomes.

Statistical Analysis

All statistical analyses were performed using R, version 4.0.4 (The R Foundation, Vienna, Austria) using the mada and meta packages.[13] We used a meta-analysis of the proportion to calculate the differences in percentages of the investigated outcome. ORs were calculated using the Mantel-Haenszel method random effects model. Also, the Haldane-Anscombe correction was applied to studies with a 0 number of cases.[14]) An I^2 value of >50% and P value of < 0.05 were considered as significant for heterogeneity.[15] The random effects model was used, regardless of the heterogeneity value.

RESULTS

Study Characteristics

A total of 18,490 subjects from 13 studies were included in the present meta-analysis (Figure 1).[4,16-27] The characteristics of the included studies are presented in Table 1. A summary of the meta-analysis findings is presented in Tables 2—4.

Severity and Mortality of TBI Cases

No statistically significant differences were found in the moderate to severe TBI case rates between the COVID-19 outbreak and before the pandemic (control group; OR, 1.13; 95% CI, 0.96—1.34; P = 0.14; I^2 = 39%; P = 0.09; Supplementary Figure 1). Similarly, although the rates of moderate to severe TBI cases were greater during the pandemic in both LMICs and HICs, the differences were not statistically significant (Table 2).

The overall aggregated risk estimates for TBI mortality showed no significant differences between before the pandemic and during the COVID-19 pandemic (OR, 1.08; 95% CI, 0.58—2.01; P = 0.81; I^2 = 73.9%; P = 0.001; Supplementary Figure 2). However, the TBI mortality rate within the LMIC group was significantly greater during the pandemic (OR, 1.65; 95% CI, 1.12—2.41; P < 0.05; I^2 = 40.8%; P = 0.18; Table 2). We did not find any differences in the occurrence of neurological deficits between the 2 periods (Supplementary Figure 3).

Radiological Findings

The overall results showed no significant differences in the radiological findings (epidural hematoma, SDH, SAH, contusion,

Figure 1. PRISMA (preferred reporting items for systematic reviews and meta-analyses) flowchart for the present study.
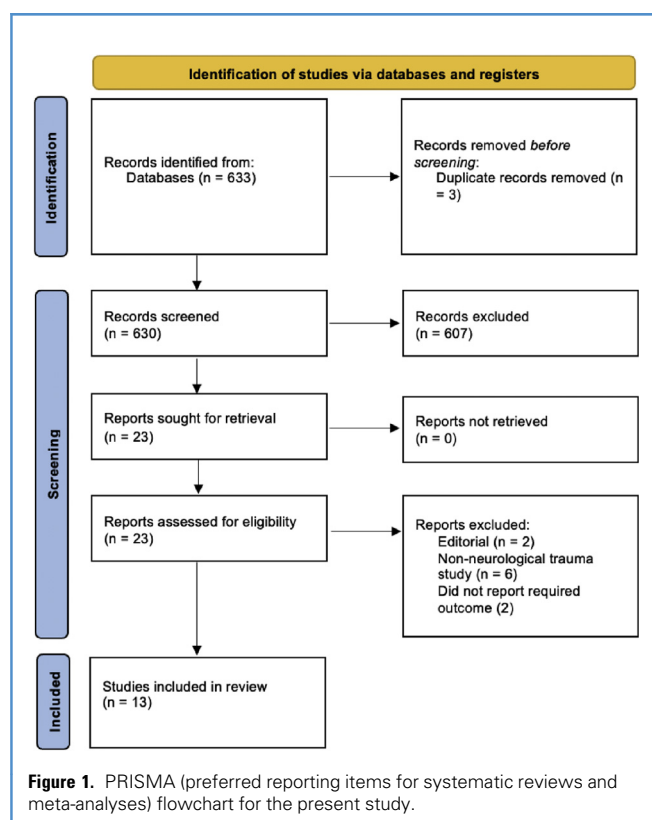
skull fracture; **Supplementary Figures 4—8**) between the 2 periods. However, the subgroup analyses showed that the rate of SDH was lower during the pandemic in the LMICs (OR, 0.79; 95% CI, 0.67—0.92; $P < 0.05$; $I^2 = 0.7\%$; $P = 0.32$). In addition, the rate of SAH was lower during the pandemic in the HICs (OR, 1.36; 95% CI, 1.00—0.84; $P < 0.05$; $I^2 = 0\%$; $P = 0.59$; **Table 3**).

Cause of Injury

The proportion of RTAs as a cause of TBI was similar between the 2 periods. Similarly, our results showed no significant differences in the rates of high falls and low and mechanical falls. In contrast, the results from our present analysis indicated that the overall rate of assault as a cause of TBI was greater during the pandemic (OR, 1.40; 95% CI, 1.06—1.86; $P = 0.02$; $I^2 = 20.8\%$; $P = 0.28$). Furthermore, the proportion of assault was greater in LMICs (OR, 1.83; 95% CI, 1.37—2.45; $P < 0.05$; $I^2 = 0\%$; $P = 0.78$; **Table 4**).

