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MORTALITY DETERMINANTS IN SEVERE TRAUMATIC BRAIN INJURY WITH PNEUMONIA: A RETROSPECTIVE STUDY

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ABSTRACT

Introduction: Traumatic brain injury (TBI) is defined as an acute brain injury caused by mechanical forces to the head, excluding those related to drugs, alcohol, medications, or other conditions, such as systemic injuries, psychological trauma, or coexisting medical issues. TBI is a global public health issue responsible for significant disability and mortality, with an estimated global incidence of 69 to over 100 million new cases annually. This burden may be higher due to underreporting, particularly in low- and middle-income countries (LMICs). Several methods have been established to classify TBI, one of them is based on its severity with the Glasgow Coma Score (GCS). Pneumonia is a frequent complication in traumatic brain injury (TBI) patients, especially those on prolonged mechanical ventilation. Pneumonia could be classified based on the source of infection into ventilator-associated pneumonia (VAP), hospital-associated pneumonia (HAP), and community-acquired pneumonia (CAP).
Objective: To evaluate the mortality and risk factors of severe traumatic brain injury (sTBI) with pneumonia.
Methods: This study is a cross-sectional study with observational analytical investigations. The sample of this study is sTBI patients who were treated in Dr. Soetomo General Academic Hospital in 2023. Descriptive statistics were used to summarize the patients' characteristics. Chi-square tests and logistic regression were used to find relationship between factors that increase the risk of death and the development of pneumonia.
Results: In 2023, we documented 832 TBI cases, of these, 479 cases (57.6%) were mild TBI, 273 cases (32.8%) were moderate brain injuries, while severe brain injuries (sTBI) with 80 cases (9.6%). Our study shows that 50% of patients with sTBI have pneumonia, and VAP itself is one of the contributing factors to mortality in this population ($p<0.001$).
Conclusion: Of all types of pneumonia in this study, there is a statistical correlation between mortality and VAP in sTBI patients.

Keywords: Developing Countries; Mortality; Pneumonia; Traumatic Brain Injury

ABSTRAK

Pendahuluan: Cedera otak traumatis (TBI) didefinisikan sebagai cedera otak akut yang disebabkan oleh kekuatan eksternal mekanik ke kepala, tidak termasuk yang terkait dengan obat-obatan, alkohol, pengobatan, atau kondisi lain seperti cedera sistemik, trauma psikologis, atau masalah medis yang terjadi bersamaan. TBI adalah masalah kesehatan masyarakat global yang bertanggung jawab atas kecacatan dan kematian yang signifikan, dengan perkiraan kejadian global 69 hingga lebih dari 100 juta kasus baru setiap tahunnya. Beban ini mungkin lebih tinggi karena kurangnya pelaporan, terutama di negara-negara berpenghasilan rendah dan menengah (LMIC). Beberapa sistem klasifikasi telah digunakan dalam praktik sehari-hari, salah satunya adalah berdasarkan derajat keparahan dengan menggunakan *Glasgow Coma Score* (GCS). Pneumonia merupakan komplikasi yang sering terjadi pada pasien cedera otak traumatis (TBI), terutama mereka yang menggunakan ventilasi mekanis dalam jangka panjang. Pneumonia dapat diklasifikasi berdasarkan dari sumber infeksinya menjadi *ventilator associated pneumonia* (VAP), *hospital associated pneumonia* (HAP), dan *community acquired pneumonia* (CAP).
Tujuan: Mengevaluasi faktor risiko yang berkontribusi pada tingkat mortalitas pada pasien cedera otak berat dengan pneumonia.
Metode: Penelitian ini merupakan penelitian cross-sectional dengan pendekatan analitik observasional. Sampel penelitian ini adalah pasien TBI yang dirawat di RSUD Dr. Soetomo pada tahun 2023. Statistik deskriptif digunakan untuk meringkas karakteristik pasien. Uji chi-square dan regresi logistik digunakan untuk mengidentifikasi hubungan antara faktor risiko mortalitas dengan kejadian pneumonia.
Hasil: Pada tahun 2023, kami mendokumentasikan 832 kasus TBI, dari jumlah tersebut, 479 kasus (57,6%) dengan cedera otak ringan, cedera otak sedang pada 273 kasus (32,8%), dan cedera otak berat (sTBI) pada 80 kasus (9,6%). Studi kami menunjukkan bahwa >50% pasien dengan sTBI menderita pneumonia, dan VAP sendiri merupakan salah satu faktor yang berkontribusi terhadap mortalitas pada populasi ini ($p<0,001$).
Kesimpulan: Dari semua jenis pneumonia, didapatkan korelasi pada tingkat mortalitas dan VAP.

