

The Detailed Analysis of the Mechanisms Resulting to Lethal Outcome in Patients with Severe Traumatic Brain Injury

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Abstract The aim of the study was to conduct a detailed analysis of the mechanisms leading to lethality in patients with severe traumatic brain injury, as well as to study the clinical epidemiology and identify the main causes of hospital mortality at different stages of experiencing severe traumatic brain injury. A detailed analysis of the main causes of fatal outcomes in victims with severe traumatic brain injury who were admitted to the neurosurgical ICU of the Republican Research Center of Emergency Medicine for the period from 2023 to 2024 was performed in this article. The total number of admitted patients was 948: 699 (74%) of them were diagnosed with severe traumatic brain injury. The overall mortality differed by years and was 15.25% and 16.67%, respectively. Ninety-two patients out of 699 victims with traumatic brain injury died at various time after receiving the injury. There were 74 (80.4%) males and 26 (19.6%) females among the deceased. The mean age was 42.3±12.5 years. In 41.2% of patients the main cause of death was cerebral edema and dislocation, in 25.3% - massive blood loss and shock (traumatic and/or hemorrhagic), in 15.9% - purulent-septic complications. Sepsis and septicemia were the main cause of death in 18.5% of the patients, and the average duration of hospital stay was 28.4±16.5 days. Almost half of the patients had a combination of two or more complications. A statistically significant relationship between the severity of trauma, the development of infectious complications, the main causes of death, on the one hand, and the terms of fatal outcomes, on the other hand, was revealed.

Keywords Severe traumatic brain injury, Combined severe traumatic brain injury, Mortality, Main causes of death, Timing of death

1. Introduction

The injury epidemic has become one of the major medical and social problems in industrialized countries, requiring huge financial expenditures for its solution [1,2]. Traumatism ranks the 3rd and the 4th after cardiovascular diseases, stroke, respiratory diseases, and infectious diseases in the mortality structure of the population of economically developed and developing countries [3,4]. Modern scientific and practical achievements of medicine have allowed to slightly reduce lethality in combined severe traumatic brain injuries (CSTBI). However, traumatic brain injury and its consequences occupy one of the leading places in the structure of neurological morbidity, and this problem, despite the great attention that is constantly paid to it, is still topical [5].

According to the World Health Organization, the incidence of severe traumatic brain injury (STBI) is increasing by 2.2% per year, with an increasing incidence of more severe types

of injury [3,6,7]. Speaking about the mechanism of traumatic brain injury, in 40-50% of cases the cause is road traffic accidents (RTAs), in 17% of cases the injury occurs as a result of fights or attacks, and in about 13% the cause is catatrauma. In most cases, STBI is associated with other injuries, often with chest trauma (30-40% of all CSTBI cases). In 3-8% of STBI there are concomitant cervical spine injuries [1,8]. The high incidence of illness and mortality caused by traumatic brain injury, especially among young and able-bodied citizens, takes this pathology beyond the scope of a purely medical problem and elevates it to the level of one of the most important social issue [5,9].

According to the data of the Institute of Health under the Ministry of Health of the Republic of Uzbekistan, severe traumatic brain injury occupies one of the leading places in the structure of lethality, making from 10 to 50% of all traumatic injuries. Mortality in TBI is 5-10%, and in STBI it can reach 41-85%. In the combined STBI group, mortality varies from 25 to 75% according to scientific and practical literature, while overall mortality in combined STBI averages 32%. [1,10,11]. Road traffic accidents (RTAs) play a leading role among the main causes of CSTBI: from 50 to 60% of all

victims are participants in RTAs. Catastrauma also contributes to the increasing number of CSTBI victims. Catastrauma also contributes to the increasing number of CSTBI victims. They together account for 85-90% of all CSTBI victims. Train and household injuries account for 10-15%.