Management of TBI

The management of TBI was categorized into surgical and nonsurgical management. We found that the rate of surgical TBI treatment was similar between before and during the COVID-19 pandemic (OR, 0.76; 95% CI, 0.53—1.08; $P = 0.13$; $I^2 = 73.6\%$; $P < 0.01$; **Table 2**). A subgroup analysis also showed no significant differences in operative treatment between before the pandemic and during the pandemic in the LMICs and HICs (**Table 2**).

DISCUSSION

In the present study, we conducted pooled analyses of the epidemiological characteristics of TBI cases during and before the COVID-19 pandemic. Because our meta-analysis included studies

from multiple countries, we divided the countries for a subset analysis by the countries' income level.

Our results showed a similar proportion of moderate to severe TBI cases during the pandemic in both the LMIC and the HIC groups, with a moderate level of heterogeneity. Thus, the healthcare management flow only slightly influenced the pattern of TBI across the centers. In addition, the massive lockdown regulations implemented by governments could have potentially caused patients with mild TBI be reluctant to visit hospitals. However, we found that many patients with mild TBI had presented to peripheral centers and were treated appropriately.[16] Although most of the studies had demonstrated a greater proportion of moderate to severe TBI cases during the pandemic, we noted a moderate level of heterogeneity in the results. A study by Manivannan et al.[23] showed a lower proportion of moderate and severe TBI cases linked to a reduced number of RTAs. The limitations on the use of mass transportation during the COVID-19 pandemic could have caused some people to switch to using bicycles to go to work, home, public places, and other places, which might account for the reduced proportion of severe TBI caused by motorized vehicles.[28-31]

Our overall analysis showed no significant differences in TBI mortality between the 2 periods. However, the TBI mortality rate was significantly greater in the LMICs. This discrepancy in the results could have been caused by the relatively greater number of COVID-19 cases in the developing countries, in addition to the limited number of medical supplies that eventually burdened the healthcare systems.[32] Pinggera et al.,[24] in their study of the Austrian population, reported that all acute neuroemergency cases were considered positive for COVID-19, with all the related consequences until proved otherwise. This policy was implemented with the aim of preventing delays in treating emergency cases caused by the lengthy COVID-19 assessments such that patient mortality could be avoided.[24] In contrast, studies in India and Indonesia showed an increase in TBI mortality during the pandemic.[17] The discrepancy between the results could also be attributed to differences in the precaution strategies that authorities have implemented to mitigate COVID-19 transmission. In addition, some studies indicated a possible causative link between the higher severity of TBI cases, which, consequently, led to significantly greater mortality during the pandemic, and the postponement of some elective surgeries during the peak of the pandemic spread in India and the requirement that surgical procedures for those who tested positive for COVID-19 should be postponed until the test results were negative, where possible.[3,28] Ultimately, the overall result has emphasized that adequate resource allocation is required among developing countries to reduce the increasing rate of TBI deaths.

The radiological manifestations in TBI might reflect the pattern of causes and the consequences of altered neurosurgical management within the hospital due to the pandemic. Overall, our pooled analyses found no significant differences in the radiological findings among TBI patients between the 2 periods. However, our subgroup analyses demonstrated a lower incidence of SDH in the LMICs and a higher incidence of SAH in the HICs. This pattern might have resulted from the marked reduction of hospital admissions for the elderly because some patients did not present with acute symptoms and COVID-19 affects elderly groups severely—urging them to stay at home to prevent viral transmission.[17,33-35] In addition, the reduced number of hospital visits could have also influenced the pattern of SAH findings owing to the decreased hypertensive control among patients with a history of cerebrovascular disease.[36,37]

