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*Original Article*

# Prevalence and patterns of infection in critically ill trauma patients admitted to the trauma ICU, South Africa

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**Abstract**

Introduction: The aim of this study was to determine if any patterns of infection or bacterial resistance existed in critically ill polytrauma patients admitted to the intensive care unit (ICU) at the CM Johannesburg Academic Hospital (CMJAH).

Methods: This was a prospective, single-center study of patient laboratory records of 73 critically injured polytrauma patients admitted to an ICU. The data collected from each patient, beginning with admission and extending until discharge from the ICU, included age, gender, admission hemoglobin levels, injury severity score, length of ICU stay, microbiological cultures and sensitivity (MCS), and types and numbers of surgical procedures.

Results: Upon admission to the ICU, the injury severity score (ISS) was 40.86 (± 15.64). In total, 73.98% of the patients required the use of a ventilator during their ICU stay. The most prevalent organisms isolated from specimens were *Pseudomonas aeruginosa* (30.1%), *Klebsiella* species (25.7%), *Acinetobacterbaumanni* (16.4%), and *Staphylococcus aureus* (5.8%). Multi-drug resistance (MDR) was identified in 63% of patients, with *Klebsiella* (73.91%) and *Pseudomonas* (65.21%) occurring most frequently. Multivariate analysis showed MDR to be the only significant predictor associated with a higher risk for hospital mortality when age, gender, ventilation, duration of ICU stay, ISS score, and the number of surgeries undergone was taken into account.

Conclusion: Critically ill polytrauma patients are at particularly high risk for Gram-negative sepsis.

**Key words:** Multidrug resistance; ICU; *Pseudomonas aeruginosa*;*Klebsiella* species; *Acinetobacterbaumanni*; *Staphylococcus aureus.*

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## Introduction

Infection and antimicrobial resistance are persistent problems in intensive care units (ICUs) and are directly associated with morbidity and mortality [1]. Traumatic wounds are likely to be an important source of contamination and infection. Reports suggest that cultures may be positive in up to 83% of open fractures. Organisms include *Pseudomonas aeruginosa* and *Staphylococcus aureus* [2]. Patients admitted to ICUs are also at high risk for nosocomial infections as a result of ventilation, surgical procedures, and daily invasive procedures. Gram-positive bacteria have been reported to be the most common cause, with *Staphylococcus aureus* beingthepredominant organism. [3].

Information regarding ward- and patient-specific prevalence of various infection and resistance patterns assists medical staff in choosing appropriate empiric and prophylactic antimicrobial therapy, thus improving the management and prevention of infection [4,5].

The spectrum of infection and antimicrobial resistance has previously been shown to depend upon a patient’s profile, risk factors associated with the patient’s comorbidities, and the admitting hospital’s infection control policies [4]. These risks factors include immunocompromised state, cancer, human immunodeficiency virus (HIV), and chronic obstructive pulmonary disease (COPD) [6]. Age and male gender have also been reported to be independent risk factors for skin infections [7]. Haley *et al*. showed that infection control policies can decrease the occurrence of nosocomial infections by 30% to 50% [8]. Therefore, effective infection control programs should also decrease the frequency of resistant infections. However, the effect of infection control policies is still unknown for resistant organisms [9]. Specific infection patterns are likely to exist in polytrauma patients in contrast with general surgical or medical patients admitted to an ICU. An understanding of infection patterns may improve rates of morbidity and mortality by anticipating the preventative measures required to reduce the incidence of acquired disease. For example, a high rate of resistant organisms may be associated with immunocompromised state (*e.g.*, HIV). Routine assessment of HIV infection is not part of current protocol in many trauma units where the general incidence is high. In certain subsets of patients, routine assessment of HIV may indicate further preventative measures (antiretroviral agents).

Multiple Gram-negative and Gram-positive organisms have been reported in patients admitted to mixed intensive care units, which included medical and general surgical patients. [1,4,10,11]. These organisms included *Pseudomonas aeruginosa*, *Escherichia coli*, *Haemophilus influenza*, coagulase-negative *Enterococcus*, *Streptococcus pneumoniae*, *Klebsiellapneumoniae*, and methicillin-resistant *Staphylococcus aureus* (MRSA) [1,4,10,11]. Gram-negative bacteria have been shown in some studies to be the most common organisms. The national Canadian Study (CAN-ICU) reported that the most common Gram-positive organism was *Staphylococcus aureus* (respiratory tract, 20.5%; wound tissue, 19.5%; and blood stream, 11.8%) [4,11]. Bayram*et al*. found that *Staphylococcus aureus* was the most common Gram-positive organisms (surgical site, 23.6%; blood stream, 16.8%; and respiratory tract, 13.6%) [11].