Kata kunci: Negara Berkembang; Mortalitas; Pneumonia; Cedera Otak Traumatis

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INTRODUCTION

Traumatic brain injury (TBI) is defined as an acute brain injury caused by mechanical forces to the head, excluding those related to drugs, alcohol, medications, or other conditions such as systemic injuries, psychological trauma, or coexisting medical issues (1). TBI is typically classified by severity (mild, moderate, or severe), mechanism of injury (closed or penetrating), and clinical presentation (focal or diffuse injuries). The severity of a traumatic brain injury is usually measured using the Glasgow Coma Scale (GCS), where a score of 13-15 indicates a mild injury, 9-12 indicates a moderate injury, and 3-8 indicates a severe injury, which can lead to long periods of unconsciousness and a higher risk of death (2).

Closed TBIs, often caused by falls, motor vehicle accidents, or sports injuries, involve non-penetrating trauma that leads to brain movement within the skull. In contrast, penetrating TBIs, typically from objects breaching the skull, are linked with severe damage and increased mortality. Clinical presentation further divides TBIs into focal injuries, like contusions and hematomas, and diffuse injuries, such as diffuse axonal injury (DAI), which results from rotational forces and carries poor outcomes (2). Understanding these classifications is critical for optimizing treatment and improving patient outcomes.

TBI is a global public health issue responsible for significant disability and mortality, with an estimated global incidence of 69 to over 100 million new cases annually. This burden may be higher due to underreporting, particularly in low- and middle-income countries (LMICs) (3). In LMICs, road traffic accidents (RTAs) account for nearly 60% of all TBIs (4), while in high-income countries (HICs), falls especially among the elderly have become the leading cause, followed by motor vehicle accidents and sports-related injuries (5). Young males, particularly those aged 15-24, are disproportionately affected by TBIs due to risky behaviors like impaired driving and poor seatbelt use (2,6), while the elderly suffer primarily from fall-related TBIs due to factors like osteoporosis and cognitive impairment (2,7).

Differences in healthcare access and rehabilitation around the world make TBI outcomes worse, especially in LMICs, where there is not enough trauma care and medical help is often delayed, leading to more deaths and worse results (3). This indicates that it requires improved prevention strategies, public health education, and continued research to address the global burden of TBI (2,5).

Pneumonia is a common complication in TBI patients, particularly those requiring prolonged mechanical ventilation. Community-acquired pneumonia (CAP) happens outside of hospitals and is usually caused by germs like Streptococcus pneumoniae and Haemophilus influenzae, while hospital-acquired pneumonia (HAP) and ventilator-associated pneumonia (VAP) occur in patients in hospitals or on ventilators, often involving tougher germs like Pseudomonas aeruginosa and MRSA, which can lead to higher death rates (3). TBI mechanisms include blunt trauma, often seen in acceleration-deceleration injuries, leading to diffuse axonal injury (DAI) and coup-contrecoup damage, commonly from falls or car accidents. Penetrating injuries from bullets or shrapnel cause localized brain damage with high infection and mortality risks (2,5). Hypoxic-ischemic injuries, such as those following cardiac arrest, and repetitive head trauma, often seen in athletes and military personnel, further complicate TBI management, leading to chronic traumatic encephalopathy (CTE) (5,7).

In Indonesia, TBI patients frequently develop VAP, especially in ICUs where prolonged mechanical ventilation is common (3). The prevalence of pneumonia in severe TBI patients is high, reaching up to 40% in some studies, which points to the important of stringent infection control and timely management. Limited healthcare resources further contribute to delayed diagnosis and treatment, worsening patient outcomes in many regions (8). The long-term

consequences of TBI include chronic physical, cognitive, and emotional impairments, which place a heavy burden on healthcare systems, particularly in under-resourced regions.

This study aims to evaluate the mortality rates comprehensively and identify the associated risk factors of severe traumatic brain injury (sTBI) in patients with pneumonia in Dr. Soetomo General Academic Hospital, taking into account the impact of various clinical findings, secondary CT-scan findings, and microbiological culture. The authors specifically chose sTBI since it has an increased risk of VAP, mainly due to low GCS scores and prolonged use of mechanical ventilation.