Table 1. Characteristics of Included Studies

Investigator	Study Design	Country	Sample Size (*n*)	Age (years)	Male Gender (%)	Control Period	Pandemic Period	NOS Score
Karthigeyan et al.,[16] 2021	Single-center, retrospective; prospective observational	India	3372	33.8	83.6	September 16, 2019 to March 24, 2020	March 25 to September 30, 2020	9
Goyal et al.,[17] 2020	Single-center, retrospective observational	India	284	33.45	75.7	March 25 to September 15, 2019	March 25 to September 25, 2020	9
Grassner et al.,[4] 2021	Multicenter, retrospective observational	Austria, Czech Republic, Switzerland	506	61.74 (NS)	57.4 (NS)	March 16 to April 15, 2017, 2018, 2019	March 16 to April 15, 2020	7
Horan et al.,[18] 2021	Single-center, retrospective observational	Ireland	658	64.7	63.07	March 1 to March 31, 2019	March 1 to March 31, 2020	8
Hecht et al.,[19] 2020	Single-center, retrospective observational	Germany	92	59.7 (NS)	50.3 (NS)	February 1 to April 15, 2019	February 1 to April 15, 2020	7
Lam et al.,[20] 2021	Single-center, retrospective observational	Taiwan	11,931	44	55.7	January 20 to April 30, 2019; May 11 to July 31, 2019	January 20 to April 30, 2020; May 11 to July 31, 2021	7
Lara-Reyna et al.,[21] 2020	Single-center, retrospective; prospective, observational	USA	150	66.2	66	November 2019 to February 2020	March to April 2020	8
Luostarinen et al.,[22] 2020	Single-center, retrospective observational	Finland	123	61.4	78.9	January to May 2019	January to May 2020	7
Manivannan et al.,[23] 2021	Single-center, retrospective observational	UK	597	65.9	59.7	April 4 to June 30, 2019	April 1 to June 30, 2020	9
Pinggera et al.,[24] 2020	Single-center, retrospective observational	Austria	122	58	60	March 16 to April 5, 2016, 2017, 2018, 2019	March 16 to April 5, 2020	8
Prawiroharjo et al.,[25] 2020	Single-center, retrospective observational	Indonesia	263	38.2	75.3	March 16 to June 14, 2019	March 16 to June 14, 2020	7
Rault et al.,[26] 2021	Single-center, retrospective observational	France	158	49.1	76.6	March 20, 2019 to March 17, 2020	March 18 to April 28, 2020	7
Santing et al.,[27] 2020	Single-center, retrospective; prospective observational	Netherlands	234	62.8	54.7	March 18 to April 6, 2019	March 18 to April 6, 2020	8

NOS, Newcastle-Ottawa scale; NS, not stated.

Table 2. Summary of Meta-Analysis Findings on General Outcomes of Traumatic Brain Injury

Outcome	OR (95% CI); P Value	Heterogeneity (%; P Value)	%	Studies (n)
Moderate to severe TBI				
LMICs	1.10 (0.90–1.36); P > 0.05	18.9; P = 0.29	49 versus 50	3
HICs	1.14 (0.80–1.61); P > 0.05	44; P = 0.10	17 versus 17	7
Overall	1.13 (0.96–1.34); P = 0.14	39%; P = 0.09	22 versus 22	10
Mortality				
LMICs	1.65 (1.12–2.41); P < 0.05*	40.8%; P = 0.18	43 versus 50	3
HICs	0.48 (0.14–1.69); P > 0.05	47.7; P = 0.15	20 versus 8	3
Overall	1.08 (0.58–2.01); P = 0.81	73.9; P = 0.001	38 versus 46	6
Neurological deficit, overall	0.64 (0.36–1.11); P = 0.11	0; P = 0.88	15 versus 9	3
Surgery				
LMICs	0.93 (0.59–1.46); P > 0.05	68.2; P = 0.08	28 versus 29	2
HICs	0.67 (0.41–1.10); P > 0.05	63.2; P = 0.02	4 versus 4	6
Overall	0.76 (0.53–1.08); P = 0.13	73.6; P < 0.001	10 versus 9	8

OR, odds ratio; CI, confidence interval; TBI, traumatic brain injury; LMICs, low- to middle-income countries; HICs, high-income countries.
*Statistically significant.

Table 3. Summary of Meta-Analysis Findings on Radiological Diagnosis

Radiological Diagnosis	OR (95% CI); P Value	Heterogeneity (%; P Value)	%	Studies (n)
EDH				
LMICs	0.76 (0.32–1.79); P > 0.05	84.8; P = 0.1	16 versus 15	2
HICs	1.35 (0.67–2.69); P > 0.05	0; P = 0.55	5 versus 5	3
Overall	0.94 (0.58–1.54); P = 0.81	51.7; P = 0.08	13 versus 13	5
SDH				
LMICs	0.79 (0.67–0.92); P < 0.05*	0.7; P = 0.32	33 versus 30	2
HICs	1.08 (0.63–1.86); P > 0.05	52; P = 0.12	44 versus 49	3
Overall	0.96 (0.67–1.37); P = 0.82	70.8; P = 0.01	35 versus 34	5
SAH				
LMICs	0.95 (0.41–2.19); P > 0.05	44.5; P = 0.18	11 versus 9	2
HICs	1.36 (1.00–1.84); P < 0.05*	0; P = 0.59	31 versus 38	2
Overall	1.15 (0.73–1.81); P = 0.56	71.4; P = 0.01	14 versus 15	4
Contusion				
LMICs	1.04 (0.90–1.19); P > 0.05	0; P = 0.57	54 versus 55	2
HICs	1.07 (0.76–1.51); P > 0.05	0; P = 0.77	18 versus 24	2
Overall	1.04 (0.92–1.18); P = 0.54	0; P = 0.93	48 versus 48	4
Skull fracture				
LMICs	0.94 (0.78–1.13); P > 0.05	0; P = 0.75	17 versus 16	2
HICs	0.71 (0.18–2.74); P > 0.05	66.3; P = 0.05	29 versus 30	2
Overall	1.01 (0.68–1.51); P = 0.94	53.6; P = 0.07	18 versus 17	4