Resistant Gram-negative bacilli remain a life-threatening concern, as the development of new antibiotics has not kept pace [12]. The CAN-ICU study identified that in the respiratory tract, the most common Gram-negative bacilli were *Haemophilus influenza*(14.1%) and *Pseudomonas aeruginosa* (12.6%). In the wound/tissue specimens, the most common Gram-negative bacteria were *Escherichia coli*(10%), *Pseudomonas aeruginosa*(9%), and *Klebsiellapneumoniae*(4.3%)[10]. Bayram*et al*. also showed that *Pseudomonas aeruginosa*was the most common Gram-negative pathogen in both respiratory tract (27.9%) and surgical site (22.2%) [11].

Studies analyzing pathogen prevalence and resistance patterns in polytrauma patients are limited, as most ICU studies have analyzed patient populations and limited their assessments to specific infections (*e.g.*, urinary or respiratory tract) [13,14].

The purpose of this study was to determine the prevalence of infection and propensity towards resistance in critically injured polytrauma patients admitted to a single-center ICU. Further, the influence of various trauma-related factors on infection patterns was assessed. Infection trends have not previously been analyzed in a high-risk, severely injured trauma population, so this information may contribute to the future use of prophylactic and empiric antibiotic therapy in patient populations such as this.

## Methodology

This study assessed the prevalence of infection and patterns of resistance in critically ill polytrauma patients admitted to a single ICU between March 2011 and July 2012

Patients were included in the study if they were over the age of 18, had sustained both a neurological injury (head or spinal cord) and a long bone fracture (as a minimum combined injury), and had survived in excess of 24 hours post admission. Injuries were objectively confirmed by radiological studies. Patients were excluded if they did not require admission to the ICU. Data was ultimately obtained on 73 critically injured polytrauma patients who were admitted to a level 1 trauma ICU at the CM Johannesburg Academic Hospital (CMJAH).Data was collected until discharge from the ICU and included admission hemoglobin levels, injury severity score, length of ICU stay, microbiological cultures and sensitivity (MCS), and types of surgical procedures. At some point in time during their ICU stay, all 73 patients each had an MCS specimen taken. All specimens were positive for organism growth, and infections were therefore considered to be nosocomial. A total of 284 MCS specimens were collected. Thirty reports were excluded from analysis as they were assessed to be duplicate samples (taken within 48 hours of the same site and reporting similar findings to previous reports). Therefore, 254 MCS specimens were analyzed. Sites included respiratory tract, blood, urine, and tissue fluid (cerebrospinal, pleural, and peritoneal). This study was approved by the ethics committee of the University of the Witwatersrand. Consent was obtained either from family members or from one of three specialists not associated with the study.

The study co-ordinator was not employed by the trauma unit and worked independently to collect all data. Data was transcribed daily from hospital records. At the end of the study period, three medical students independently double-checked all MCS data by comparing the transcribed data to computerized reports. The Kirby-Bauer method, microdilution assay, and E-test were used to test the samples for the antibiotic resistance.

Data from ACCESS was analysed using Statistica version 10. The following variables were investigated as independent risk factors for infection: age, gender, ventilation, time of admission to casualty, duration of

ICU stay, ISS score, acute physiology and chronic health evaluation II (APACHE II) score, predicted death rate, and number of surgeries undergone. In addition to these variables, infection was investigated as a risk factors for hospital mortality. These risk factors were compared between patients who survived and those who died, and between those with and without MDR using student's *t*-test or Mann-Whitney test as appropriate, and categorical variables were compared using a Chi-squared test with Fischer's exact test where numbers were small (n < 5). A p value of less than 0.05 was considered significant. The multivariate logistic regression analysis was used to determine the risk for mortality.

