Ventilator-associated pneumonia rates in a level I trauma intensive care unit in KwaZulu-Natal Province, South Africa, compared with international benchmarks

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Background. Ventilator-associated pneumonia (VAP) is a common nosocomial infection in critically ill patients in intensive care units (ICUs) worldwide. Despite the huge healthcare economic burden and the significant negative morbidity and mortality impact of VAP, its incidence and outcomes in the trauma ICU (TICU) population were poorly documented in South Africa (SA).

Objectives. To determine the incidence of VAP in a level I trauma centre at Inkosi Albert Luthuli Central Hospital in Durban, SA, compared with international benchmarks. Determining mortality rates, the average length and cost of ICU stay, ventilator days and antibiotic consumption was a secondary objective.

Methods. This retrospective chart review of the trauma registry at the centre examined the incidence of VAP and secondary outcomes over the period January 2017 - December 2019. A data pro forma was used with VAP diagnoses as per the 2015 Centers for Disease Control and Prevention definitions. The comparator was international literature-based benchmark VAP rates in TICUs.

Results. The study included 395 patients, of whom 143 (36.2%) were diagnosed with VAP. The VAP rate was calculated to be 35.6 per 1 000 ventilator days. Thirty-one patients with VAP (21.7%) died in the ICU, a similar figure to that for the non-VAP group (22.6%). There were no statistically significant differences in age, sex, mechanism of injury or Injury Severity Score between the VAP and non-VAP groups ($p>0.05$). There were statistically significant differences between the two groups in number of days on mechanical ventilation, ICU length of stay and ICU cost. The VAP group had a median of 12 ventilation days v. 5 days for the non-VAP group ($p<0.001$), and spent a median of 7 days longer in the ICU ($p<0.001$). The median cost of ICU stay for VAP patients was almost double that for non-VAP patients ($p<0.001$).

Conclusion. VAP rates in this local TICU were similar to international rates. Trauma patients, especially those with traumatic brain injury, are at higher risk of VAP than general ICU patients, so strict adherence to evidence-based VAP prevention bundles is necessary among TICU staff.

Keywords. Pneumonia, benchmarks, trauma, intensive care.

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Contribution of the study

This study is the first to assess ventilator-associated pneumonia rates in a South African trauma-specific intensive care unit compared with national and international benchmarks, and sets the standard for local morbidity and mortality norms.

Ventilator-associated pneumonia (VAP) is a life-threatening hospital-acquired infection frequently encountered in critically ill patients admitted to intensive care units (ICUs) worldwide.[1] The incidence of VAP varies from 5% to 67%, depending on patient case mix and the diagnostic criteria used.[1] VAP has an estimated attributable mortality rate of 8 - 12%.[2] The cost of hospitalisation for VAP patients was reported to be three times higher than that for non-VAP patients in developing countries.[3] The mean length of stay for VAP patients was reported to be four times higher than that for non-VAP patients.[3] This infection undoubtedly puts an additional burden on the already limited healthcare resources of developing countries. Despite the huge economic burden of VAP on healthcare systems and the negative impact on patient morbidity and mortality, the incidence and outcomes of this condition in the trauma ICU (TICU) population have been poorly documented in South African (SA) literature.

The US-based National Health and Safety Network in 2012 reported VAP rates ranging from 0.0 to 4.4 per 1 000 ventilator days.[4] The European Centre for Disease Prevention and Control in 2014 reported pooled VAP rates of 10 per 1 000 ventilator days.[4] The World Health Organization reported VAP rates of 23.9 per 1 000 ventilator days from low- and middle-income countries from 1995 to 2010.[5] A study published in 2015 from two major surgical and medical ICUs in Durban, SA, reported VAP rates of 9.9 episodes per 1 000 ventilator days.[6] VAP rates from major trauma centres in a multi-institutional US study were reported to be 17.2 per 1 000 ventilator days.[7] In a 2019

meta-analysis by Li *et al.*,[8] which included studies from European, North American, Asian and a few African countries, the incidence of VAP among patients with traumatic brain injury (TBI) was 36%.[8] In a prospective observational study from 2016 conducted in multiple European ICUs, the incidence of VAP among trauma patients was noted to be 36.5%.[9] A retrospective chart review by Dricken *et al.*[10] found VAP rates among trauma patients without TBI to be 23 per 1 000 ventilator days (incidence 23%), and among those with TBI to be 28.2 per 1 000 ventilator days (incidence 30%).