OR, odds ratio; CI, confidence interval; EDH, epidural hematoma; LMICs, low- to middle-income countries; HICs, high-income countries; SDH, subdural hematoma; SAH, subarachnoid hemorrhage.
*Statistically significant.

Table 4. Summary of Meta-Analysis Findings on Cause of Traumatic Brain Injury

Cause of TBI	OR (95% CI); *P* Value	Heterogeneity (%; *P* Value)	%	Studies (*n*)
RTA				
LMICs	1.04 (0.79—1.38); $P > 0.05$	48.1; $P = 0.15$	62 versus 60	3
HICs	0.89 (0.42—1.91); $P > 0.05$	73.4; $P < 0.01$	14 versus 9	5
Overall	1.00 (0.72—1.38); $P = 0.99$	63.4; $P = 0.01$	48 versus 43	8
High fall, overall	1.17 (0.93—1.48); $P = 0.18$	0; $P = 0.43$	37 versus 42	3
Low and mechanical falls, overall	0.63 (0.39—1.03); $P = 0.07$	42.7; $P = 0.17$	52 versus 47	3
Assault				
LMICs	1.83 (1.37—2.45); $P < 0.05$*	0; $P = 0.78$	4 versus 7	2
HICs	1.14 (0.81—1.60); $P > 0.05$	0; $P = 0.59$	32 versus 40	4
Overall	1.40 (1.06—1.86); $P = 0.02$*	20.8; $P = 0.28$	6 versus 8	6

TBI, traumatic brain injury; CI, confidence interval; OR, odds ratio; RTA, road traffic accident; HICs, high-income countries; LMICs, low- to middle-income countries.
*Statistically significant.

Although the manifestation of TBI during the pandemic had altered, this could also have resulted from differences in the pattern of the mechanism of the injury itself. Overall, we did not find any differences in the proportion of RTAs and falls. In some of the HICs, the rate of RTA-related trauma had increased during the pandemic.[21] This could have been influenced by various factors that correlate with public mobility. A decrease in traffic as the result of country lockdowns and quarantines could yield empty roads and, thus, trigger speed-related vehicle collisions.[28,38] However, this shifted pattern was also found to vary across countries and was influenced by geographic differences, urban planning, and seasonal variations. States with hilly areas with narrow and curvaceous roads were more likely to have a higher rate of RTAs.[38,39]

Although most of the included studies had reported a decrease in surgical volumes, our pooled analysis found no significant differences in surgical interventions between the 2 periods (Supplementary Figure 4). A reduction in the surgical volume for TBI cases might have occurred from the measures taken by the authorities to maximize the resources required to manage the pandemic. However, we also noted that some studies had reported a greater proportion of surgical interventions, which affected our aggregated results and the heterogeneity.[16,20] This was likely because these studies had included patients from a period in which the lockdown regulations had been lifted. Recommendations, reviews, and viewpoints from many surgical bodies have emerged to guide hospitals to reallocate resources by postponing any elective cases and mobilizing more staff to join the COVID-19 care team.[4,40] In addition, the decreasing proportion of surgeries has also been attributed to the conversion of intensive care units from caring for elective patients to caring for patients with severe COVID-19.[1,41] Moreover, some hospitals were converted to dedicated COVID-19 isolation centers because the number of patients outweighed the availability of the hospitals.[42] Outpatient care management for nonemergency cases also gradually transitioned to telemedicine

because many spaces were dedicated to use for COVID-19 patients.[28,43,44] Taken together, these measures will eventually compromise the necessity for early management of TBI patients, causing them to progress to more severe TBI.

The present study had several limitations. Because the epidemiological pattern of TBI could vary greatly owing to differences in geographic factors, we have attempted to describe the current overall representation of how the pandemic influenced patients with TBI. In addition, the paucity of reported studies meant that we performed subset analyses according to the countries' income level. Also, because some countries had different regulations for requiring lockdown periods, this could have affected the pattern of admitted patients with TBI. Ultimately, more studies from different centers are required to strengthen the evidence illustrating the results of the measures taken to manage neurosurgical trauma cases at different centers.

