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Emerging Trends in Antimicrobial Resistance

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ABSTRACT

Burn injury is associated with high morbidity, long term disability and mortality. This phenomenon is seen all over the world, but is more pronounced in economically developing countries. Treatment of burn patients has evolved to a great extent today, but infection still continues to be the main cause of morbidity and mortality in the burn patients. Invasion of the burn wound by microbial pathogens leads to burn wound infections in burn patients. The risk of contracting a life threatening infection is high in burn patient due to the nature of the injury, an immunocompromised state, prolonged hospital stay and multiple interventions. Septic processes account for approximately 73% of all deaths within the initial five days of post-burn.

Burn patients usually have a prolonged stay in the burn unit. The microbiological profile of the organisms invading the burn wounds changes over time. A burn wound typically has large amounts of protein rich fluid exudate, which forms a healthy medium for bacterial growth. New burn admissions usually show the predominance of gram positive organisms in their wounds. Gram negative organisms become more prevalent as the duration of treatment increases. These organisms are potentially more invasive. Endogenous gram-negative flora from the patient's gut colonize the wounds within a few days of the burn. The gram-positive flora, are the natural inhabitants of the skin. Infection in burn patient is not only one of the major reasons for mortality, but also for prolonging the hospital stay and delay skin cover procedures such as skin grafting. It is hence considered prudent for every burn institute to determine the changing anti-microbial profile of the burn patients and their sensitivity pattern over time.

The microbial flora affecting the burn wound is a dynamic entity and continues to evolve as the burn wound progresses. This change in the microbiological profile of the wound varies with each patient over the duration of his admission for the treatment of his burn injury and also in each burn unit over the time. Nosocomial organisms are commonly seen infecting the burn wounds and have multi-drug resistance antimicrobial profiles.

In addition, there was no comprehensive study done on the changing trends in the burn wound microbiology with emphasis on changing trends in the microbiological profile of burn wounds

KEYWORDS: *wounds, microbiology, noscomial, patients, immunocompromised, burn*

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INTRODUCTION

Antimicrobial resistance (AMR) is one of the most serious public health threats of the twenty-first century [1]. Globally, about 700,000 people die due to AMR related illnesses every year. It is estimated that by 2050 these deaths will reach10 million, costing the world US$100 trillion [2]. In 2014, the World Health Organisation (WHO) reported > 25% resistance to penicillin by *Streptococcus pneumoniae*

in all its six regions. Five out of the six regions reported > 50% resistance to 3rd generation cephalosporins by *Eschericia coli*. WHO reported resistance to last resort antibiotics like vancomycin, 3rd generation cephalosporins, clindamycin and carbapenems by some organisms. Resistance to these last line antibiotics led the WHO to advocate for research and development of more antimicrobials for treatment of these priority organisms in 2017 [4]. We estimated deaths and disability-adjusted life-years (DALYs) attributable to and associated with bacterial AMR for 23 pathogens and 88 pathogen–drug combinations in 204 countries and territories in 2019. We obtained data from systematic literature reviews, hospital systems, surveillance systems, and other sources, covering 471 million individual records or isolates and 7585 study-location-years. We used predictive statistical modelling to produce estimates of AMR burden for all locations, including for locations with no data. Our approach can be divided into five broad components: number of deaths where infection played a role, proportion of infectious deaths attributable to a given infectious syndrome, proportion of infectious syndrome deaths attributable to a given pathogen, the percentage of a given pathogen resistant to an antibiotic of interest, and the excess risk of death or duration of an infection associated with this resistance. [1,2]

