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## **Evaluating initial antimicrobial use in an adult intensive care unit at an Academic Teaching Hospital in Pretoria, South Africa**

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### **Abstract**

Antimicrobial resistance is increasing globally. It is estimated that in hospitals around the world 50% of antimicrobial usage is either unnecessary or inappropriate. The study aimed to explore factors surrounding initially prescribed antibiotics and direct medicine related costs in the adult Medical Intensive Care Unit (MICU), at Steve Biko Academic Hospital (SBAH). A clinically trained pharmacist was included as part of the multi-disciplinary team and evaluated antibiotics prescribed *after* admission. These were considered as the initial course of antibiotics. The antimicrobial agents that the patient was admitted with were documented and are referred to as "*antibiotics prior to review*". Just less than half of the patients, 23 (44.2%; n = 52) were initiated on antibiotics on the first day of admission to the MICU. The majority of antibiotics 46 (60.5%) were prescribed appropriately during the study period. The total cost of initial antibiotic use for the treatment period during the study was R209 140.40, with an average cost of R31 240.77 per day for all initial antibiotics. A coordinated effort from the infectious diseases specialist and clinical pharmacist within the multi-disciplinary team, assisted in appropriate prescribing of antibiotics to patients that were admitted to the MICU.

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### **Introduction**

Antimicrobial resistance is increasing globally. It is estimated that in hospitals around the world 50% of antimicrobial usage is either unnecessary or inappropriate (Doron & Davidson, 2011; Martin, Goff, Karam, Dombrowski & DeChant, 2009). The timely selection and administration of appropriate antimicrobial therapy can significantly impact treatment outcomes, especially in patients with severe or life-threatening infections (Drew, 2009).

Antimicrobial stewardship is a coordinated effort to ensure the judicious and effective use of antimicrobial therapy that includes, but is not limited to the appropriate selection, dosing, route of administration, and duration of antimicrobial therapy (Martin et al., 2009). The goal of an antimicrobial stewardship programme (ASP) is to optimise clinical outcomes while minimizing unintended consequences of antimicrobial use, and to reduce health care costs without adversely affecting quality of care (Martin et al., 2009). The implementation of an ASP can present a challenge due to limited resources and other barriers such as lack of physician participation, insufficient diagnostic facilities, absence of formal mechanisms of data collection, and lack of cooperative strategies from health care workers. Institutional needs and available resources should therefore be taken into consideration when planning a strategy for ASP implementation. The goal of an ASP is to optimize the use of limited resources, overcome barriers to implementation, and improve clinical outcomes (Martin et al., 2009). Part of antibiotic stewardship includes the use of appropriate biomarkers especially when treating bacterial infection and sepsis. Procalcitonin (PCT) have been used as a biomarker to shorten antimicrobial therapy without adversely affecting clinical outcomes (Martin et al., 2009).

The Surviving Sepsis Campaign guidelines recommend prompt antimicrobial therapy in high-risk patients. Inappropriate antimicrobial therapy for septic shock is known to be associated with a five-fold reduction in survival (Dellinger et al., 2012). Appropriate antibiotic use is of both clinical and economic significance to any health care system and should be given adequate attention (Ojeniran, Shouval, Miskin, Moses & Shmueli, 2010). Pharmacists play an important role in reducing the threat to public health and costs of hospital-acquired antibiotic-resistant infections through antimicrobial stewardship (Martin et al., 2009). Antimicrobial resistance is increasing; however, antimicrobial drug development is slow. Now, more than ever before, antimicrobial stewardship is of the utmost importance as a way to optimize the use of antimicrobials, prevent the development of resistance and improve patient outcomes (Martin et al., 2009).

In SBAH a need for an ASP was identified by the Head of Infectious Diseases, as at the time of the study, an antibiotic policy was not available for the adult MICU. The study intended to investigate the use of initially prescribed antimicrobial agents in an adult intensive care unit at SBAH as part of an antimicrobial stewardship roll out programme. Initially prescribed antibiotics are extremely important in high risk patients (ventilator associated pneumonia (VAP), septic shock, etc.), and every hour of delay in antibiotic administration after diagnosis, is associated with an average decrease in survival of 7.6% (Pong & Bradley, 2005).