Severe traumatic brain injury is a complex diagnosis that combines multiple pathologic conditions, including diffuse axonal injury, localized contusion foci, and hematomas located in the epi- and subdural spaces. Numerous scientific and practical studies have focused on identifying the causes of adverse outcomes and risk factors contributing to mortality [1,12,13]. After the initial injury caused by the traumatic agent, various pathophysiologic mechanisms come into play, leading to the development of secondary organic lesions. These secondary damaging factors aggravate the condition in more than half of STBI patients. Posttraumatic hypotension observed in the early posttraumatic period significantly worsens the prognosis of the disease, provoking the development of chronic intracranial hypertension. Chronic intracranial hypertension is an extremely dangerous and destructive factor, causing up to 70% of deaths and increasing disability [14]. In patients with STBI, mortality is dramatically increased with simultaneous hypoxia and hypercapnia. At the same time, pathogenetic factors are not simply added up (for example: hypoxia and hypotension), but mutually enhance each other due to the commonality of individual pathogenetic mechanisms. As a result, an aggravating effect is created, leading to an even more unfavorable development of each of the coexisting processes. As a consequence, the course of trauma in victims of this group is more severe, with a greater risk of infectious complications and characterized by high mortality, especially in patients with CSTBI, where the number of adverse and fatal outcomes can exceed 80% [2,3,7,15].

Despite the successes achieved in recent decades, mortality in the group of STBI victims, according to various authors, remains high and reaches 70% [5,8,16]. Reducing mortality is a socially significant problem, as these are mostly patients of working age. In spite of this, we are still often unable to prevent fatal outcomes or serious lesions even in patients who are not initially considered severe. All this forces us to carefully analyze the reasons that led to the tragic outcome in order to prevent their repetition in the future.

The aim of the study was to conduct a detailed analysis of the mechanisms leading to lethality in patients with

severe traumatic brain injury, as well as to study the clinical epidemiology and identify the main causes of hospital mortality at different stages of experiencing severe traumatic brain injury.

2. Material and Methods

We conducted a retrospective analysis of 92 case histories and the results of forensic medical examination of patients who died with severe traumatic brain injury and were treated in the neurosurgical ICU of the Republican Research Center of Emergency Medicine for the period from 2023 to 2024.

The total number of admitted patients was 948: 699 (74%) of them were diagnosed with severe traumatic brain injury. The overall mortality differed by years and was 15.25% and 16.67%, respectively. Ninety-two patients out of 699 victims with traumatic brain injury died at various time after receiving the injury. Ninety-two patients out of 699 victims with traumatic brain injury died at various time after receiving the injury. There were 74 (80.4%) males and 26 (19.6%) females among the deceased. The mean age was 42.3 ± 12.5 years.

The age of the patients varied as follows: 14.9% of patients were from 17 to 20 years old, between 21 to 40 years old - 38.9%, between 41 to 50 years old - 35.9%, and over 50 years old there were 10.2%. TBI was associated with RTAs in 62.7% of the cases, 18.2% of the cases were related to catastrauma, 15.6% of the cases were household in nature, and 3.5% of the cases had an injury under unclear circumstances (Fig. 1).

Mortality was analyzed, including the main causes and timing of fatal outcomes (taking into account the results of forensic medical examination). Depending on the main causes of death, all deceased were divided into the five most common types of fatal outcomes:

- massive blood loss and shock,
- cerebral edema and dislocation,
- infectious pulmonary complications,
- purulent intoxication,
- other causes.

Depending on the time of death, all victims were divided into four groups: I (n=19) - up to 24 hours, II (n=20) - from 1 to 3 days, III (n=28) - from 3 to 10 days and IV (n=25) - more than 10 days. The structure of the victims' diagnosis is presented in Table 1.

Table 1. Structure of diagnosis of patients with severe traumatic brain injury

Diagnosis	Admitted		Died	
	2023	2024	2023	2024
Total number of admitted patients	402	546	63	91
Isolated blunt TBI	83	102	11	7
Isolated Penetrating TBI	70	100	4	11
Combined injury	113	164	8	27
Polytrauma	28	39	12	12
Total, %	294 (73.1%)	405(74.1%)	35(55.5%)	57(62.6%)