Using these components, we estimated disease burden based on two counterfactuals: deaths attributable to AMR (based on an alternative scenario in which all drug-resistant infections were replaced by drug-susceptible infections), and deaths associated with AMR (based on an alternative scenario in which all drug-resistant infections were replaced by no infection). We generated 95% uncertainty intervals (UIs) for final estimates as the 25th and 975th ordered values across 1000 posterior draws, and models were cross-validated for out-of-sample predictive validity. We present final estimates aggregated to the global and regional level. The six leading pathogens for deaths associated with resistance (*Escherichia coli*, followed by *Staphylococcus aureus, Klebsiella pneumoniae, Streptococcus pneumoniae, Acinetobacter baumannii*, and *Pseudomonas aeruginosa*) were responsible for 929 000 (660 000–1 270 000) deaths attributable to AMR and 3·57 million (2·62–4·78) deaths associated with AMR in 2019. One pathogen–drug combination, meticillin-resistant *S aureus*, caused more than 100 000 deaths attributable to AMR in 2019, while six more each caused 50 000–100 000 deaths: multidrug-resistant excluding extensively drug-resistant tuberculosis, third-generation cephalosporin-resistant *E coli, carbapenem-resistant* A baumannii, *fluoroquinolone-resistant E coli*, carbapenem-resistant *K pneumoniae*, and third-generation cephalosporin-resistant *K pneumoniae*.[3,4]

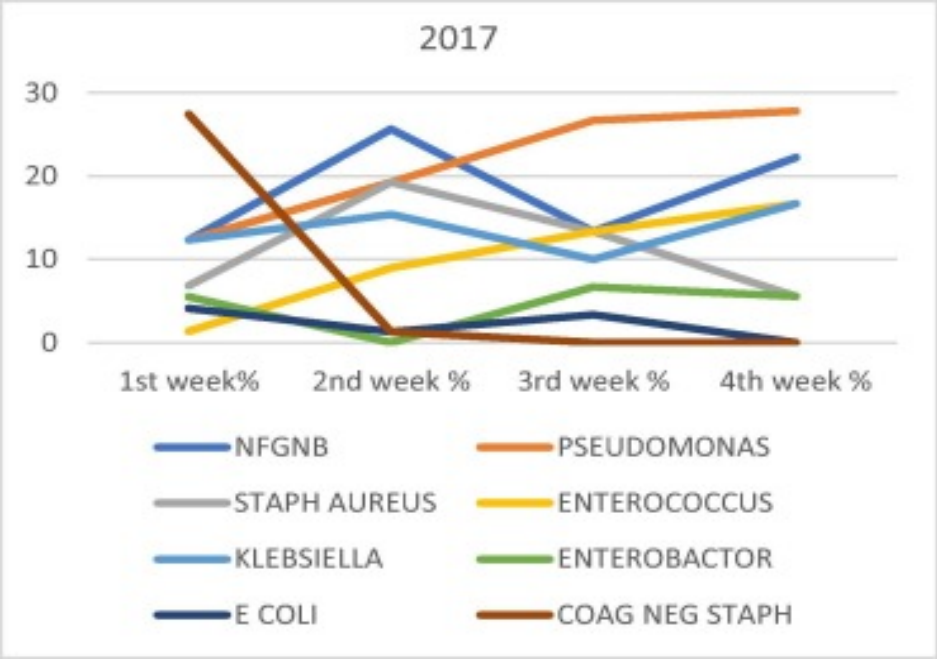
Antimicrobial resistance experiment

Many bacteria are demonstrating increasing levels of resistance to commonly used antibiotics. While this has implications for the healthcare system as a whole, many patients infected with these resistant organisms will initially present to the emergency department (ED).[5]