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### **Methods**

#### *Study site*

The study was conducted in the adult MICU at SBAH in Pretoria, situated in the Gauteng Province of South Africa. The hospital has 832 beds, including 53 ICU beds and 21 high care beds, and it has a theatre complex with 21 operating theatres, with 19 operational (Statistical information from SBAH, 2014). The MICU is a 9-bed ward and the only ICU in the hospital admitting medical patients. Although the MICU has nine beds, at the time of the study it never had more than six beds occupied at any given time, because of a shortage of ICU-trained nursing staff.

#### *Study period and design*

This was an operational study with a descriptive and observational design, conducted through daily ward rounds over a period of seven months.

#### *Study population and sample*

According to the hospital statistics at the time of the study, the MICU admitted an average of 24 patients per month, depending on the staff complement and availability of trained ICU staff (Statistical documentation MICU SBAH, 2014). All patients newly admitted to the adult MICU at SBAH and who were initiated on antimicrobial therapy (received a prescription), were included in the study. This resulted in a final sample size of 52 patients, enrolled over the study period of seven months.

#### *Data collection and data collection instruments*

For the purposes of the study, antibiotics prescribed and initiated *after* admission to the MICU were considered as the “*initially prescribed antibiotics*”. The antibiotic agents that patients were admitted with, were documented and are referred to as “*antibiotics prior to review*”. Only antibiotics that were initiated *in* the MICU were included in the study for review and evaluation. Direct costs were calculated for the duration of therapy using the tender prices from the National Department of Health and were related to treatment days.

Initial antimicrobial use was evaluated using the parameters showed in Table 1. These prescribing markers and the patient’s clinical condition were discussed by the pharmacist with the treating physician or infectious diseases specialist during daily ward rounds. A collective decision was made by the health care team on the appropriate antimicrobial therapy and subsequently implemented.

**Table 1:** Antibiotic prescribing markers

<b>Drug factors</b>	<b>Infectious biomarkers</b>	<b>Patient factors</b>
• Dose	• WBC count*	• Diagnosis
• Duration of use	• CRP**	• Weight
• Indication of use	• Temperature	• Renal markers
	• Blood culture	• Hepatic markers
	• Procalcitonin	

\*WBC: White blood cell; CRP: \*\*C-reactive protein

Data were collected using a validated data collection instrument developed by the American Society of Hospital Pharmacists (American Society of Hospital Pharmacists, 1992). Over the years, the instrument had been used in multiple studies and further validated for use in the South African setting (Untiedt, 2004; Leteka, 2005; Baaisi, 2007; Schellack and Gous, 2010; Bronkhorst, 2012; Pretorius, 2012).

Patients were followed for the duration of their initially prescribed antibiotic course. For example: Patient X is admitted to the MICU on amoxicillin, and switched in the unit to meropenem. The amoxicillin was recorded as “*antibiotic prior to review*” and meropenem as the “*initially prescribed antibiotic*”. Patient X was then followed for the duration of meropenem therapy, e.g. either stopped or de-escalated. Laboratory data were obtained from the National Health Laboratory System (N HLS), providing services to the patients at SBAH.

#### *Statistical analysis*

Data were captured on Microsoft Excel™ spread sheets and exported to SAS® (SAS institute Inc. Cary, NC), Release 9.3 for statistical analysis, which was explorative and descriptive. Continuous variables were summarised by mean with standard deviation (SD), range with minimum and maximum values, and median with interquartile range (IQR). Categorical variables were summarised by frequency counts and percentage calculations.

The initially-prescribed antibiotics were categorised and summarised descriptively. The direct costs of patients’ initial antimicrobial usage were calculated according to the total daily dose and based on the tender prices of the National Department of Health for 2012. The cost for each item was derived from the following equation: Daily cost = (Antibiotic pack size x dosing interval) x days on antibiotics.

#### *Ethical considerations*

Ethical clearance for the study was obtained from the University of Pretoria (Number 178/2012) and the University of Limpopo, Medunsa Campus (Number MREC/H/212/2012: PG). As this was an observational study with review of patient records and no direct patient interaction, participant consent was not obtained. Participants’ personal information was only used to match the

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laboratory report obtained from the laboratory dataset with the dataset that is hosted at SBAH. Once this was done, no personal information was used further in the study.

### **Results**

#### *Patient demographics*

Of the 52 patients included during the study, slightly more were female (55.8%). The mean age was 40.1 years, ranging from 13 to 77 years, with one adolescent aged 13 years included in the study. The mean weight of the patients admitted to the study was 74.3 kg, with a range of 37 kg to 120 kg. Demographic characteristics are shown in Table 2.