METHODS

This study employed a retrospective observational design with a case-control approach. Data collection occurred from January to December 2023, focusing on patients diagnosed with severe traumatic brain injury (sTBI) admitted to Dr. Soetomo General Academic Hospital. All patients meeting the predetermined inclusion criteria throughout the designated study period were systematically enrolled, ensuring complete population capture rather than representative sampling. This thorough method removes any bias from sampling and gives strong evidence for assessing how VAP affects the risk of death in sTBI patients. The Commission of Ethics, Dr. Soetomo Academic General Hospital, granted the ethical clearance for this study on October 29th, 2024. (1808/LOE/301.4.2/X/2024)

The study population consisted of all patients with severe traumatic brain injury (GCS 3-8) admitted to Dr. Soetomo General Academic Hospital from January to December 2023. The inclusion criteria required patients to have a confirmed diagnosis of TBI and be admitted to the ICU. Exclusion criteria included penetrating craniocerebral injuries and cases complicated by coexisting conditions such as chronic infections and malignancies. The final sample consisted of all eligible patients during the study period.

Data were collected from patients' medical records, including written informed consent, demographic information, clinical history, types of surgical interventions, types of pathogens identified, pneumonia classification (community-acquired, hospital-acquired, or ventilator-associated), post-traumatic seizure history, CT imaging findings, and the presence of cranial base or impression fractures. Pneumonia diagnosis was confirmed through clinical criteria, radiological evidence, and microbiological testing. Patients with incomplete medical records or missing essential variables were excluded from the study to ensure data completeness.

Data were analyzed using both descriptive and inferential statistical methods with SPSS Statistics 30.0.0. Descriptive statistics were applied to summarize the characteristics of the patients, while chi-square tests and logistic regression were employed to identify associations between risk factors and pneumonia development. Odds ratios (ORs) and 95% confidence intervals (CIs) were calculated to determine the strength of associations. A p-value of < 0.05 was considered statistically significant.

RESULTS AND DISCUSSION

The demographic data for brain-injured patients at Dr. Soetomo General Academic Hospital show a total of 832 documented cases, classified according to the Glasgow Coma Score (GCS). Of these, 479 cases (57.6%) were categorized as mild, representing the majority of brain injuries. Moderate brain injuries accounted for 273 cases (32.8%), while severe brain injuries (sTBI) were the least common, with only 80 cases (9.6%). Due to incomplete patient data, this study focused on 74 cases of sTBI.

The survival outcomes of the 74 patients with severe traumatic brain injury (sTBI) with pneumonia incidence were also analyzed. Among these patients, 39 developed pneumonia, while 35 did not. Overall, 38 patients succumbed to their injuries, while 36 survived. Of the 39 patients with pneumonia, 25 (64.1%) passed away, compared to

13 (37.1%) fatalities among the 35 patients who did not develop pneumonia. This suggests that pneumonia, particularly ventilator-associated pneumonia (VAP), may significantly contribute to mortality in sTBI patients.

Table 1 records the sTBI patients with epidural hemorrhage (EDH) and their rate of mortality. For patients with EDH, 30 cases were documented. Among them, 11 patients had EDH without any other associated lesions. However, for the remaining 19 patients who had additional lesions, the mortality rate reached up to 84%, suggesting that the presence of additional lesions may worsen the outcome in EDH cases.

Table 1. Demographics of sTBI patients with EDH

EDH incidence		Survive N (%)	Dead N (%)	Total N (%)
EDH (N=30)	With other lesions (n=19)	3 (16)	16 (84)	19 (100)
	Without other lesions (n=19)	7 (64)	4 (36)	11 (100)
Non-EDH (N=50)		32 (64)	18 (36)	50 (100)

In SAH cases, there were 26 patients, three of whom had no other lesions. The survival rate for patients without additional lesions, the percentage was 33%. However, for the 23 patients with additional lesions, the mortality rate reached 61%, indicating that SAH in conjunction with other injuries is associated with poorer outcomes. The details are shown in Table 2.

Table 2. Demographics of sTBI patients with SAH

SAH incidence		Survive N (%)	Dead N (%)	Total N (%)
SAH (N=26)	With other lesions (n=23)	9 (39)	14 (61)	23 (100)
	Without other lesions (n=3)	1 (33)	2 (67)	3 (100)
Non-SAH (N=54)		35 (59)	22 (41)	54 (100)

Subdural hemorrhage (SDH) involved 41 patients, of whom only 3 had isolated SDH without other lesions, as shown in Table 3. The mortality rate in this group was 47%. Among the remaining 38 patients with additional lesions, the mortality rate was 45%, further highlighting the high mortality risk associated with SDH, with or without associated lesions.

Table 3. Demographics of sTBI patients with SDH

SDH Incidence		Survive N (%)	Dead N (%)	Total N (%)
SDH (N=41)	With other lesions (n=38)	21 (55)	17 (45)	38 (100)
	Without other lesions (n=3)	0 (0)	3 (100)	3 (100)
Non-SDH (n=39)		21 (53)	18 (47)	39 (100)

Intracranial hemorrhage (ICH) was present in 29 patients, with 4 cases involving isolated ICH. The survival rate in isolated ICH is 75%. However, among the 25 patients with ICH and additional lesions, the survival rate dropped dramatically to 36% (only 9 out of 25 survived). This suggests that while isolated ICH may have a favorable prognosis, the presence of additional lesions significantly worsens the outcome. Table 4 demonstrates sTBI patients with pneumonia and ICH.