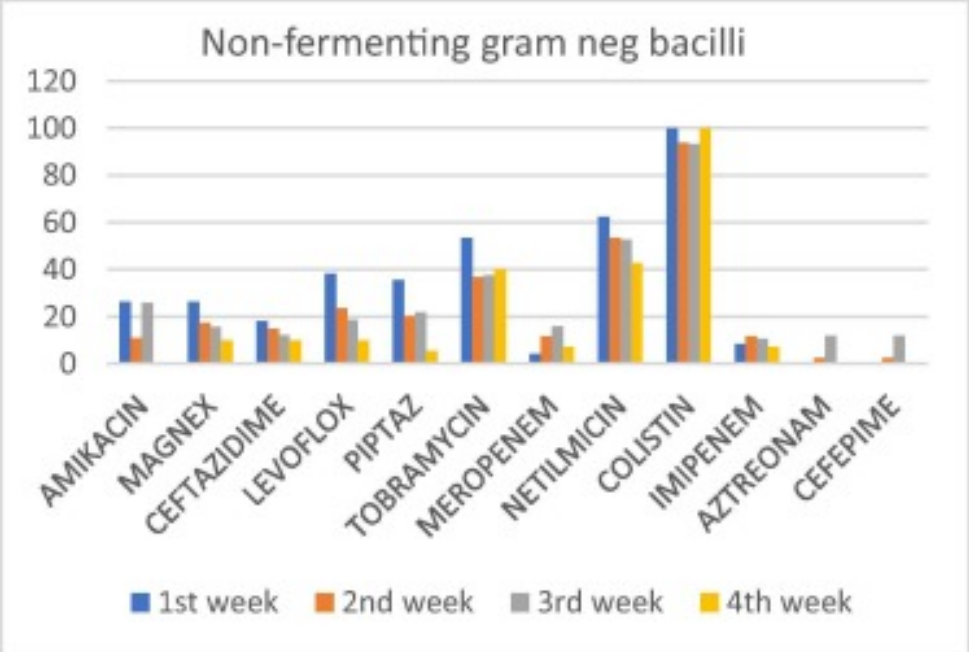
Discussion and Results

Burn wound infection is a dynamic entity that is one of the major determining factors of the patient's hospital stay, mortality and morbidity. The analysis of the changing trends in the burn wounds microbiological profile will help deciding a more effective empirical therapy for burn wound infection. The gram-positive organisms have become more common in 2017 in the first week of burn admission as compared to previous years. From the second week onwards the gram-negative organisms are the more prevalent organisms. Non-fermenting gram-

negative bacilli, *Pseudomonas aeruginosa* and *Staphylococci* are the most commonly seen organisms. The patients with a rapid progression of sepsis with burn wound infected with *Pseudomonas* and non-fermenting gram-negative bacilli will benefit from starting of Colistin at an early stage. Similarly, those with *Staphylococci* growing in the burn wounds can benefit from Linezolid, Chloramphenicol.[6,7]