CONCLUSIONS

Compared with before the pandemic, the TBI mortality rate had increased during the COVID-19 pandemic in the LMICs. In addition, the radiological findings showed a reduced rate of SDH in LMICs and an increased incidence of SAH in HICs. Our overall analysis showed an increased rate of assaults as the cause of TBI, especially in LMICs. We did not find any significant difference in surgical volumes between the 2 periods.

CRediT AUTHORSHIP CONTRIBUTION STATEMENT

Fachreza Aryo Damara: Conceptualization, Methodology, Formal analysis, Investigation, Writing — original draft, Writing — review & editing. **Galih Ricci Muchamad:** Investigation, Resources, Writing — original draft. **Anton Anton:** Writing — original draft. **Alfya Nandika Ramdhani:** Writing — original draft. **Ivan Christian Channel:** Writing — original draft. **Ahmad Faried:** Conceptualization, Resources, Supervision, Writing — review & editing.

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SUPPLEMENTARY DATA

APPENDIX

Search terms

(("Brain Injuries, Traumatic"[Mesh] OR Traumatic Brain Injury [tiab] OR "Brain Concussion"[Mesh] OR "Brain Injuries"[Mesh] OR Brain Injury[tiab] OR "Accidents, Traffic"[Mesh]) AND (Pandemic OR COVID-19 OR "COVID-19"[Mesh]))

R programming script

library(meta)

library(mada)

library(readxl)

#Odds ratio for Severity outcome

Document_name<- read_excel("Document location/Document_name.xlsx", sheet = "Severity")

View(Document_name)

data <- Document_name

OR_outcome <- metabin(Document_name$modsevere_pandemic, Document_name$total_pandemic, Document_name$modsevere_prepandemic, Document_name$total_prepandemic, sm = "OR", method = "I", comb.fixed = F, comb.random = T, data = Document_name, studlab = Document_name$study_id)

forest(OR_outcome, digits = 2, rightcols = c("effect", "ci"), xlab = " Odds Ratio", col.predict.lines = "red", col.random = "red")

#Odds ratio for Mortality outcome

Document_name<- read_excel("Document location/Document_name.xlsx", sheet = "Mortality")

View(Document_name)

data2 <- Document_name

OR_mortality <- metabin(Document_name$mortality_pandemic, Document_name$total_pandemic, Document_name$mortality_prepandemic, Document_name$total_prepandemic, sm = "OR", method = "I", comb.fixed = F, comb.random = T, data = Document_name, studlab = Document_name$study_id)

print(OR_mortality)

forest(OR_mortality, digits = 2, rightcols = c("effect", "ci"), xlab = " Odds Ratio", col.predict.lines = "red", col.random = "red")

#Odds ratio for Neurological deficit outcome

Document_name<- read_excel("Document location/Document_name.xlsx", sheet = "Neurological_deficit")

View(Document_name)

data3 <- Document_name

OR_ND <- metabin(Document_name$ND_pandemic, Document_name$total_pandemic, Document_name$ND_prepandemic, Document_name$total_prepandemic, sm = "OR", method = "I", comb.fixed = F, comb.random = T, data = Document_name, studlab = Document_name$study_id)

print(OR_ND)

forest(OR_ND, digits = 2, rightcols = c("effect", "ci"), xlab = "Odds Ratio", col.predict.lines = "red", col.random = "red")

#Odds ratio for Epidural hematoma

Document_name<- read_excel("Document location/Document_name.xlsx",sheet = "EDH")

View(Document_name)

Document_name$EDH_prepandemic <- Document_name$EDH_prepandemic + 0.5

Document_name$total_prepandemic <- Document_name$total_prepandemic + 0.5

Document_name$EDH_pandemic <- Document_name$EDH_pandemic + 0.5

Document_name$total_pandemic <- Document_name$total_pandemic + 0.5

OR_EDH <- metabin(Document_name$EDH_pandemic, Document_name$total_pandemic, Document_name$EDH_prepandemic, Document_name$total_prepandemic, sm = "OR", method = "I", comb.fixed = F, comb.random = T, data = Document_name, studlab = Document_name$study_id)

print(OR_EDH)

forest(OR_EDH, digits = 2, rightcols = c("effect", "ci"), xlab = "Odds Ratio", col.predict.lines = "red", col.random = "red")

#Odds ratio for Subdural hematoma

Document_name<- read_excel("Document location/Document_name.xlsx",sheet = "SDH")

View(Document_name)

OR_SDH <- metabin(Document_name$SDH_pandemic, Document_name$total_pandemic, Document_name$SDH_prepandemic, Document_name$total_prepandemic, sm = "OR", method = "I", comb.fixed = F, comb.random = T, data = Document_name, studlab = Document_name$study_id)

print(OR_SDH)

forest(OR_SDH, digits = 2, rightcols = c("effect", "ci"), xlab = "Odds Ratio", col.predict.lines = "red", col.random = "red")