**Table 2:** Demographic characteristics

<b>Gender</b>	<b>Female, n (%)</b>	23 (44.2%)
	<b>Male, n (%)</b>	29 (55.8%)
<b>Age (years)</b>	<b>Mean (SD)</b>	40.1 (18.0)
	<b>Range</b>	13 - 77
	<b>Median (IQR)</b>	34 (26.5; 55.5)
<b>Weight (kg)</b>	<b>Mean (SD)</b>	74.3 (16.90)
	<b>Range</b>	37 - 120
	<b>Median (IQR)</b>	74.3 (65.0; 82.5)

SD: Standard deviation; IQR: Interquartile range.

#### *Initiation of antibiotics*

Over the study period 76 antibiotics were initiated for the 52 patients. Nearly half of the patients 23 (44.2%) were initiated on antibiotics on day one of admission to the MICU. Twelve (23.1%) of the 52 patients were initiated on day two and five (9.6%) on day three. The remainder of the patients were initiated on day four (2%), day five (6%), day six (4%), day seven (8%) and day eight (2%).

Of the 76 antibiotics prescribed initially, the majority 54 (71.1%) were started on the same day that the prior antibiotics were discontinued. Eight (10.5%) antibiotics were started one day after the prior antibiotics were stopped. The remainder of the ten patients' antibiotics were started 3-12 days after the prior antibiotics were stopped. The majority of patients 42 (80.8%; n=52) were transferred from the wards to the ICU and 10 patients (19.2%) were admitted from home.

#### *Length of hospital stay (LOS)*

The median length of hospital stay (LOS) in the MICU for all patients was 10.50 days (IQR: 6.0; 14.0) with a mean of 10.6 (SD: 4.9) days, ranging from 3 to 23 days.

*Antibiotics frequently prescribed and related costs*

During the study period 76 antibiotics were started for the 52 patients. Table 3 illustrates the frequently prescribed antibiotics and costs associated with antibiotic use in the MICU. The three antibiotics most frequently prescribed during the study period were Meropenem, (19 times), Piperacillin/Tazobactam (10 times), and Clarithromycin (9 times).

**Table 3:** Frequency and costs of antibiotics initiated in the MICU

Anti-infectives for systemic use		Number of patients (n=52)	Mean days on antibiotic	Mean total daily dose (g)	Mean cost per day on antibiotic (R)	Mean cost per treatment (R)
ATC code	INN of Antibiotic (n=16)					
J01D	Meropenem	19	7.5	3.26	890.68	6 335.31
H02						
J01C	Piperacillin/tazo bactam	10	5.3	14.85	354.09	1 867.02
R05						
J01F	Clarithromycin	9	8.4	1	253.06	2 136.95
A09						
J01X	Linezolid	5	5.2	1.20	601.76	3 129.15
X08						
J01D	Ceftriaxone	5	5.4	2	45.12	243.65
D04						
J01C	Cloxacillin	4	6.0	11	193.16	1 229.20
F02						
J01D	Imipenem	3	6.7	3	762.96	5 001.63
H51						
J01X	Teicoplanin	3	6.7	0.80	299.26	1 995.07
A02						
J01X	Vancomycin	3	6.7	2	89.04	593.60
A01						
J01C	Co-amoxiclav	6	6.0	3.6	47.25	283.50
R02						
J01E	Co-trimoxazole	2	3.0	2.4	5.88	17.63
E01						
J01G	Gentamicin	2	5.5	0.18	7.11	42.62
B03						
P01A	Metronidazole	2	6.0	1.5	16.98	101.88
B01						
J01D	Ceftazidime	1	7.0	3	155.79	1 090.53
D02						
J01F	Clindamycin	1	5	1.8	36.96	184.80
F01						
J01A	Tigecycline	1	6	0.1	691.40	4 148.40
A12						
<b>Mean (SD)</b>					278.16 (298.01)	1 775.06 (1 949.56)
<b>Range</b>					5.88 - 890.68	17.63 - 6 335.31
<b>Median (IQR)</b>						
		6	2	174.48	1 159.87	

ATC: Anatomical Therapeutic Chemical Classification System; INN: International Nonproprietary Name; SD: Standard Deviation; IQR: Interquartile Range

In eight cases, Clarithromycin was used as part of dual therapy with either one of the following agents: i) Meropenem or Ceftriaxone for three patients; ii)

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combination of Piperacillin/Tazobactam or Cloxacillin in two patients; iii) Vancomycin, Linezolid or Co-trimoxazole respectively as part of the combination for three patients.