Benchmarking is a process of comparing services and practices with industry leaders. When applied to a healthcare setting, particularly VAP, it encourages improvement of infection control policies, and allows comparison of risk factors, prevention measures, clinical trends and treatment choices and their impact on outcomes.[11] The incidence of VAP across multiple studies of the trauma population, with and without head injury, ranges from 17% to 36.5%, and is generally higher in patients with TBI. The incidence of VAP in severely injured trauma patients has been too poorly reported on locally to establish accurate benchmarks.

TICU patients are a unique set of patients compared with those in medical and surgical ICUs. This retrospective observational study at Inkosi Albert Luthuli Central Hospital (IALCH) in Durban, SA, aimed to determine VAP rates in a TICU in the only Trauma Society of South Africa (TSSA)-accredited level I trauma centre in the state sector, to address this gap in the literature. These VAP rates in patients with severe trauma were compared with international benchmark VAP rates.

Methods

A single-centre, retrospective, observational chart review was conducted using information retrieved from the IALCH Trauma Registry, as approved by the University of KwaZulu-Natal Biomedical Research Ethics Committee (ref. no. BCA207/09). The study included all adult patients admitted to the TICU between January 2017 and December 2019. All patients who met the study inclusion criteria were included in the data analysis. Data were collected from an existing electronic database of TICU patients and the electronic patient records, and recorded in a data pro forma. The clinical diagnosis of VAP was at the discretion of the on-call trauma intensivist, as this is a closed ICU. Semi-quantitative culture results were used as reported by the local microbiology unit. Microbiological cultures were endotracheal tube aspirates, except for one case in which a specimen from bronchoalveolar lavage was used. Data points such as temperature and white blood cell count were readily available on the electronic database and were recorded retrospectively by a single author (BN).

Patients included in the study were of both sexes, aged ≥18 years, and admitted secondary to either blunt or penetrating trauma that required at least 48 hours of mechanical ventilation. Exclusion criteria were patients considered to be children (<18 years of age) and burn patients. The 2015 Centers for Disease Control and Prevention (CDC) criteria for possible or probable VAP were used to differentiate groups with and without VAP. The CDC definition of VAP is a three-tiered algorithm that aims to provide objective and trustworthy values for monitoring, surveillance and benchmarking.[12] According to the American Thoracic Society guidelines, VAP can be divided into early (occurring within 4 days of commencement of mechanical ventilation) and late (starting on day 5 or thereafter).[13]

There are three surveillance definition syndromes, described in each tier of the CDC algorithm.[14] The most inclusive is ventilator-associated condition (VAC). A subset of VAC is infection-related ventilator-associated complication (IVAC), and subsets of IVAC were possible VAP (PoVAP) and probable VAP (PrVAP). In 2015, PoVAP and PrVAP were combined into a single definition of possible VAP (PVAP) (Fig. 1).

The primary objective was to determine the incidence of VAP in the TICU. This would also be reported as a VAP rate per 1 000 ventilator days using the formula: total number of patients meeting criteria for VAP/total number of ventilator days for whole sample × 1 000. Use of VAP rates as a benchmarking tool may be a valuable quality marker. However, accuracy in reporting requires large sample sizes, high-quality data and an objective method of reporting.