#Odds ratio for Subarachnoid hemorrhage

Document_name<- read_excel("Document location/Document_name.xlsx", sheet = "SAH")

View(Document_name)

Document_name$SAH_prepandemic <- Document_name$SAH_prepandemic + 0.5

Document_name$total_prepandemic <- Document_name$total_prepandemic + 0.5

Document_name$SAH_pandemic <- Document_name$SAH_pandemic + 0.5

Document_name$total_pandemic <- Document_name$total_pandemic + 0.5

OR_SAH <- metabin(Document_name$SAH_pandemic, Document_name$total_pandemic, Document_name$SAH_prepandemic, Document_name$total_prepandemic, sm = "OR", method = "I", comb.fixed = F, comb.random = T, data = Document_name, studlab = Document_name$study_id)

print(OR_SAH)

forest(OR_SAH, digits = 2, rightcols = c("effect", "ci"), xlab = "Odds Ratio", col.predict.lines = "red", col.random = "red")

```
#Odds ratio for Contusion

Document_name<-    read_excel("Document    location/Doc-
ument_name.xlsx", sheet = "contusion")

View(Document_name)

Document_name$contusion_prepandemic <- Document_name$
contusion_prepandemic + 0.5

Document_name$total_prepandemic    <-    Document_name$
total_prepandemic + 0.5

Document_name$contusion_pandemic   <-   Document_name$
contusion_pandemic + 0.5

Document_name$total_pandemic <- Document_name$total_
pandemic + 0.5

OR_contusion   <-   metabin(Document_name$contusion_pan-
demic,   Document_name$total_pandemic,   Document_name$
contusion_prepandemic,    Document_name$total_prepandemic,
sm = "OR", method = "I", comb.fixed = F, comb.random = T,
data = Document_name, studlab = Document_name$study_id)

print(OR_contusion)

forest(OR_contusion, digits = 2, rightcols = c("effect", "ci"), xlab =
"Odds Ratio", col.predict.lines = "red", col.random = "red")

#Odds ratio for Skull fracture

Document_name<-    read_excel("Document    location/Doc-
ument_name.xlsx", sheet = "skull_fracture")

View(Document_name)

OR_SF    <-    metabin(Document_name$SF_pandemic,    Doc-
ument_name$total_pandemic,    Document_name$SF_prepan-
demic,   Document_name$total_prepandemic,   sm   =   "OR",
method = "I", comb.fixed = F, comb.random = T, data = Doc-
ument_name, studlab = Document_name$study_id)

print(OR_SF)

forest(OR_SF, digits = 2, rightcols = c("effect", "ci"), xlab =
"Odds Ratio", col.predict.lines = "red", col.random = "red")

#Odds ratio for Road traffic accident

Document_name<-    read_excel("Document    location/Doc-
ument_name.xlsx", sheet = "RTA")

View(Document_name)
OR_rta   <-   metabin(Document_name$rta_pandemic,   Doc-
ument_name$total_pandemic,    Document_name$rta_prepan-
demic,   Document_name$total_prepandemic,   sm   =   "OR",
method = "I", comb.fixed = F, comb.random = T, data = Doc-
ument_name, studlab = Document_name$study_id)

print(OR_rta, digits = 2)

forest(OR_rta, digits = 2, rightcols = c("effect", "ci"), xlab =
"Odds Ratio", col.predict.lines = "red", col.random = "red")

#Odds ratio for High fall

Document_name<-    read_excel("Document    location/Doc-
ument_name.xlsx", sheet = "high fall")

View(Document_name)

OR_fall   <-   metabin(Document_name$fall_pandemic,   Doc-
ument_name$total_pandemic,    Document_name$fall_prepan-
demic,   Document_name$total_prepandemic,   sm   =   "OR",
```

```
method = "I", comb.fixed = F, comb.random = T, data = Doc-
ument_name, studlab = Document_name$study_id)

print(OR_fall, digits = 2)

forest(OR_fall, digits = 2, rightcols = c("effect", "ci"), xlab =
"Odds Ratio", col.predict.lines = "red", col.random = "red")

#Odds ratio for Low fall

Document_name<-    read_excel("Document    location/Doc-
ument_name.xlsx", sheet = "low or mechanical fall")

View(Document_name)

OR_lowfall    <-    metabin(Document_name$lowfall_pandemic,
Document_name$total_pandemic,    Document_name$lowfall_
prepandemic, Document_name$total_prepandemic, sm = "OR",
method = "I", comb.fixed = F, comb.random = T, data =
Document_name, studlab = Document_name$study_id)

print(OR_lowfall, digits = 2)

forest(OR_lowfall, digits = 2, rightcols = c("effect", "ci"), xlab =
" Odds Ratio", col.predict.lines = "red", col.random = "red")

#Odds ratio for Assault/Violence

Document_name<-    read_excel("Document    location/Doc-
ument_name.xlsx", sheet = "assault")

View(Document_name)

OR_assault    <-    metabin(Document_name$assault_pandemic,
Document_name$total_pandemic,    Document_name$assault_
prepandemic, Document_name$total_prepandemic, sm = "OR",
method = "I", comb.fixed = F, comb.random = T, data =
Document_name, studlab = Document_name$study_id)

print(OR_assault, digits = 2)

forest(OR_assault, digits = 2, rightcols = c("effect", "ci"), xlab =
" Odds Ratio", col.predict.lines = "red", col.random = "red")

#Odds ratio for Surgical management

Document_name<-    read_excel("Document    location/Doc-
ument_name.xlsx", sheet = "surgery")

View(Document_name)

Document_name$surgery_prepandemic   <-   Document_name$
surgery_prepandemic + 0.5

Document_name$total_prepandemic <- Document_name$total_
prepandemic + 0.5

Document_name$surgery_pandemic <- Document_name$surgery_
pandemic + 0.5

Document_name$total_pandemic   <-   Document_name$total_
pandemic + 0.5

OR_surgery   <-   metabin(Document_name$surgery_pandemic,
Document_name$total_pandemic,    Document_name$surger-
y_prepandemic,   Document_name$total_prepandemic,   sm   =
"OR", method = "I", comb.fixed = F, comb.random = T, data =
Document_name, studlab = Document_name$study_id)

print(OR_surgery, digits = 2)

forest(OR_surgery, digits = 2, rightcols = c("effect", "ci"), xlab =
" Odds Ratio", col.predict.lines = "red", col.random = "red")
```