Table 4. Demographics of sTBI patients with ICH

ICH Incidence		Survive N (%)	Dead N (%)	Total N (%)
ICH (N=29)	With other lesions (n=25)	9 (36)	16 (64)	25 (100)
	Without other lesions (n=4)	1 (25)	3 (75)	4 (100)
Non-ICH (N=51)		31 (68)	19 (32)	51 (100)

The study also classified pneumonia types in sTBI patients and examined their association with survival outcomes. Of the 40 cases of pneumonia, 27 resulted in death, and 13 patients survived. Ventilator-associated pneumonia (VAP) was linked to the highest mortality, with 24 out of 33 patients succumbing to their illness. Hospital-acquired pneumonia (HAP) was observed in 4 cases, with only 1 fatality and 3 survivors. Community-acquired pneumonia (CAP), which was documented in 3 patients, showed the most favorable outcome, with all patients recovering. This data indicates that VAP is strongly associated with higher mortality rates compared to HAP and

CAP. The distribution of sTBI patients with and without pneumonia is described in Table 5.

Table 5. The distribution of sTBI patients associated with pneumonia

Characteristics	VAP	HAP	CAP	Non-pneumonia	Total
Number of patients (n (%))	33 (41.25)	4(5)	3 (3.75)	40(50)	80 (100)
Mortality (n (%))					
Survive	9(11)	1(1)	3(3)	27(34)	42(52)
Dead	24(30)	3(3)	0(0)	11(16)	38(48)

In terms of pathogens, *Klebsiella pneumoniae* was the most common organism identified, responsible for 11 infections. *Pseudomonas aeruginosa* and *Enterobacter cloacae* each accounted for 5 cases. Other significant pathogens included *Acinetobacter baumannii*, *Staphylococcus aureus, and Staphylococcus coagulase*, each causing 2 infections. Additionally, there was 1 case of infection caused by COVID-19. The "Others" category, which included rare pathogens such as *Stenotrophomonas maltophilia*, *Proteus mirabilis*, and *Klebsiella aerogenes*, accounted for 12 cases. This distribution highlights *Klebsiella pneumoniae* as the leading pathogen in these pneumonia cases, as shown in Table 6.

Table 6. Etiology of pneumonia in sTBI patients

Microbacteria	Total
Klebsiella pneumoniae	11
Pseudomonas aeruginosa	5
Enterobacter cloacae	5
Acinetobacter baumannii	2
Staphylococcus aureus	2
Staphylococcus coagulase	2
Covid-19	1
Others (Stenotropomonas maltophilia, Proteus mirabilis, Klebsiella aerogenes)	12

Patients with acute neurological impairment, such as traumatic brain injury (TBI), and stroke, are at a higher risk of developing pneumonia due to compromised protective reflexes and the increased likelihood of aspiration (9). In a study involving 74 patients with severe TBI (sTBI), those who developed pneumonia had a significantly higher mortality rate of 64.1% compared to 37.1% in those without pneumonia. Ventilator-associated pneumonia (VAP) was particularly lethal, with a mortality rate of 77.4%, underscoring its severity. Hospital-acquired pneumonia (HAP), although less deadly, still had a notable mortality rate of 20%. These findings align with other studies that have shown VAP to be associated with longer ICU stays, increased complications, and worsened outcomes in sTBI patients (10).

Our study confirms that VAP significantly impacts mortality in sTBI patients ($p < 0.001$, CI = 95%), driven by prolonged mechanical ventilation and extended ICU stays, as shown in Table 7. This multivariate analysis of sTBI mortality factors reveals pneumonia as the sole statistically significant predictor (OR = 1.854, $p = 0.01$), nearly doubling mortality risk. Notably, ventilator-associated pneumonia (VAP) showed the strongest univariate association ($p < 0.001$) but lost significance in multivariate modeling, suggesting confounding variables. Other factors, including multitrauma, culture positivity, various hemorrhage types (ICH, SAH, SDH, EDH), skull base fractures, and surgical interventions, demonstrated no significant independent association with mortality outcomes.

This is supported by Marjanovic et al. (11), who found that VAP in sTBI patients leads to higher illness rates and a trend towards increased mortality. Furthermore, Plurad et al. (12) demonstrated that bilateral dependent consolidation observed on chest CT scans upon admission can predict VAP occurrence and is independently associated with increased mortality in severe TBI cases. This suggests that VAP has a profound impact on patient outcomes, especially in those with predisposing factors.