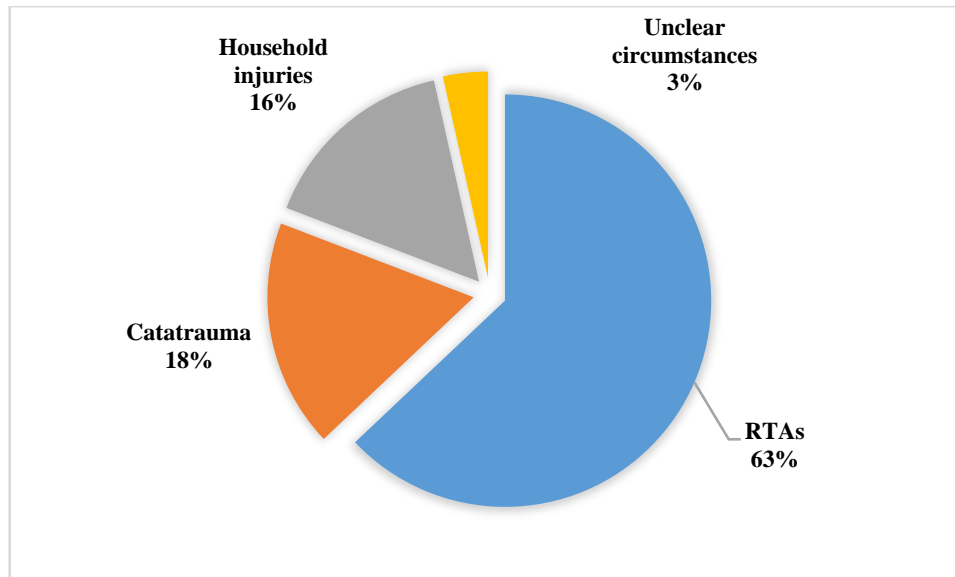


Figure 1. Mechanisms leading to severe traumatic brain injury

The level of consciousness was estimated using the Glasgow Coma Scale (GCS), and the severity of injuries was evaluated using the Injury Severity Score (ISS). Наряду с этим проанализирована частота развития инфекционных осложнений и их связь со сроками смерти.

Statistical processing of the data was performed using Excel program and Medcalc package. Data are presented as mean plus or minus standard deviation. To determine the relationship between factors, Spearman's rank correlation coefficient and Chi-square test for conjugation tables of traits were used.

3. Results

The structure of STBI in the considered sample of patients was as follows: a combination of head and chest injuries was present in 49 (56.5%) patients, abdominal injury - in 28 (30.4%) cases, musculoskeletal system injury - in 48 (52.17%) ones, facial injury - in 32 (34.7%), combination with spinal injury was revealed in 22 (24%) patients. At the same time, it should be noted that one third of the victims had injuries of three or more anatomical areas of the body.

The severity of injuries in patients was evaluated by ISS scale from 33 to 75 points (mean 54.4 ± 12.8 points), and the level of consciousness was assessed by GCS (mean 5.2 ± 2.4 points). In 6 patients compression of brain cisterns was detected at the initial CT scan, in 46 patients - displacement of medial structures more than 5 mm, intracerebral hematomas with the volume from 15 to 120 ml (evacuated surgically).

Those who died in the first 24 hours after trauma were patients with very severe injuries and depression of consciousness level to deep coma. The severity of their injuries was estimated at 64.6 ± 13.2 points on the ISS scale, and the level of consciousness according to the GCS was 4.2 ± 1.6 points. No infectious complications were noted. It was noticed

that as the severity of injuries decreased, the length of stay in the intensive care unit increased, but at the same time the incidence of infectious complications increased significantly. If by the 3rd day of patient's stay in the intensive care unit pneumonia was developed in 30% of them, then by the 10th day nosocomial pneumonia occurred in 100% of patients. Nineteen (20.6%) patients died in the first day, and 11 (57.9%) of those patients died within the first 7 hours of admission. There were 20 (21.7%) patients who died on days 1 to 3; 28 (30.4%) patients died on days 3 to 10 and 25 (27.2%) patients died on days more than 10. There was a statistically significant correlation between the severity of ISS scale injuries and the timing of death: the Spearman rank correlation coefficient was -0.637 (-0.718 ; -0.538), $p < 0.0001$ (Fig. 2).

The distribution of the injured depending on the main causes of death revealed the following: 41.2% ($n=38$) had brain edema and dislocation, 25.3% ($n=23$) - massive blood loss and shock, 13.2% ($n=12$) - purulent intoxication, 15.9% ($n=15$) - infectious pulmonary complications, and 4.4% ($n=4$) died from other causes (Fig. 3).