Secondary objectives were to determine mortality rates, number of days spent on mechanical ventilation, number of days spent on antibiotics, average length of ICU stay, and average cost of hospitalisation. Daily procalcitonin (PCT) screening in all patients with an index PCT level >2 µmol/L was used in the unit to guide antibiotic duration. The average cost of ICU stay was estimated from a previous study that estimated the average cost of admission per inpatient day to be ZAR12 727.56.[15] The figure included the cost of surgical procedures, imaging, laboratory tests, pharmaceuticals, and compensation of employees.

Statistical analysis was performed using SPSS version 28 (IBM, USA). Categorical variables were described using frequency counts and percentages. Intergroup comparison was done using Pearson's χ^2 tests. Continuous variables that were normally distributed were summarised using means and standard deviations (SDs) and compared between the two groups using two-sided *t*-tests. Numerical variables that were not normally distributed were summarised using medians and interquartile ranges (IQRs) and compared between the groups using non-parametric Mann-Whitney tests. For all statistical tests, $p<0.05$ was considered significant.

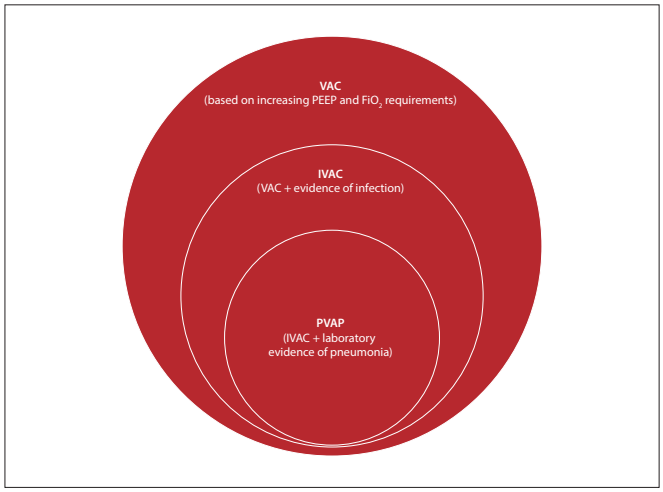

Fig. 1. VAP definitions according to the 2015 Centers for Disease Control and Prevention guidelines.[12] A VAC is considered to be worsening of oxygenation on ventilator (evidenced by increasing PEEP and FiO_2 requirements) after a period of stability of at least 2 days. An IVAC is a VAC plus: (i) abnormal white blood cell count or temperature around the date of onset of worsening oxygenation; and (ii) new antimicrobial commencement around the date of worsening oxygenation. PVAP is presence of an IVAC plus laboratory evidence of pneumonia (positive culture from sputum, endotracheal tube aspirate, bronchoalveolar lavage or lung tissue, OR objective evidence of purulent respiratory secretions, positive test for selected respiratory viruses).[14] (VAP = ventilator-associated pneumonia; VAC = ventilator-associated condition; PEEP = positive end-expiratory pressure; FiO_2 = fraction of inspiratory oxygen; IVAC = infection-related ventilator-associated complication; PVAP = possible VAP.)

Results

A total of 827 patients were admitted to the TICU during the study period. All patients who were admitted for <48 hours or died within 48 hours of admission (so that the minimal time required for potential development of VAP was not met), were aged <18 years, or were not mechanically ventilated during the ICU stay, were excluded. Three hundred and ninety-five patients (47.7% of all admissions) were eventually included in the primary analysis.

When the registry was reviewed, 36.2% of the total sample met criteria for VAP (n=143/395). The 95% confidence interval for this estimate is 31.5 - 41.2%. The VAP rate calculated was 35.6 per 1 000 ventilator days (total number of VAP cases 143/total number of ventilator days 4 022 × 1 000).

The mean (SD) ages of patients with and without VAP were similar (36 (13) years), and there was no significant difference between the groups (t=1.523; two-sided p=0.128).