Study	Experimental Events Total	Control Events Total	Odds Ratio	OR	95%-CI
category = LMIC					
Karthigeyan et al, 2021	587 1113	1182 2259		1.02	[0.88; 1.17]
Goyal et al, 2020	70 129	69 155		1.48	[0.92; 2.36]
Prawiroharjo et al, 2020	30 157	17 106		1.24	[0.64; 2.38]
Random effects model	1399	2520		1.10	[0.90; 1.36]
Heterogeneity: $I^2 = 19\%$, $\tau^2 = 0.0098$, $p = 0.29$					
category = HIC					
Lam et al, 2021	697 4757	904 7190		1.19	[1.07; 1.33]
Lara-Reyna et al, 2020	12 49	16 101		1.72	[0.74; 4.00]
Luostarinen et al, 2020	46 67	34 56		1.42	[0.67; 2.98]
Manivannan et al., 2021	24 280	42 317		0.61	[0.36; 1.04]
Pinggera et al, 2020	4 13	32 109		1.07	[0.31; 3.72]
Rault et al, 2021	4 11	22 147		3.25	[0.88; 12.03]
Santing et al, 2020	1 91	5 143		0.31	[0.04; 2.67]
Random effects model	5268	8063		1.14	[0.80; 1.61]
Heterogeneity: $I^2 = 44\%$, $\tau^2 = 0.0789$, $p = 0.10$					
Random effects model	**6667**	**10583**		**1.13**	**[0.96; 1.34]**
Heterogeneity: $I^2 = 39\%$, $\tau^2 = 0.0176$, $p = 0.10$			0.1 0.5 1 2 10 Odds Ratio		

Supplementary Figure 1. Forest plot of traumatic brain injury severity. CI, confidence interval; HIC, high-income country; LMIC, low- to middle-income country; OR, odds ratio.

Study	Experimental Events Total	Control Events Total	Odds Ratio	OR	95%-CI
category = LMIC					
Karthigeyan et al, 2021	657.0 1113.0	1062.0 2259.0		1.62	[1.40; 1.88]
Goyal et al, 2020	29.0 129.0	16.0 155.0		2.52	[1.30; 4.89]
Prawiroharjo et al, 2020	12.0 157.0	9.0 106.0		0.89	[0.36; 2.20]
Random effects model	1399.0	2520.0		1.65	[1.12; 2.41]
Heterogeneity: $I^2 = 41\%$, $\tau^2 = 0.0541$, $p = 0.18$					
category = HIC					
Grassner et al, 2021	7.0 93.0	72.0 413.0		0.39	[0.17; 0.87]
Pinggera et al, 2020	2.0 13.0	11.0 109.0		1.62	[0.32; 8.27]
Rault et al, 2021	0.5 11.5	51.5 147.5		0.08	[0.00; 1.47]
Random effects model	117.5	669.5		0.48	[0.14; 1.69]
Heterogeneity: $I^2 = 48\%$, $\tau^2 = 0.5951$, $p = 0.15$					
Random effects model	**1516.5**	**3189.5**		**1.08**	**[0.58; 2.01]**
Heterogeneity: $I^2 = 74\%$, $\tau^2 = 0.3585$, $p < 0.01$			0.01 0.1 1 10 100 Odds Ratio		

Supplementary Figure 2. Forest plot of traumatic brain injury mortality. CI, confidence interval; HIC, high-income country; LMIC, low- to middle-income country; OR, odds ratio.