The elevated risk of pneumonia following TBI can be attributed to both mechanical factors, such as the increased likelihood of aspirating oropharyngeal contents and immunological factors. TBI often leads to immune suppression, making patients more vulnerable to infections. Vermeij et al. demonstrated in an experimental

model that TBI-induced immune suppression is driven by an imbalance in acetylcholine, linked to increased vagal tone, resulting in immunoparalysis. This condition complicates the body's ability to fight off infections like pneumonia.

Table 7. Multivariate analysis of related factors to mortality in sTBI patients

Determinant	Univariate Analysis		Multivariate Analysis	
	Chi-square (χ^2)	p-value	Odds Ratio (OR)	p-value
Pneumonia	15.557	**0.001***	1.854	0.11**
VAP	11.707	**<0.001***	-	-
HAP	0.094	0.759	-	-
CAP	1.397	0.237	-	-
Multitrauma	0.222	0.683	0.473	0.386
Culture	12.65	0.081	1.084	0.58
SBF	0.343	0.558	**2.826**	0.078
Impression	0.802	0.37	2.552	0.344
Constusio	1.928	0.165	0.462	0.187
ICH	2.256	0.133	1.784	0.334
SAH	0.622	0.43	2.252	0.251
SDH	0.222	0.638	0.975	0.971
ICH	0.334	0.563	0.685	0.538
Surgical intervention	4.766	0.312	1.11	0.566

VAP: ventilator-associated Pneumonia; HAP: hospital-acquired pneumonia.; CAP: community-acquired pneumonia; SBF: skull base fracture; ICH: intracranial hemorrhage; SAH: subarachnoid hemorrhage; SDH: subdural hemorrhage; EDH: epidural hemorrhage

*Based on the chi-square test, significant if $\alpha < 0.05$

**Based on the logistic regression test, significant if $\alpha < 0.05$

The connection between the central nervous system (CNS) and the immune system plays a pivotal role in the development of immunoparalysis following TBI. When the blood-brain barrier (BBB) is disrupted, immune cells and inflammatory mediators enter the CNS, activating microglia and attracting peripheral immune cells. While this immune response is initially aimed at limiting further damage and initiating repair, it can become dysregulated, resulting in excessive inflammation. This heightened inflammatory response not only exacerbates brain injury but also weakens systemic immune function, a hallmark of immunoparalysis (13).

The autonomic nervous system (ANS) also contributes significantly to immune regulation post-TBI. During the acute phase of TBI, the sympathetic nervous system (SNS) is activated, leading to the release of catecholamines like adrenaline and noradrenaline, which suppress immune cell function. This reduces the body's ability to combat infections. Conversely, the parasympathetic nervous system (PNS) exerts an anti-inflammatory effect through the cholinergic anti-inflammatory pathway, mediated by the vagus nerve, which inhibits pro-inflammatory cytokine production (14).

Additionally, neurohormonal changes, particularly in the hypothalamic-pituitary-adrenal (HPA) axis, play a critical role in immunosuppression following TBI. The activation of the HPA axis leads to increased cortisol levels, which suppress immune responses by reducing cytokine production and limiting immune cell proliferation. These neurohormonal effects further compromise the immune system's ability to respond to infections such as pneumonia (15).

Ventilator-associated pneumonia (VAP) was defined as pneumonia occurring 48 hours or more after endotracheal intubation, meeting at least two of the following criteria: fever greater than 38.3°C, leukocytosis or leukopenia, and purulent tracheal secretions. Among patients with severe traumatic brain injury (sTBI), the mortality rate for VAP in patients with severe traumatic brain injury (sTBI) is particularly high, with 77.4% (24 out of 31) of those affected succumbing to the condition, often

exacerbated by prolonged mechanical ventilation and the resultant complications. In comparison, hospital-acquired pneumonia (HAP) showed a mortality rate of 20% (1 out of 5), indicating a considerably lower impact than VAP. Notably, none of the three patients who developed community-acquired pneumonia (CAP) died, reflecting a relatively better prognosis for sTBI patients with CAP. However, it is important to acknowledge the limited sample size for CAP and HAP, which introduces bias into these findings.

Previous studies corroborate the detrimental effect of pneumonia, especially VAP, on outcomes in TBI patients. Kesinger et al. (16) demonstrated that hospital-acquired pneumonia significantly worsened long-term outcomes in sTBI patients. Similarly, Li et al. (17) identified VAP as a frequent complication in TBI patients, associated with extended ICU stays and increased morbidity.