A clear male predominance was noted in both the VAP and non-VAP groups (90.2% and 85.3%, respectively). Blunt mechanism of injury appeared more common than penetrating trauma in both the VAP and non-VAP groups, with similar percentages (83.2% and 80.6%, respectively). The presence of TBI was also more common than no TBI in both groups, with VAP patients having a higher percentage of 73.4%, compared with 69.4% in the non-VAP group.

There was no significant difference in Injury Severity Score (ISS) between the VAP and non-VAP groups (t=1.17; p=0.243). The median (IQR) ISS for the VAP group was 34 (26 - 43), and that for the non-VAP group was 34 (25 - 41) (Fig. 2).

There was a 21.7% death rate in the VAP group and a 22.6% death rate in the non-VAP group, with no statistical difference noted between the two groups (Fig. 3). Overall, 22.3% of the total patient cohort died. It was not possible to clearly differentiate probable from possible VAP based on the retrospective data.

There was a statistically significant difference between the groups in number of days spent on mechanical ventilation (p<0.001). The VAP group spent a significantly longer time, on average 7 days longer, on mechanical ventilation than non-VAP group (Table 1 and Fig. 4).

The median number of days of treatment with antibiotics was 5 days, with a range of 0 - 14 days. This variable was only measured in the VAP group; however, it was not possible to distinguish between empirical and directed therapy in the possible VAP subgroup, as these were not clearly defined in the notes. The most commonly cultured organisms were *Klebsiella pneumoniae* (35%), *Acinetobacter baumannii* (28%), *Staphylococcus aureus* (27%) and *Escherichia coli* (10%). The majority (63%) of VAP cases were late onset, occurring after day 4 of admission.

There was a statistically significant difference in ICU length of stay between the groups (p<0.001). The VAP group spent on average 7 days longer in the ICU than the non-VAP patients, in keeping with the longer ventilation days period, as illustrated in Fig. 5. The mean ICU length of stay for VAP patients was 16 days.

A statistically significant difference in cost of ICU stay was noted between the groups (p<0.001). The VAP group generated much higher hospitalisation costs, with a median cost of ICU stay of ZAR203 640.96, while the non-VAP group had a median cost of ZAR114 548.04.

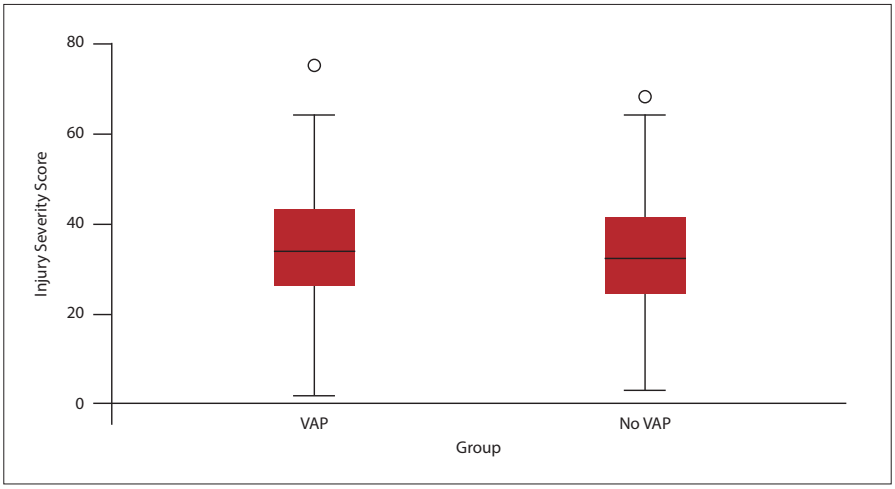

Fig. 2. Interquartile ranges of Injury Severity Scores in the VAP v. no VAP groups. (VAP = ventilator-associated pneumonia.)