In group I patients ($n=19$), the main cause of death was massive blood loss and shock; the severity of injuries was estimated as 69.9 ± 8.7 points, and the level of consciousness was 3.9 ± 1.5 points. Their mean age was 42.4 ± 16.8 years. Upon admission of patients to the department, the monetized mean arterial pressure (MAP) was 23.0 mm Hg, heart rate (HR) was 60.2 beats/min, which indicated the extreme severity of this category of patients; 8 (8.7%) victims from this group were taken to the intensive care unit in a the condition of clinical death. Blood aspiration was noted in 10 patients (10.8%) and gastric contents were aspirated in one patient (1.08%). Thus, in the injured, whose main cause of death was massive blood loss and shock, the condition was evaluated as extremely severe and agonal. They died mostly in the first hours from the time of admission to the hospital

(more than 70% of them died in the first 3 hours from injuries incompatible with life) due to massive trauma of internal organs and main vessels. It should be noted that 65% of those who died were of working age (under 50 years). The average time of stay in the ICU for group I was 10.4 ± 2.1 hours.

When analyzing the medical records of 20 deceased (21.7%) included in group II, it turned out that the severity of their injuries was 48.7 ± 10.8 points, and the depression of the level of consciousness was noted at a level of 4.4 ± 1.2 points.

The mean age of the patients was 40.9 ± 12.9 years. Their hospital stay ranged from 24 to 72 hours. Upon admission of patients of group II to the intensive care unit, MAP was 74.6 mmHg, HR – 83.2 beats/min. Four patients in the group were admitted to hospital in a state of clinical death and experienced post-resuscitation illness. Blood aspiration was noted in 11 (55%) cases, and gastric contents were aspirated in 3 (15%) patients. Purulent tracheobronchitis and nosocomial pneumonia were diagnosed in 2 patients (11.9%).

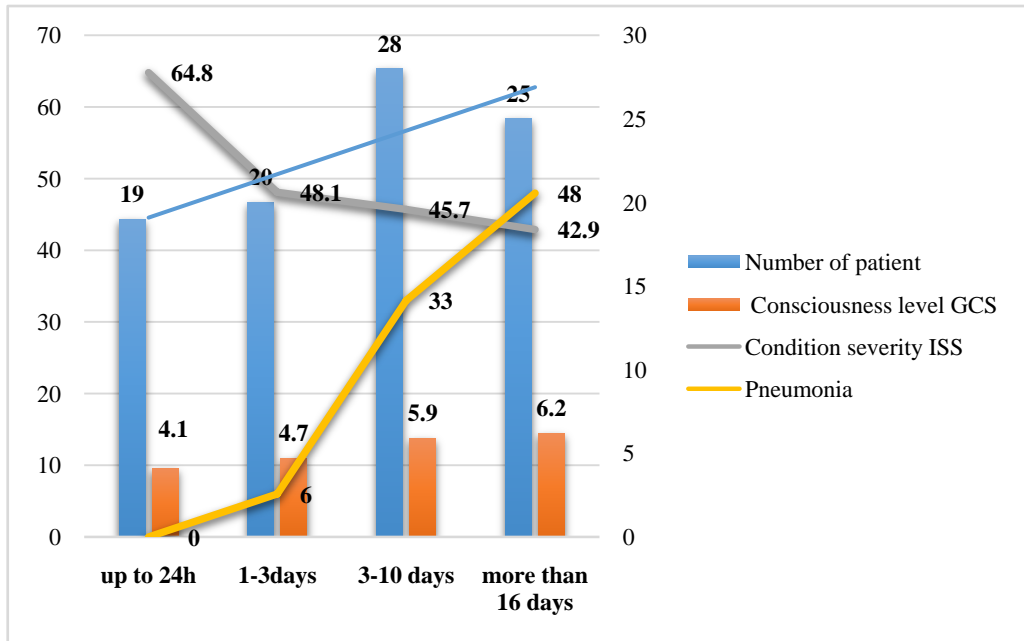


Figure 2. Characteristics of injury severity, level of consciousness and frequency of nosocomial pneumonia development in patients depending on the time of death