### Total costs for initial antibiotic use

As summarised in Table 3, the total costs for all initial antibiotics used during the study period were R209 140.40 and a cost of R4 021.9 per patient. The average cost of all initial antibiotics was R31 240.77 per day and R600.8 per patient day. The mean costs per treatment period for the three most frequently prescribed antibiotics were R63 35.31 for Meropenem, R1 867.02 for Piperacillin/Tazobactam, and R2 136.95 for Clarithromycin.

### Organ systems affected and diagnoses

Figure 1 illustrates the different organ systems and disease states affected for the 52 patients. In many cases, more than one organ system per patient were affected. Evidently '*infectious diseases*' were diagnosed most frequently, followed by diagnoses made related to the endocrine-metabolic, cardiovascular, renal and respiratory system.

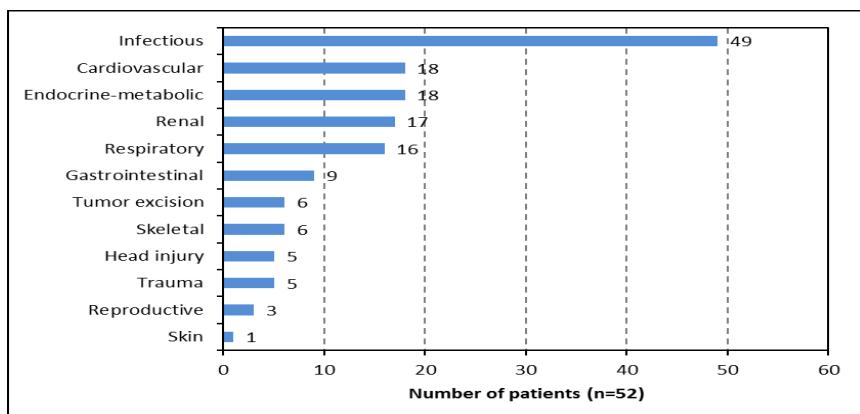


Figure 1: Organ systems and disease states affected.

During the study period a total number of 167 diagnoses were made for the 52 patients with an average of 3.2 diagnoses per patient. The most common diagnosis made during the study period was sepsis (11 times; 6.6%), followed by community-acquired pneumonia (CAP), hypertension and respiratory failure, which was eight times (4.8%) in each case.

### Number of antibiotics used during the hospital stay

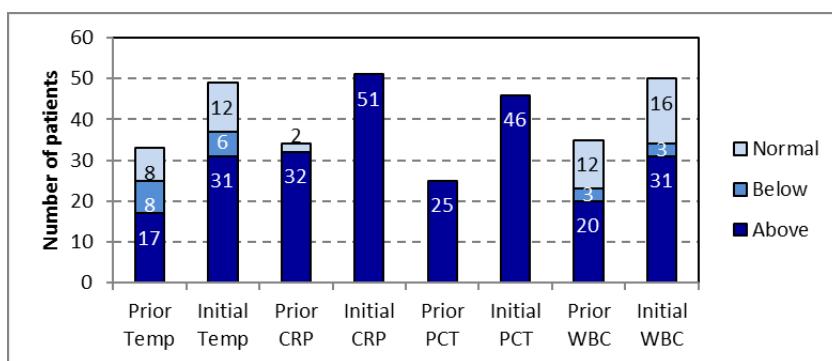
Overall, 76 antibiotics were prescribed for the 52 patients over the study period with an average of 1.4 antibiotics prescribed per patient. The antibiotics were prescribed according to the following classes:

- $\beta$ -lactams, 48 (63.2%):
- Carbapenems, 22 (28.9%)
- Penicillins, 20 (26.3%)
- Cephalosporins, 6 (7.9%)
- Macrolides, 9 (11.8%)
- Glycopeptides, 6 (7.9%)
- Oxazolidinones, 5 (6.6%)
- Aminoglycosides, 2 (2.6%)
- Trimethoprim/sulfamethoxazole, 2 (2.6%)
- Metronidazole, 2 (2.6%)
- Clindamycin, 1 (1.3%)
- Tigecycline, 1 (1.3%)

The majority of patients (38; 73.1%) were started in the MICU on one antibiotic, 10 (19.2%) were started on two antibiotics, three (5.8%) were started on three antibiotics and one (1.9%) patient was started on four antibiotics (Ceftriaxone, Cloxacillin, Co-trimoxazole and Claritromycin).