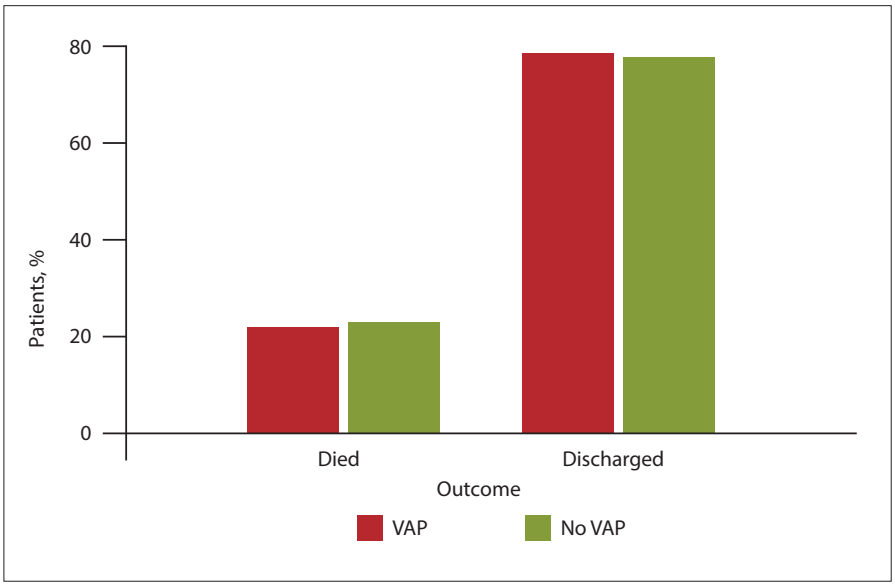

Fig. 3. Mortality and discharged alive comparison of VAP v. no VAP groups. (VAP = ventilator-associated pneumonia.)

Table 1. Days on ventilation, VAP v. no VAP

	VAP	No VAP	Total
Days spent on MV			
Median	12	5	8
25th percentile	9	4	4
75th percentile	17	9	13

VAP = ventilator-associated pneumonia; MV = mechanical ventilation.

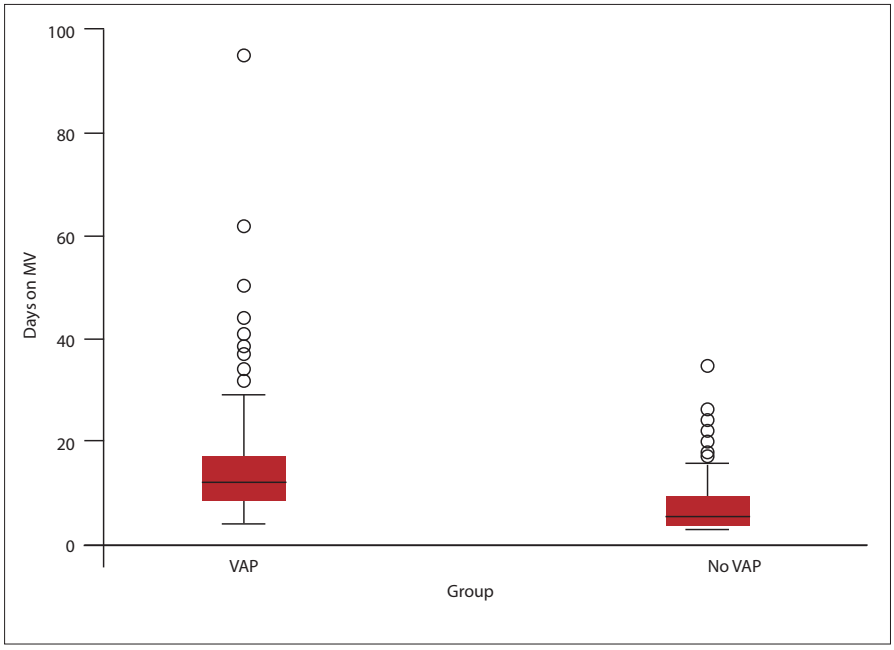

Fig. 4. Days on MV for the VAP v. no VAP groups. (MV = mechanical ventilation; VAP = ventilator-associated pneumonia.)