## Results

*Patient demographics*

The average age of the patients was 32.73 years (standard deviation [SD], 12.83; range, 18–80), and 16.4% of the patients were female. The average ISS was 40.86 (SD, 15.64). The average APACHE II score was 19 (SD, 6.7), corresponding to a mean predicted death rate of 35.4% (SD, 18.2%). None of the patients were on immunosuppressive therapy. In total, during their ICU stay, the 73 patients underwent 111 general surgical procedures, 90 orthopedic procedures, 32 vascular procedures, and 10 neurosurgical procedures. The total number of ICU days analyzed for the study population was 908. Fifty-four patients (73.98%) were ventilated for a variable period during the course of their ICU stay. The majority of the patients (80%) had had a car accident, and 15% had had a motorbike accident.

*Patterns of infection*

During the study period, a total of 254 MCS specimens were analyzed. The distribution of infection was analyzed by site of culture: respiratory tract (57%), blood (25%), urine (9%), catheter tip (5%), or tissue/fluid (4%). All patients had a positive MCS culture at some point during their ICU stay. Of 73 patients, 47 (64.4%) required inotropes at some point

**Table 1.** The five most common organisms isolated by specimen site

| Specimen site | Organism | No. of Isolates | % of total |
|---|---|---|---|
| **Respiratory** | | | |
| | *Pseudomonas aeruginosa* | 40 | 34.78 |
| | *Klebsiella*species | 33 | 28.69 |
| | *Acinetobacterbaumannii* | 17 | 14.78 |
| | Other | 15 | 13.04 |
| | *Proteus mirabilis* | 10 | 8.69 |
| **Blood** | | | |
| | *Pseudomonas aeruginosa* | 14 | 25.9 |
| | *Staphylococcus aureas* | 13 | 24 |
| | Other | 11 | 20.37 |
| | Acinetobacterbaumannii | 9 | 16.66 |
| | *Klebsiella*species | 7 | 12.96 |
| **Tissue** | | | |
| | *Pseudomonas aeruginosa* | 8 | 34.78 |
| | *Klebsiella*species | 7 | 30.43 |
| | *Enterobacter*species | 3 | 13.04 |
| | Other | 3 | 13.04 |
| | *Acinetobacterbaumannii* | 2 | 8.69 |
| **Catheter tip** | | | |
| | *Acinetobacterbaumannii* | 5 | 31.25 |
| | *Klebsiellapneumoniae* | 3 | 18.75 |
| | *Pseudomonas aeruginosa* | 3 | 18.75 |
| | Other | 3 | 18.75 |
| | CoNS | 2 | 12.5 |
| **Urine** | | | |
| | *Klebsiella*species | 8 | 44.44 |
| | *Acinetobacterbaumannii* | 4 | 22.22 |
| | *Pseudomonas aeruginosa* | 3 | 16.66 |
| | *Escherichia coli* | 2 | 11.11 |
| | *Proteus mirabilis* | 1 | 5.55 |

CoNS: coagulase-negative *Staphylococci* during their ICU stay (30 MDR, 17 non-MDR).

Overall, the most common organisms were *Pseudomonas aeruginosa* (30.1%), *Klebsiella*species (25.7%), *Acinetobacterbaumanni* (16.4%), and *Staphylococcus aureus* (5.8%). The distribution of infection per site is shown in Table 1. *Pseudomonas aeruginosa* was the predominant infection in respiratory tract, blood, and tissue/fluid cultures. *Acinetobacter* and *Klebsiella* were the most common organisms in catheter tip and urine cultures, respectively. The only site where *Staphylococcus aureus* prevailed was in blood cultures (24%, compared with 25.9% for *Pseudomonas*).

The most common antibiotics used are shown in Table 2. Prophylactic antibiotics used prior to surgical procedures were included. The penicillins and cephalosporins predominated, and the macrolides included drugs that were used to enhance gastrointestinal motility. Only two patients had no documentation of antibiotic usage during their ICU stays.

*Multi-drug-resistant (MDR) infections*

For the purposes of the study, MDR was defined as resistance to three or more first-line classes of antibiotics (beta-lactams, aminoglycosides, fluoroquinolones) or resistance to carbapenems [5,15].

Accordingly, 46 patients (63%) had positive cultures for drug-resistant strains. In the 254 samples, 740 drug resistance patterns were analyzed. Ampicillin and cotrimoxazole were the most common non-sensitive antibiotics (11.75% and 9.59%, respectively). Cefepime and meronem together comprised approximately 15% of the total. *Klebsiella* and *Pseudomonas* predominated as the most common resistant organisms in each of these classes. The most common MDR isolate was *Klebsiella*(73.91%), followed by *Pseudomonas* (65.21%). In 56.52% of MDR patients, both *Pseudomonas* and *Klebsiella*demonstrated resistance.