#### *Inflammatory biomarkers*

Figure 2 illustrates the infection biomarkers (CRP, PCT, WBC and temperature) available for patients one day *prior* to initiation of initially-prescribed antibiotics (the day before antibiotics was prescribed). This is compared to the inflammatory biomarkers that were taken *on the day* of antibiotic initiation in the MICU. Not all of the biomarkers were available or recorded for the patients, and only the ones recorded in the file are displayed in Figure 2.



Temp: Temperature; CRP: C-reactive protein; PCT: Procalcitonin; WBC: White blood cell  
Normal values: Temp: 37.0°C; CRP: below 5mg/l; PCT: 0.00–0.05ng/ml; WBC: 3.92–9.88 10<sup>9</sup>/l

**Figure 2:** Inflammatory biomarkers prior to and on the day of antibiotic initiation in the MICU

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**Temperature:** Almost a third of all patients (17; 32.7%) were admitted to the MICU with a mean *prior* temperature value of 37.2°C. Sixty percent (31) of the patients that were initiated on antibiotics in the MICU, had a slightly raised *initial* temperature with a mean value of 37.6°C.

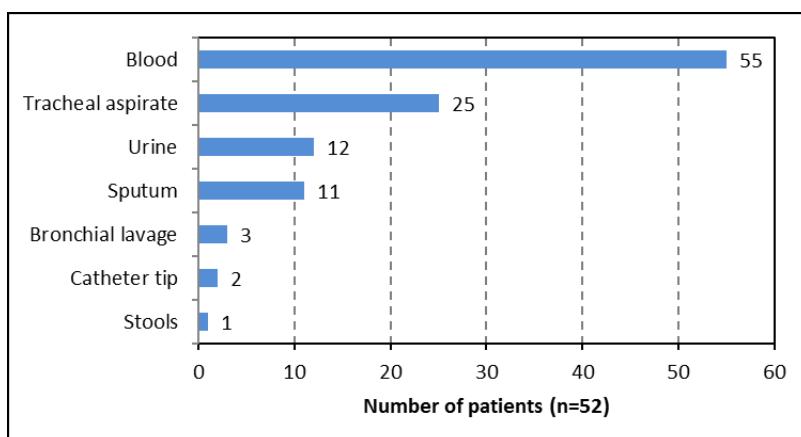
**C-reactive protein (CRP):** Nearly two thirds of the patients (32; 61.5%) were admitted to the MICU with a raised prior CRP and a mean value of 198.2mg/l (considered as above 5mg/l). Almost all patients (51; 98.1 %), initiated on antibiotics in the MICU had a raised initial CRP with a mean value of 208.9mg/l.

**Procalcitonin (PCT):** Nearly half of the patients (25, 48.1%), were admitted with an elevated prior PCT, with a mean value of 42.3ng/ml (considered as above 0.00-0.05ng/ml). In the majority of the study population 46 (88.5%) the initial PCT was elevated on the day antibiotics were initiated with a mean value of 31.8ng/ml.

**White blood cell (WBC) count:** Less than half of the patients (20; 38.5%) were admitted with a raised prior WBC count with a mean value of  $11.9 \times 10^9/l$  (considered as above  $3.92-9.88 \times 10^9/l$ ). For 31 patients (59.6%) the initial WBC count was elevated on the day antibiotics were initiated, with a mean value of  $14.5 \times 10^9/l$ .

### Microbiological cultures obtained

A total number of 109 positive cultures were obtained during the study period. The number of positive cultures for all micro-organisms, according to specimen origin before or on the day when the initial antibiotic was prescribed, are illustrated in Figure 3.



**Figure 3:** Number of positive cultures and specimen origin

Of the cultures taken before the initially-prescribed antibiotic was started, 109 were positive, of which 64 were positive for bacteria. The remainder of the 45 positive organisms were of viral, fungal, mycobacterial and parasitic origin. Of the 64 positive cultures taken, 35 (54.7%) were from gram-negative *bacilli* and 19 (36.5%) were from gram-positive cocci. *Acinetobacter baumannii* was cultured nine times.

Table 4 provides a summary of all micro-organisms cultured before and on the day the initially-prescribed antibiotic was started. For the majority of patients (43; 82.7%) cultures were taken prior to initiation of the antibiotics in the MICU.