Although our study did not establish a statistically significant relationship between specific pathogens and mortality, it was observed that Klebsiella pneumoniae was the most common pathogen responsible for VAP (35.4%). *K. pneumoniae* is a globally recognized pathogen, often associated with VAP and heightened mortality, particularly due to its multidrug-resistant (MDR) strains. Studies highlight the global prevalence of *K. pneumoniae* in ICU patients, especially in countries such as China, India, and Iran, where carbapenem resistance has become a growing concern (18,19). The mortality rate in patients with K. pneumoniae VAP can exceed 40%, particularly when carbapenem-resistant strains or Klebsiella pneumoniae carbapenemase (KPC)-producing strains are involved (20). Early detection and tailored antimicrobial therapy, including the use of polymyxins, have been shown to improve outcomes, although MDR pathogens continue to present major treatment challenges (21).

In patients with severe TBI, Klebsiella pneumoniae VAP is associated with poor clinical outcomes, particularly when MDR strains are involved. A meta-analysis by Li et al. (22) reported a 36% incidence of VAP in TBI patients, risk factors such as blood transfusion and high injury severity scores contribute to the increased likelihood of VAP, with the odds ratio (OR) for the injury severity score being 4.65 (95% CI: 1.96–7.34, $p < 0.001$), indicating a strong correlation between more severe injuries and the risk of VAP. Moreover, patients with VAP had significantly longer mechanical ventilation (OR: 5.45; 95% CI: 3.78–7.12) and hospital stays (OR: 10.92; 95% CI: 9.12–12.72), indicating the heavy burden of this complication.

Xu et al. (19) further emphasized the role of carbapenem-resistant K. pneumoniae (CRKP) in VAP among TBI patients, identifying ICU stays longer than 7 days (OR: 2.793; 95% CI: 1.439–5.421, $p < 0.01$) and previous antibiotic use (OR: 1.977; 95% CI: 1.025–3.812, $p < 0.05$) as major risk factors for CRKP infection. Mortality was significantly higher in CRKP-infected patients, highlighting the complexity of managing such resistant infections.

Chen et al. (23) reported a 42% incidence of VAP in TBI patients, highlighting its substantial impact on survival, particularly in critically injured patients. Tsikritsaki et al. (24) supported these findings by showing that VAP extended mechanical ventilation and ICU stays, while also increasing mortality, especially in older patients with comorbidities. These findings collectively underscore the urgent need for effective prevention and control measures for VAP in sTBI patients.

While community-acquired pneumonia (CAP) theoretically leads to high mortality, especially within the first 30 days of hospitalization (25,26), factors such as advanced age, comorbidities, and illness severity are critical contributors to poor outcomes (27–29). Studies also indicate long-term mortality associated with CAP, suggesting that its effects extend beyond the initial hospitalization period (30). Early intervention is key to reducing mortality in CAP cases (31,32).

Hospital-acquired pneumonia (HAP) is another significant cause of mortality, particularly in hospitalized patients with severe underlying conditions. HAP, occurring after at least 48 hours

in the hospital, is often caused by multidrug-resistant bacteria, complicating treatment and increasing mortality rates. Research indicates that HAP-related mortality can reach up to 30%, with more aggressive bacteria and compromised immune systems contributing to poorer outcomes (33). Despite these associations, our study was unable to demonstrate statistically significant relationships between CAP (p = 1.397, CI = 95%) and HAP (p = 0.094, CI = 95%) with mortality in sTBI patients, which is a limitation of the research.

While VAP had a statistically significant effect on mortality, our study did not establish a statistically significant relationship between CAP or HAP and mortality, likely due to the limited sample size. Nonetheless, pneumonia remains a critical complication in sTBI, emphasizing the need for enhanced prevention, early intervention, and targeted antimicrobial therapy to improve patient survival and reduce the burden of infection in this vulnerable population.

CONCLUSION

This study reinforces the significant impact of pneumonia, particularly ventilator-associated pneumonia (VAP), on mortality in patients with severe traumatic brain injury (sTBI). VAP, driven by prolonged mechanical ventilation and immune suppression, was associated with a higher mortality rate, highlighting the need for early detection and prevention strategies. Hospital-acquired pneumonia (HAP) also contributed to increased mortality, albeit to a lesser extent. The high prevalence of multidrug-resistant pathogens, especially *Klebsiella pneumoniae*, further complicates treatment and underscores the importance of stringent infection control measures in reducing VAP-related mortality.

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Conflict of Interest

The authors declare there are no conflicts of interest in this study.