**Table 2.** The most common antibiotic classes used by patients during their stay in the ICU

| Class of antibiotics | % of total |
|---|---|
| Penicillin | 30.08 |
| Cephalosporin | 18.70 |
| Macrolide | 16.26 |
| Carbapenem | 13.82 |
| Glycopeptide | 5.70 |
| Aminoglycoside | 4.88 |
| Other | 4.88 |
| Quinolone | 3.25 |
| Sulfonamide | 1.62 |
| Lincosamide | 0.81 |

When comparing patients with MDR infection to those without MDR infection, the latter were older, had a higher mortality rate, and stayed in the ICU longer (Table 3). However, the average ISS, APACHE II score, predicted death rate, and the average number of surgical procedures were not significantly different in the two groups. Patients with an ISS greater than 50, those who underwent more than four surgical procedures, and those with higher APACHE II scores seemed to be at higher risk of MDR infections (Tables 4, 5, and 6).

*Mortality*

The hospital mortality rate was 23.3% (17 patients). Multivariate analysis showed that MDR and lower admission hemoglobin levels were the only significant predictors associated with a higher risk for death when age, gender, ventilation, time of admission to casualty, duration of ICU stay, ISS score, and number of surgical procedures were taken into account.

**Table 3.** Demographics of the ICU patients

| | All patients (n = 73) | MDR patients (n = 46) | Non-MDR patients (n = 27) | P values |
|---|---|---|---|---|
| Female, % | 16.4 | 17.4 | 14.81 | 0.52 |
| Male, % | 83.56 | 82.6 | 85.19 | |
| Age (years), mean ±SD | 32.73 ± 12.83 | 35.55 ± 15.58 | 28.5 ± 8.23 | 0.0358* |
| Mortality rate, % | 23.3 | 32.6 | 7.4 | 0.0118* |
| ISS, mean ± SD | 40.86 ± 15.64 | 43.82 ± 15.64 | 35.61 ± 14.30 | 0.6314 |
| Ventilated % | 73.98 | 73.92 | 74.07 | 0.89 |
| Not ventilated, % | 26.02 | 26.08 | 25.93 | |
| Duration of ICU stay, mean ± SD | 15.09 ± 12.94 | 18.25 ± 14.55 | 9.10 ± 5.70 | 0.0055* |
| Hb, mean ± SD | 12.38 ± 2.21 | 12.24 ± 2.35 | 12.65 ± 1.94 | 0.5 |

MDR: multidrug resistant; Hb: *hemoglobin*; ISS:injury severity score; *p < 0.05

**Table 4.** Injury severity score (ISS) in MDR and non-MDR patients

| ISS range | MDR patients (n = 46) | Non-MDR patients (n = 27) |
|---|---|---|
| 1–25 | 13% | 29.62% |
| 26–50 | 54.40% | 55.55% |
| 51–75 | 32.60% | 11.11% |

**Table 5.** Number of surgeries patients had in MDR and non-MDR groups

| Number of surgeries | MDR patients (n = 46) | Non-MDR patients (n = 27) |
|---|---|---|
| 0–3 | 56.20% | 70.40% |
| 4–6 | 34.72% | 18.15% |
| 7–20 | 8.69% | 3.89% |

**Table 6.** APACHE II scores and predicted death rate (PDR) in MDR and non-MDR patients

| | APACHE II SCORE ± SD | PDR % ± SD |
|---|---|---|
| All patients (n = 73) | 19 ± 6.07 | 35.4 ± 18.2 |
| MDR patients (n = 46) | 19.3 ± 7.1 | 36.8 ± 19 |
| Non-MDR patients (n = 27) | 17.5 ± 5.4 | 29.8 ± 14.7 |

## Discussion

This study analyzed infection patterns and resistance in a specific high-risk trauma population. Gram-negative organisms predominated, and the most common organism overall was *Pseudomonas* (30.1%), followed by *Klebsiella* (25.7%) and *Acinetobacter* (16.4%). A high rate of *Pseudomonas* infection was detected in sputum, blood, and urine. Although *Staphylococcus aureus* infections were comparable to *Pseudomonas* infections in blood cultures (24% and 25.9%, respectively), the overall *Staphylococcus aureus* infection rate was only 5.8%. In line with the high prevalence of Gram-negative organisms, the MDR bacteria was found in 63% of the patients analyzed. The most common MDR bacteria were *Klebsiella* and *Pseudomonas*. As expected, this was associated with higher mortality and longer ICU stay. The MDR group also appeared to be slightly older.