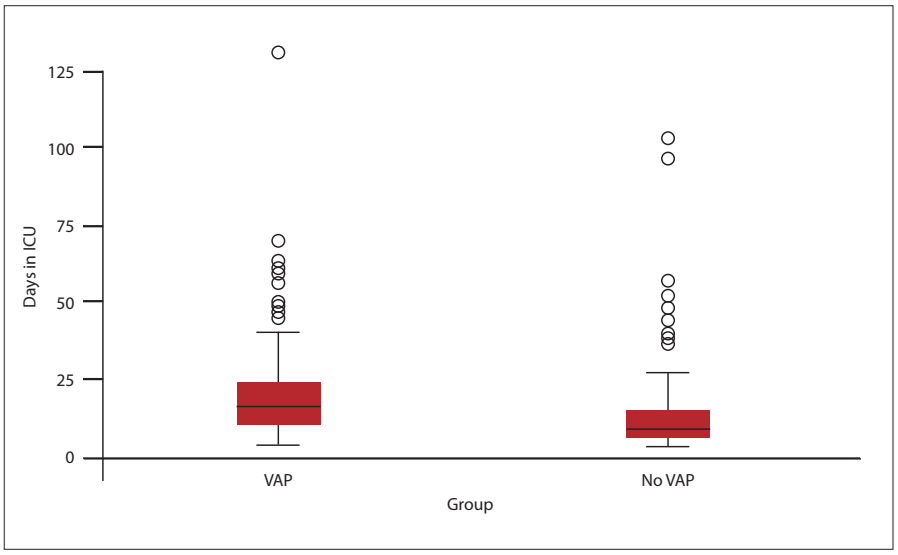

Fig. 5. Length of stay in the ICU for the VAP v. no VAP groups. (ICU = intensive care unit; VAP = ventilator-associated pneumonia.)

Discussion

The main objective of the study was to determine the incidence of VAP in this TSSA-accredited level I trauma centre, and compare it with international benchmarks. The study revealed that VAP rates in the local setting are similar to those reported internationally. The incidence of VAP in our study was 36.2%, corresponding to a rate of 35.6 per 1 000 ventilator days. These rates were higher than those in a multi-institutional US study from major trauma centres, which reported pooled mean VAP rates of 17.2 per 1 000 ventilator days.[7] However, the VAP incidence was similar to the 36% among TBI patients noted in a meta-analysis that included studies from Europe, North America, Asia and Africa.[8] It was also similar to the 36.5% noted in a prospective observational study from multiple European ICUs.[9] The incidence of VAP in our study was higher compared with that in local surgical and medical ICUs, which was reported as 25% in a study published in 2015.[6] This finding is to be expected, as trauma patients have a much higher risk of developing pneumonia than ventilated patients in non-trauma ICUs.[16] Severely injured patients are at increased risk of VAP because they may require earlier airway acquisition and longer mechanical ventilation than other patients. Moreover, severely injured patients may have reduced resistance to infection owing to a compensatory anti-inflammatory response phase associated with a systemic inflammatory response syndrome. A high ISS, use of vasopressors and nasogastric tube malposition were also recognised as risk factors in this special ICU population.[16] The presence of chest trauma (rib fractures, pulmonary contusions) and failed prehospital intubation were identified as significant predictors of pneumonia in a study by Mangram *et al.*[17] published in 2015, and a suggestion was made to redefine VAP in trauma patients to 'trauma-associated pneumonia'.[17]

A 2021 study by Keneally *et al.*[18] suggests that high ISSs and male sex are risk factors associated with VAP. However, in the present study we found that ISSs were similar in the VAP and non-VAP groups, with a median of 34 in both. There was also the usual male predominance in both groups, with 90.2% male patients in the VAP group and 85.3% in the non-VAP group.