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Authors' Contributions

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REFERENCES

1. Lefevre-Dognin C, Cogné M, Perdrieau V, Granger A, Heslot C, Azouvi P. Definition and epidemiology of mild traumatic brain injury. Neurochirurgie. 2021;67(3):218–21. [PubMed]
2. Maas AIR, Menon DK, Adelson PD, Andelic N, Bell MJ, Belli A, et al. Traumatic brain injury: integrated approaches to improve prevention, clinical care, and research. Lancet Neurol. 2017; 16(12): 987–1048. [PubMed]
3. Dewan MC, Rattani A, Gupta S, Baticulon RE, Hung YC, Punchak M, et al. Estimating the global incidence of traumatic brain injury. J Neurosurg. 2018; 130(4): 1080–97. [PubMed]
4. Hyder AA, Wunderlich CA, Puvanachandra P, Gururaj G, Kobusingye OC. The impact of traumatic brain injuries: a global perspective. NeuroRehabilitation. 2007; 22(5): 341–53. [PubMed]
5. Roozenbeek B, Maas AIR, Menon DK. Changing patterns in the epidemiology of traumatic brain injury. Nat Rev Neurol. 2013; 9(4): 231–6. [PubMed]
6. Rubiano AM, Carney N, Chesnut R, Puyana JC. Global neurotrauma research challenges and opportunities. Nature. 2015; 527(7578): S193–7. [PubMed] [Website]
7. Stocchetti N, Maas AIR. Traumatic intracranial hypertension. New England Journal of Medicine. 2014; 370(22): 2121–30. [PubMed]
8. Najem D, Rennie K, Ribecco-Lutkiewicz M, Ly D, Haukenfrers J, Liu Q, et al. Traumatic

brain injury: classification, models, and markers. Biochemistry and cell biology. 2018; 96(4): 391–406. [PubMed]
9. Vermeij JD, Aslami H, Fluiter K, Roelofs JJ, van den Bergh WM, Juffermans NP, et al. Traumatic brain injury in rats induces lung injury and systemic immune suppression. J Neurotrauma. 2013; 30(24): 2073–9. [PubMed]
10. Jovanovic B, Milan Z, Djuric O, Markovic-Denic L, Karamarkovic A, Gregoric P, et al. Twenty-eight-day mortality of blunt traumatic brain injury and co-injuries requiring mechanical ventilation. Medical principles and practice. 2016; 25(5): 435–41. [PubMed]
11. Marjanović V, Novak V, Veličković L, Marjanović G. The incidence and risk factors of ventilator-associated pneumonia in patients with severe traumatic brain injury. Med Pregl. 2011; 64(7–8): 403–7. [PubMed] [Website]
12. Plurad DS, Kim D, Bricker S, Lemesurier L, Neville A, Bongard F, et al. Ventilator-associated pneumonia in severe traumatic brain injury: the clinical significance of admission chest computed tomography findings. Journal of surgical research. 2013; 183(1): 371–6. [PubMed] [Science Direct]
13. Thal SC, Neuhaus W. The blood–brain barrier as a target in traumatic brain injury treatment. Arch Med Res. 2014; 45(8): 698–710. [PubMed] [Science Direct]
14. Purkayastha S, Stokes M, Bell KR. Autonomic nervous system dysfunction in mild traumatic brain injury: a review of related pathophysiology and symptoms. Brain Inj. 2019; 33(9): 1129–36. [PubMed]
15. Sribnick EA, Popovich PG, Hall MW. Central nervous system injury–induced immune suppression. Neurosurg Focus. 2022; 52(2): E10. [PubMed] [Website]
16. Kesinger MR, Kumar RG, Wagner AK, Puyana JC, Peitzman AP, Billiar TR, et al. Hospital-acquired pneumonia is an independent predictor of poor global outcome in severe traumatic brain injury up to 5 years after discharge. Journal of Trauma and Acute Care Surgery. 2015; 78(2): 396–402. [PubMed]
17. Gao B, Li X, Yang F, Chen W, Zhao Y, Bai G, et al. Molecular epidemiology and risk factors of ventilator-associated pneumonia infection caused by carbapenem-resistant enterobacteriaceae. Front Pharmacol. 2019; 10: 262. [PubMed] [Website]
18. Gu D, Dong N, Zheng Z, Lin D, Huang M, Wang L, et al. A fatal outbreak of ST11 carbapenem-resistant hypervirulent Klebsiella pneumoniae in a Chinese hospital: a molecular epidemiological study. Lancet Infect Dis. 2018; 18(1): 37–46. [PubMed] [Website]
19. Xu H, Huo C, Sun Y, Zhou Y, Xiong Y, Zhao Z, et al. Emergence and molecular characterization of multidrug-resistant Klebsiella pneumoniae isolates harboring bla CTX-M-15 extended-spectrum β-lactamases causing ventilator-associated pneumonia in China. Infect Drug Resist. 2018; 33–43. [PubMed] [Website]
20. Wirtz MR, Moekotte J, Balvers K, Admiraal MM, Pittet JF, Colombo J, et al. Autonomic nervous system activity and the risk of nosocomial infection in critically ill patients with brain injury. Intensive Care Med Exp. 2020; 8: 1–14. [PubMed] [Website]
21. Hasan MJ, Sumi CD, Huq SMR, Anam AM, Rabbani R. Aerosolized plus intravenous polymyxin B versus colistin in the treatment of pandrug-resistant klebsiella pneumonia-mediated ventilator-associated pneumonia: A retrospective cohort study in Bangladesh. The Journal of Critical Care Medicine. 2023; 9(2): 106–15. [PubMed]
22. Li Y, Liu C, Xiao W, Song T, Wang S. Incidence, Risk Factors, and Outcomes of Ventilator-Associated Pneumonia in Traumatic Brain Injury: A Meta-analysis. Neurocrit Care. 2020; 32(1): 272–85. [PubMed]
23. Chen S, Gao G, Xia Y, Wu Z. Incidence rate and risk factors of ventilator-associated pneumonia in patients with traumatic brain injury: a systematic review and meta-analysis