**Table 4:** Cultures prior to the initiation of initial antibiotics in the MICU

Organism	Frequency
<b>Gram negative bacilli</b>	
<i>Acinetobacter baumannii</i>	9
<i>Klebsiella pneumoniae</i>	7
<i>Pseudomonas aeruginosa</i>	7
<i>Enterobacter cloacae</i>	6
<i>Citrobacter freundii</i>	2
<i>Escherichia coli</i>	1
<i>G negative bacilli<sup>a</sup></i>	1
<i>Stenotrophomonas maltophilia</i>	1
<i>Serratia</i>	1
<b>Gram positive cocci</b>	
<i>Coagulase-negative staphylococci</i> (CoNS)	9
<i>Staphylococcus epidermidis</i>	3
<b>Methicillin-resistant Staphylococcus aureus (MRSA)</b>	2
<i>Enterococcus faecalis</i>	1
<i>Staphylococcus aureus</i>	1
<i>Staphylococcus</i>	1
<i>Streptococcus</i>	1
Vancomycin resistant enterococci (VRE)	1
<b>Gram negative cocci</b>	
G negative cocci	2
<b>Miscellaneous</b>	
No growth	18
Fastidious Antibiotic Neutralization Anaerobic	9
G positive and G negative cocci	7

#### *Appropriate use of antibiotics*

Antibiotic use would be considered appropriate when evaluated according to the parameters as listed in Table 1. For example if it was the appropriate drug, at the right dose and for the right indication as specified in the South African Essential Medicines List at Hospital Level, (Standard Treatment Guidelines for Adults. 1996) and if the patient had raised infectious biomarkers, and if the patient did not

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have any risk factors (e.g. impaired renal function) for the use of the drug, then the antibiotic would be considered appropriate for the particular patients.

**Table 4** (continued): Cultures prior to the initiation of initial antibiotics in the MICU

<b>Organism</b>	<b>Frequency</b>
<i>Candida albicans</i>	5
No bacteria	3
Cytomegalovirus positive	2
Fastidious Antibiotic Neutralization Aerobic (FAN)	2
Hepatitis B positive	2
<i>Negative acid-fast bacilli</i>	2
Bacteria observed	1
H1N1 positive	1
Malaria positive	1

<sup>a</sup>No specific strain was listed, reflected as stated on the laboratory report

After the above parameters were taken into consideration by the pharmacist, and following consultation with the infectious diseases specialist, the results indicated that 46 (60.5%), of all initially-prescribed antibiotics in the MICU (n =76) were prescribed appropriately. Reasons for inappropriate antibiotic 30 (39.5%) use were as follows:

- Three antibiotics were initiated in patients with normal inflammation biomarkers
- Six antibiotics were initiated in patients with no positive cultures and no raised inflammation markers
- Ten antibiotics were initiated for patients with no positive cultures
- Eleven antibiotics were inappropriately prescribed according to the sensitivity patterns.

## **Discussion**

The mean age of the patients admitted to the MICU and enrolled in this study was 40.1 years, with females (55.8%) predominating slightly, which was in line with a similar study (Statistics South Africa. 2011; Song et al., 2013). This age group constitutes patients that are economically active in the society.

The mean duration of hospital stay in this study was 10.6 days (range 3 to 23 days). This is in line with international (Wilke, Grube & Bodmann, 2011) and local literature as a similar study conducted at Groote Schuur Hospital in Cape Town, South Africa, also reported similar results with regards to length of hospital stay (Meyer, Smith & Mayosi, 2012).

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The infection biomarkers obtained (WBC, CRP, PCT and temperature) for the patients in this study on admission to the MICU, were all raised and used to guide antibiotic use. Over the past two decades PCT, CRP, WBC have been extensively studied as serum markers of systemic infection and sepsis (Assink-de Jong et al., 2013). The researchers further reported that PCT-guided therapy is not only beneficial for respiratory tract infections but also provide useful guidance for antimicrobial treatment in critically ill patients in the ICU who are treated for suspected bacterial infections.

For half of the 52 patients, sepsis or an infective diagnosis was based on blood cultures. Specifically, positive “sterile site” cultures (such as blood cultures) better represent true infection than positive “non-sterile site” cultures (such as wound and sputum cultures). Non-sterile sites are more likely to reflect colonization or contamination (Katsios et al., 2012). According to the Surviving Sepsis Campaign (2014), at least two sets of blood cultures (both aerobic and anaerobic bottles) should be obtained before antimicrobial therapy is initiated (Dellinger et al., 2012).