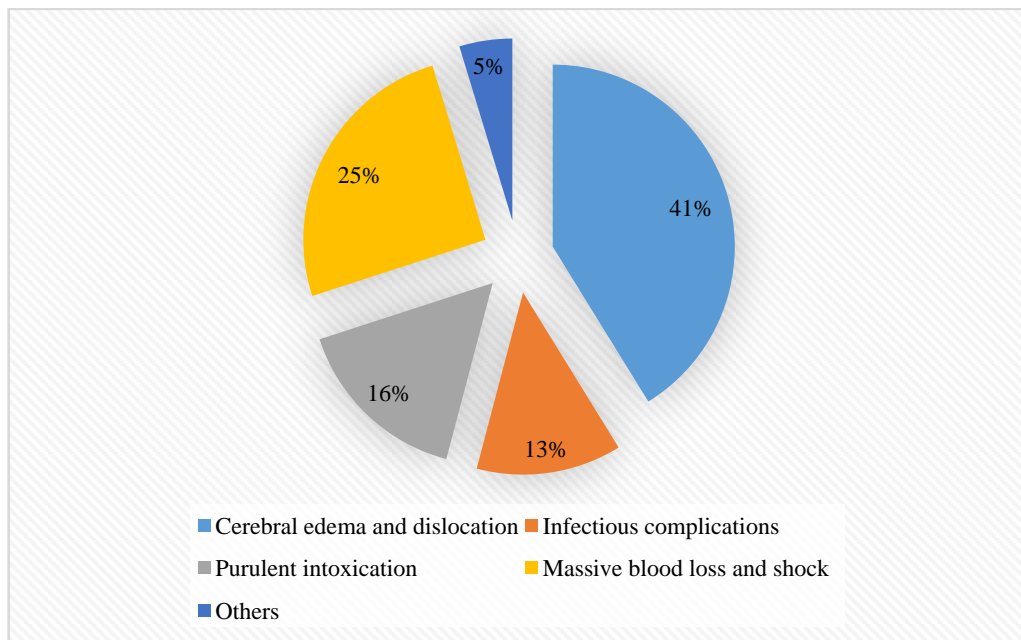


Figure 3. Distribution of patients depending on the main causes of death

Complications that developed in the deceased patients depending on the time of fatal outcomes are presented in Table 2.

Table 2. Infectious complications occurred in patients depending on the timing of fatal outcomes

Indices	Groups				Total
	I	II	III	IV	
Number of deceased patients	19	20	28	25	92
Nosocomial pneumonia	-	6	28	25	59
Vascular thrombosis	1	1	2	1	5
Pulmonary embolism	-	1	3	7	11
Pancreatitis	-	1	2	3	6
Bedsore	-	-	5	12	17
Acute erosions of the gastric mucosa	-	1	-	-	1
Purulent meningitis, ventriculitis and encephalitis	-	1	2	15	18
Sepsis	-	3	4	10	17

Thus, in group II, 6 (30%) patients died, and it should be noted that out of 6 patients, only 3 were found to have pneumonia at autopsy. One patient was diagnosed with mural thrombosis of the aorta and iliac arteries. One patient was found to have acute erosions of the gastric mucosa that were not diagnosed during life.

With increasing duration of stay in the intensive care unit, the incidence of infectious complications increases. Thus, out of 28 (30.4%) of those who died in group III, 100% were found to have nosocomial pneumonia. The following complications were also detected in patients of these two groups: postcatheterization thrombophlebitis of the brachial and superior vena cava in two patients; deep vein thrombosis of the shins with pulmonary embolism (TELA) - in 3 patients; thrombosis of the dura mater sinuses - in 1 patient and fat embolism of cerebral and pulmonary vessels - in 1 patient. In another 2 patients, the course of the injury was complicated by pancreatitis. Also in 3 patients pressure sores were formed due to tissue trophic disorder. The main cause of death in the patients was the increasing edema, ischemia and dislocation of the brain. The severity of STBI was aggravated by massive blood loss and shock, and in a part of the patients - by infectious complications, in 2 patients - by TELA and fat embolism - in one patient. When analyzing the case histories of group III, whose death occurred as a result of infectious complications (nosocomial pneumonia of varying severity (from small focal to focal-confluent abscessing, purulent tracheobronchitis), the severity of injury in 12 deceased was estimated at up to 49 points and in 13 - over 49 points. The mean age of the victims was 47.1 ± 15.2 years. Depression of the level of consciousness (GCS) up to 7 points was noted. The duration of hospital stay ranged from 3 to 10 days. Upon admission to the intensive care unit, MAP was 81.5 mmHg and HR was up to 94 beats/min. It should be noted that many patients had a combination of 2 and more clinical forms of complications. The main cause of death in all patients of this group was nosocomial pneumonia.