of observational studies. J Thorac Dis. 2023; 15(4): 2068. [PubMed] [Website]
24. Tsikritsaki K, Koukoulitsios G, Dimakou K, Lavdas K, Tsoulou V, Kalatzis I, et al. A41 Incidence and Outcome of Ventilator Associated Pneumonia in Traumatic Brain Injury Patients. European Journal of Anaesthesiology. 2012; 29: S12. [Website]
25. Eurich DT, Marrie TJ, Minhas-Sandhu JK, Majumdar SR. Ten-Year Mortality after Community-acquired Pneumonia. A Prospective Cohort. Am J Respir Crit Care Med. 2015; 192(5): 597–604. [PubMed]
26. Morgan A, Glossop A. Severe community-acquired pneumonia. BJA Educ. 2016; 16(5): 167–72. [PubMed] [Website]
27. Torres A, Niederman MS, Chastre J, Ewig S, Fernandez-Vandellos P, Hanberger H, et al. International ERS/ESICM/ESCMID/ALAT guidelines for the management of hospital-acquired pneumonia and ventilator-associated pneumonia: Guidelines for the management of hospital-acquired pneumonia (HAP)/ventilator-associated pneumonia (VAP) of the European Respiratory Society (ERS), European Society of Intensive Care Medicine (ESICM), European Society of Clinical Microbiology and Infectious Diseases (ESCMID) and Asociación Latinoamericana del Tórax (ALAT). European Respiratory Journal. 2017; 50(3). [PubMed] [Website]
28. Kózka M, Sega A, Wojnar-Gruszka K, Tarnawska A, Gniadek A. Risk Factors of Pneumonia Associated with Mechanical Ventilation. Int J Environ Res Public Health. 2020; 17(2): 656. [PubMed] [Website]
29. Blot S, Koulenti D, Dimopoulos G, Martin C, Komnos A, Krueger WA, et al. Prevalence, Risk Factors, and Mortality for Ventilator-Associated Pneumonia in Middle-Aged, Old, and Very Old Critically Ill Patients*. Crit Care Med. 2014; 42(3): 601–9. [PubMed]
30. Cangemi R, Calvieri C, Falcone M, Bucci T, Bertazzoni G, Scarpellini MG, et al. Relation of Cardiac Complications in the Early Phase of Community-Acquired Pneumonia to Long-Term Mortality and Cardiovascular Events. Am J Cardiol. 2015; 116(4): 647–51. [PubMed]
31. Cilloniz C, Ferrer M, Liapikou A, Garcia-Vidal C, Gabarrus A, Ceccato A, et al. Acute respiratory distress syndrome in mechanically ventilated patients with community-acquired pneumonia. European Respiratory Journal. 2018; 51(3): 1702215. [PubMed][Website]
32. Yu Y, Fei A. Atypical pathogen infection in community-acquired pneumonia. Biosci Trends. 2016; 10(1): 7–13. [PubMed]
33. Lizaur-Utrilla A, Gonzalez-Parreño S, Gil-Guillen V, Lopez-Prats FA. Debridement with prosthesis retention and antibiotherapy vs. two-stage revision for periprosthetic knee infection within 3 months after arthroplasty: a case–control study. Clinical Microbiology and Infection. 2015; 21(9): 851.e11-851.e17. [PubMed] [Science Direct]