The two antibiotics mostly prescribed, Meropenem and Piperacillin/Tazobactam, are both members of the  $\beta$ -lactam group. A recent study conducted in 2012, similarly reported  $\beta$ -lactams, including Carbapenems, as the most frequently prescribed antibiotics in empiric therapy for patients with severe sepsis and septic shock (Diaz-Martin et al., 2012). Meropenem was most frequently prescribed (25%; n=76) as initial antibiotic therapy for patients admitted to the MICU. This is in line with the Surviving Sepsis Campaign guidelines (2014) stating that a broad-spectrum antibiotic is indicated as first-line therapy in patients with sepsis (Dellinger et al., 2012). Furthermore it was also the most expensive first line therapy at a mean daily cost of R890.68. According to a study conducted in a large tertiary care academic medical centre, Meropenem was also the most expensive antibiotic (Standiford, Chan, Tripoli, Weekes & Forrest, 2012). Meropenem as first line therapy was approved by the infectious diseases specialist for patients with contributing co-morbidities that could lead to their demise before administration.

Of the 52 patients included in the study, ten patients (19.2%) were prescribed Piperacillin/Tazobactam with an average daily cost of R354.09. In a study conducted in Spain  $\beta$ -lactams are the mainstay of empiric therapy in patients with severe sepsis and septic shock (Diaz-Martin et al., 2012). The combination Piperacillin/Tazobactam was also used as empiric therapy for patients treated in an ICU setting with community acquired pneumonia (CAP) (Fariba, 2015). Empiric therapy should attempt to provide antimicrobial activity against the most likely pathogens based upon each patient’s presenting illness and local patterns of infection (Dellinger et al., 2012). Clarithromycin was mostly used as part of dual therapy in CAP. Clarithromycin is effective against commonly encountered

pathogens and is well tolerated (McCarthy, 2000). Azithromycin was not freely available in SBAH to use for CAP, and Clarithromycin was therefore used instead. A patient with CAP in an ICU setting will benefit from the addition of either Azithromycin or Clarithromycin (Fariba, 2015).

In this study, 60.5% of antibiotics (n=76) were mostly prescribed appropriately, while 39.5% of antibiotics were prescribed inappropriately, according to weight, renal function (creatinine clearance), hepatic function, infection biomarkers (WBC count CRP, temperature, blood cultures and Procalcitonin). Antibiotic indication, dose and duration of treatment were compared to the Standard Treatment Guidelines and Essential Medicine List for Adults at Hospital Level and other relevant literature (National Department of Health, 1996).

A multi-centre hospital-based study carried out in 2011, reported that 221 patients were identified with hospital acquired pneumonia (HAP) and ventilator-associated pneumonia (VAP), of whom approximately half (107; 48.4%) received adequate initial intravenous antibiotic therapy as opposed to 114 (51.6%) who received inadequate initial intravenous antibiotic therapy (Song et al., 2013). A study that was conducted in 2012 on antibiotic prescription practices and their relationship to outcomes in South African intensive care units, revealed that therapeutic antibiotics were initiated in 182 patients, with more than half (54.9%) of them receiving inappropriate initial antibiotic therapy (Paruk et al., 2012).

The total cost of initial antibiotic use during the study period was R209 140.40 (R4021.90 per patient for the study period), with an average cost for all initial antibiotics during the study period of R31 240.77 (R600.80 average cost per patient during the study period). No similar studies have been performed in any of the academic hospitals in South Africa to be able to compare rand values in terms of cost of initial antibiotic use in the ICU. However, a similar study that was conducted within a tertiary care academic medical center in the USA in 2012, reported higher costs of antibiotics, when compared to this study (Standiford et al., 2012).

## **Conclusions**

From this study it was evident that the  $\beta$ -lactams were the mainstay of initially-prescribed antimicrobial therapy in the MICU. The majority of initially-prescribed antibiotics were prescribed appropriately when considering drug factors, infectious biomarkers, costs, and patient factors, contrary to what is generally described in literature in terms of appropriateness of initially prescribed antibiotics. It is therefore, suggested that the presence of a clinical pharmacist and infectious diseases specialist, with the addition of an antibiotic policy and training might ensure continuous rational antibiotic use.

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