When analyzing the case histories of 25 deceased patients of group IV, whose death was due to purulent intoxication, the severity of injuries in 20 patients was estimated up to 49, and in 5 cases - over 49 points. The mean age of the patients was 45.2 ± 13.7 years. The level of consciousness was estimated at 7.1 points. The duration of hospital stay ranged from 10 to 16 days. At admission to the intensive care unit, MAP was 83.1 ± 13.4 mm Hg and HR was up to 120 beats/min. The complications which developed in group IV patients depending on the time of fatal outcomes differed from those who died in other groups: in addition to the fact that all of them had nosocomial pneumonia of different severity (from small-focal to focal-confluent abscessing) and purulent tracheobronchitis, there were many cases of purulent-septic complications. Septic thromboendocarditis of the mitral valve with septicopyemia was detected at autopsy in 3 patients, brain abscesses, purulent meningitis, encephalitis and ventriculitis were found in 15 patients. In 4 patients with multiple rib fractures pleural empyema was developed. Inflammation in the area of rib fracture sites, pelvic bones and lower limbs was detected in 2 patients. It should be noted that almost all patients who were treated for more than 10 days had a combination of two or more clinical forms of complications. The main cause of death in group IV patients who died in the remote period was purulent-septic complications that were developed against the background of multiorgan failure.

Seven patients died from combined STBI (ISS score 38) complicated by thromboembolism of large branches of the pulmonary artery. They were not diagnosed with deep vein thrombosis of the lower leg veins. Thus, a 36-year-old patient with combined STBI, pelvis and extremities (ISS score 45) died on the 11th day from acute renal failure.

4. Discussion

Analysis of the data showed that a greater number of victims die early from blood loss and shock (traumatic, hemorrhagic), but significantly more often fatal outcomes occur as a result of edema and dislocation of the brain, although at a later stage. According to the data, there is a statistically significant relationship between the timing of death depending on its main causes. According to the 5×4 contingency table, Chi-square is 164.007, the number of degrees of freedom is 12, and $p < 0.0001$.

Analyzing all groups of patients regardless of the time of admission, we can say that 41.2% of patients had brain edema and dislocation as the main cause of death, 25.3% had massive blood loss and shock (traumatic and/or hemorrhagic), and 15.9% had purulent-septic complications. Sepsis and septicemia were the main cause of death in 18.5% of the patients, and the mean time of the hospital stay was 28.4 ± 16.5 days. Almost half of the patients had a combination of two or more complications.

Thus, the retrospective detailed analysis of the case histories of STBI victims, as well as the features of their

clinical course and lethality, including the main causes and terms of death, showed that the combination of head and musculoskeletal system trauma prevailed in the overall structure of STBI (79%). This was followed by patients with a combination of head and chest injury (72%); combination of STBI with abdominal injury was noted in 31% and combination with spinal injury was present in 17% of cases. The performed forensic medical studies revealed that the main causes of death in 25.3% of cases were massive blood loss and shock mainly in the first 24 hours, with up to 75% of them dying in the first 6 hours after the injury. It should be noted that two thirds of patients had a combination of injuries of four or more anatomical areas of the body. These victims were extremely severe, one third of whom were brought to the hospital in a state of clinical death, the rest were in agonal and extremely severe condition, and the severity of injuries according to ISS was more than 70 points.

5. Conclusions

Edema and dislocation of the brain was the largest group of deceased patients, which accounted for 41.2% of the total. More than half of them died within 3 days from increasing edema, ischemia and dislocation of the brain, massive blood loss and shock; in the remaining victims, the severity of STBI was complicated by additional infectious complications. In these patients (12.9% of the total number), against the background of massive blood loss and prolonged shock, as well as prolonged mechanical ventilation, the severity of the injury was complicated by nosocomial pneumonia, which played a leading role in thanatogenesis.

Ethical Approval and Consent to Participate

The Research Ethics Board of our institution does not require review or approval of case reports. Our research was carried out in accordance with the World Medical Association Code of Ethics (Declaration of Helsinki).

Conflict of Interests

The authors declare no conflict of interest.

This study does not include the involvement of any budgetary, grant or other funds.

The article is published for the first time and is part of a scientific work.

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