This trend towards Gram-negative prevalence has been documented in large regional and global ICU surveillance studies in mixed ICU populations. In the MYSTIC study, *Pseudomonas aeruginosa* (33%) was the most common isolate obtained, followed by *Acinetobacter baumanni* (17.1%), *Klebsiella pneumoniae* (12.1%), and *E. coli* (10.5%) [17]. In a Turkish surgical ICU, Bayram*et al*. identified *Pseudomonas aeruginosa* as the most common isolate (23%) [11].

In other global studies evaluating patients in mixed ICUs, *Staphylococcus aureus* has predominated. In the point prevalence EPIC II study, *Staphylococcus aureus* and *Pseudomonas aeruginosa* had a similar prevalence (20.5% and 19.9%, respectively) [1]. In Deshpande *et al.*'s study of the SENTRY antimicrobial surveillance program, the incidence of *Staphylococcus aureus* was 24.1%, *Pseudomonas aeruginosa* 12.2%, and *E. coli* 10.1% [16]. The Canadian National Intensive Care Unit Study revealed that *Staphylococcus aureus* was the most common isolate (16.4%), followed by *Escherichia coli* (12.8%) and *Pseudomonas* (10%) [10]. In Vincent *et al*.'s report of the SOAP Study, *Staphylococcus aureus* predominated (30%), followed by *Pseudomonas aeruginosa* at 14% and *Escherichia coli* at 13%. In this study, *Pseudomonas* was associated with high mortality [18]. Unlike the other studies, the current study only included patients who were afflicted by severe trauma, and analyzed all microbiology specimens until the patients' discharge from the ICU. It highlights the devastating effect of Gram-negative sepsis and MDR strains on mortality and impacts on ICU stay. MDR strains were found in 43 patients (63%). *Klebsiella* and *Pseudomonas* were the most common MDR bacteria. The most common drug resistance patterns included penicillin, cotrimoxazole, ceftazidime, cefepime, and meronem. Although we were not able to show conclusively that an ISS greater than 50 and multiple surgical procedures were risks for MDR infection, it makes intuitive sense that there is likely to be a relationship. The trauma ICU implements strict infection surveillance and prevention programs. This includes audits of hand washing, use of barrier methods in nursing in cubicles, and adherence to septic techniques. A microbiologist and an infection control supervisor monitor these activities. In view of the current findings, these strategies may need to be reassessed.

Topical or systemic prophylactic antibiotics are not routinely used in the trauma ICU when patients are admitted. This is due to the concern of propagating resistant bacteria [18,19]. Cefazolin is the most common prophylaxis used in surgical procedures.

There is also no standard protocol for the use of empiric antibiotics when a patient has features of infection. Generally, an intravenous beta-lactam is used at the discretion of the attending physician. Based on our findings, the use of aminoglycosides and/or piperacillin/tazobactam as empiric therapy needs to be investigated.

Current statistics indicate that the HIV rate of infection is likely to be relatively high. Obtaining appropriate consent for this test from all patients was not possible. This was not analyzed and may have exacerbated the MDR rate.

The effect of an ISS greater than 50 and number of surgical procedures on MDR infection needs evaluation in a larger study. A larger study will also clarify the relationship between MDR infection and mortality.

## Conclusions

This study highlights the global impact of multidrug-resistant Gram-negative sepsis. Critically ill polytrauma patients are a particularly vulnerable group, and the high rate of Gram-negative sepsis demonstrated in this study may be more widespread than we realize. The association between MDR infection and mortality mandates a reappraisal of infection control policy. The development of new antibiotics to combat such sepsis does not appear to be imminent. In the interim, similar studies are necessary to reaffirm the global life-threatening impact of resistant bacteria in specific patient populations. Under these circumstances, choosing the most appropriate prophylactic and empiric drug strategies is crucial.

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