Study	Experimental Events	Total	Control Events	Total	Odds Ratio	OR	95%-CI
Hecht et al, 2020	6	41	9	51		0.80	[0.26; 2.47]
Luostarinen et al, 2020	9	67	11	56		0.63	[0.24; 1.66]
Santing et al, 2020	8	91	21	143		0.56	[0.24; 1.32]
Random effects model		199		250		0.64	[0.36; 1.11]
Heterogeneity: $I^2 = 0\%$, $\tau^2 = 0$, $p = 0.89$							

Supplementary Figure 3. Forest plot of neurological deficit. CI, confidence interval; OR, odds ratio.

Study	Experimental Events	Total	Control Events	Total	Odds Ratio	OR	95%-CI
category = LMIC							
Karthigeyan et al, 2021	323.0	1113.0	610.0	2259.0		1.11	[0.94; 1.30]
Goyal et al, 2020	36.0	129.0	56.0	155.0		0.68	[0.41; 1.13]
Random effects model		1242.0		2414.0		0.93	[0.59; 1.46]
Heterogeneity: $I^2 = 68\%$, $\tau^2 = 0.0784$, $p = 0.08$							
category = HIC							
Lam et al, 2021	44.0	4757.0	57.0	7190.0		1.17	[0.79; 1.73]
Lara-Reyna et al, 2020	6.0	49.0	21.0	101.0		0.53	[0.20; 1.42]
Luostarinen et al, 2020	32.0	67.0	31.0	56.0		0.74	[0.36; 1.50]
Manivannan et al., 2021	121.0	280.0	193.0	317.0		0.49	[0.35; 0.68]
Pinggera et al, 2020	0.5	13.5	34.5	109.5		0.08	[0.00; 1.45]
Rault et al, 2021	1.0	11.0	14.0	147.0		0.95	[0.11; 7.98]
Random effects model		5177.5		7920.5		0.67	[0.41; 1.10]
Heterogeneity: $I^2 = 63\%$, $\tau^2 = 0.1841$, $p = 0.02$							
Random effects model		6419.5		10334.5		0.76	[0.53; 1.08]
Heterogeneity: $I^2 = 74\%$, $\tau^2 = 0.1440$, $p < 0.01$							

Supplementary Figure 4. Forest plot of traumatic brain injury surgical intervention. CI, confidence interval; HIC, high-income country; LMIC, low- to middle-income country; OR, odds ratio.

Study	Experimental Events	Total	Control Events	Total	Odds Ratio	OR	95%-CI
category = LMIC							
Karthigeyan et al, 2021	180.0	1113.0	333.0	2259.0		1.12	[0.92; 1.36]
Goyal et al, 2020	15.5	129.5	35.5	155.5		0.46	[0.24; 0.88]
Random effects model		1242.5		2414.5		0.76	[0.32; 1.79]
Heterogeneity: $I^2 = 85\%$, $\tau^2 = 0.3334$, $p = 0.01$							
category = HIC							
Lara-Reyna et al, 2020	4.5	49.5	5.5	101.5		1.75	[0.48; 6.37]
Manivannan et al., 2021	12.0	280.0	10.0	317.0		1.37	[0.58; 3.23]
Pinggera et al, 2020	0.5	13.5	12.5	109.5		0.30	[0.02; 5.35]
Random effects model		343.0		528.0		1.35	[0.67; 2.69]
Heterogeneity: $I^2 = 0\%$, $\tau^2 = 0$, $p = 0.55$							
Random effects model		1585.5		2942.5		0.94	[0.58; 1.54]
Heterogeneity: $I^2 = 52\%$, $\tau^2 = 0.1395$, $p = 0.08$							

Supplementary Figure 5. Forest plot of epidural hematoma. CI, confidence interval; HIC, high-income country; LMIC, low- to middle-income country; OR, odds ratio.

Supplementary Figure 6. Forest plot of subdural hemorrhage. CI, confidence interval; HIC, high-income country; LMIC, low- to middle-income country; OR, odds ratio.

Supplementary Figure 7. Forest plot of subarachnoid hemorrhage. CI, confidence interval; HIC, high-income country; LMIC, low-to middle-income country; OR, odds ratio.

Supplementary Figure 8. Forest plot of contusion. CI, confidence interval; HIC, high-income country; LMIC, low- to middle-income country; OR, odds ratio.