Mortality in our study was similar between the VAP and non-VAP cohorts, with rates of 21.7% and 22.6%, respectively. This finding seems to suggest that VAP is of lesser consequence in the trauma population compared with critically ill patients in other ICUs, and concurs with a study by Cook *et al.*[19] in which it was found that trauma represented a 3.9 odds ratio of developing VAP. It is therefore important to consider these factors prior to using VAP as a quality indicator among TICU patients.

Similar to findings of previous studies, the development of VAP in our study was strongly associated with longer duration of mechanical ventilation and longer length of ICU stay.[16] VAP patients spent an average of 7 days longer on mechanical ventilation, as well as 7 days longer in the ICU, than non-VAP patients. This finding emphasises the need to avoid mechanical ventilation where possible. When invasive ventilation is unavoidable, daily assessments for the possibility of early weaning with daily sedation hold and use of other care bundles to reduce VAP are important. However, early weaning off the ventilator may not be possible in some trauma patients, e.g. those with TBI with neurological indications for prolonged ventilation.[20]

The appropriate use of antimicrobial therapy in the treatment of VAP is an important focus point in many studies, as delays in initiation of antibiotics and inappropriate treatment may result in longer ICU stay and increased mortality.[4] Although the optimal duration of antimicrobial therapy for the treatment of VAP is not known, evidence shows that shorter courses, averaging 7 days, are effective and reduce antibiotic resistance and adverse effects,

as well as cost of care.[4] In the present study, patients with VAP spent an average of 5 days on antibiotics. Treatment was tailored according to micro-organisms cultured and the sensitivities of the organisms. Discontinuation of antimicrobial therapy was based upon both clinical and laboratory (PCT trends) evidence of improvement. International guidelines for management of hospital-acquired pneumonia and VAP recommend the use of biomarkers such as serial PCT measurements in conjunction with clinical assessment to determine the optimal duration of antimicrobial therapy.[21]

The cost of ICU stay was 1.8 times higher for VAP patients than for the non-VAP group. These findings are in keeping with those of Alp *et al.*,[3] who reported that the total cost of VAP patients was three times higher than that for non-VAP patients. This economic burden places a further strain on the already limited healthcare resources in our upper-middle-income country, where the trauma burden is far higher than in many high-income regions with better systems of care. This situation emphasises the need for strict adherence to cost-effective VAP prevention bundles to reduce the incidence of this complication. Implementation of ventilator care bundles was associated with reduced VAP episodes and a reduced duration of mechanical ventilation in adult ICU patients in a recent meta-analysis.[22]

Study limitations

Limitations of this study are that it was a retrospective chart review, along with the single-centre status, so generalisation to other facilities is not necessarily possible. This drawback is mitigated by the fact that the data were from an electronic record linked to a registry with broad data points, reducing the risk of selection bias and missing data. The database also has links to laboratory data for sensitivity to antibiotics; however, the documentation did not differentiate possible from probable VAP. The other important aspect is that because the study was retrospective, observational causality cannot be ascertained.

Conclusion

The study has shown that VAP rates in a local TICU are higher than those reported from local non-trauma ICUs, and yet not dramatically worse than rates in TICUs in higher-income countries internationally. Although there is a need to reduce the incidence of this complication in the TICU by strict adherence to VAP care bundles, it remains a potentially predictable complication, particularly in those with TBI, as these patients had a higher incidence.

Data availability. The datasets generated and analysed during the present study are available from the corresponding author (BN) on reasonable request. Any restrictions or additional information regarding data access can be discussed with the corresponding author.

Declaration. The research for this study was done in partial fulfilment of the requirements for BN's MMed (Anaes) degree at the University of KwaZulu-Natal.

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Author contributions. TCH and BN conceptualised the study, TCH provided the data from the registry, and BN analysed the data and retrieved the clinical data. TCH and BN wrote the article draft, and both authors agreed on the final submission. TCH was the MMed supervisor for BN.

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