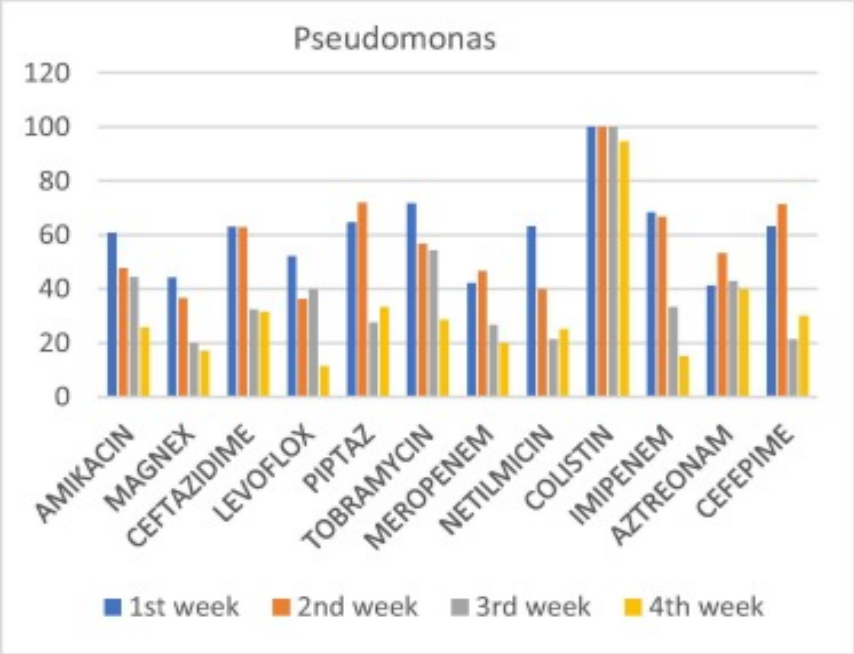


Percentage of different organisms isolated from burn wounds over 1st to 4th week

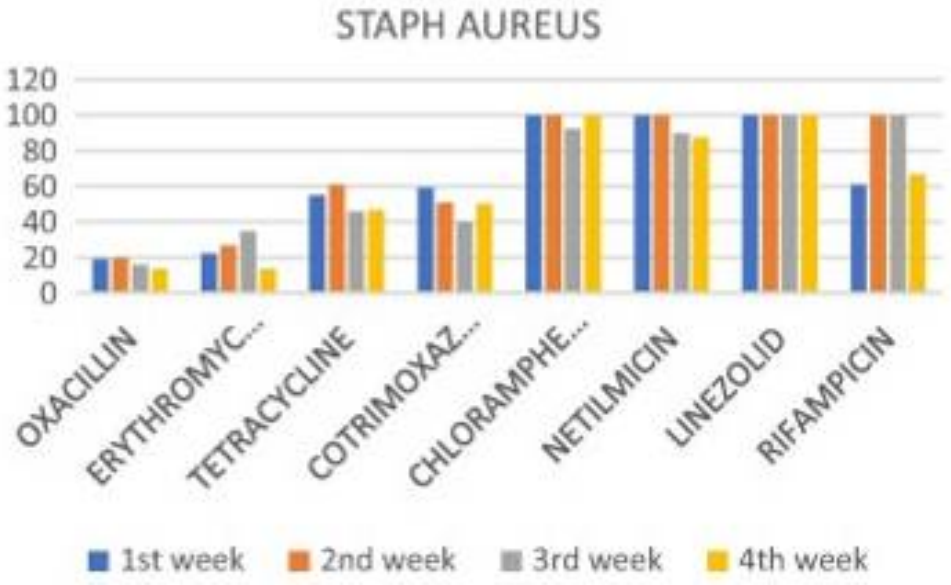


Susceptibility of Non-fermenting gram negative bacilli to different antibiotics over 1st to 4th week

Non-fermenting gram-negative bacilli (*NFGNB*) were the most commonly isolated organisms over all in the 5 years of the study. In the first week Enterococcus, *NFGNB* and coagulase negative *staphylococci* were isolated from the burn wounds. In the second week, the most common organism isolated was *NFGNB* in all 5 years. In the 3rd week and 4th week, *Pseudomonas Aeruginosa* was the most common organism isolated in all 5 years. The most common bacterial isolate (in numbers) from cultures was Non-fermenting gram negative bacilli with 212 isolates, which was in contrast with the other studies. Gram negative bacteria were resistant to majority of antibiotics with the sensitivity progressively diminishing as the duration of the burn injury progresses.[8,9] However, they remained sensitive to Colistin. This was in contrast to other studies which found Polymixin to be effective drug for the treatment of gram negative bacilli.



Complete sensitivity is shown by *Pseudomonas aeruginosa* only to Colistin in the first week. 1st line drugs i.e. Amikacin, Magnex, Ceftazidime, Levoflox and Piperacillin tazobactam show sensitivity in the range of 50–70% and resistance of 20–30%. This trend continues almost the same over the 2nd and the 3rd week. In the 4th week, minimal Colistin resistance is noted (5.6%) with sensitivity of 94.4%. All the first line drugs mentioned above show a higher level of resistance ranging between 65 and 80%.[10]



In the first week, *Methicillin Resistant Staphylococcus aureus* (MRSA) was present in high percentage of nearly 81%. Chloramphenicol, Netilmicin, Linezolid and Rifampicin have 100% sensitivity. Similar trend continues over 2nd and 3rd week with minimal resistance developing towards Chloramphenicol (7.69%) and Netilmicin (10%). In the 4th week MRSA has gone up to 86.67% with developing resistance against Netilmicin (12.5%) and Rifampicin (33.33%) but it was still 100% sensitive to Chloremphenicol and Linezolid.

Pseudomonas and *NFGNB* species were sensitive to Colistin, throughout the course of the admission. Their resistance to 1st line drugs like Amikacin, Ceftazidime, Magnex, Piptaz was noted, on an increasing scale from the 1st culture to the 4th culture.

There is an increase in the presence of MRSA from 80% in the first culture to 86% in the 4th culture. Though it still carries 100% of sensitivity for Linezolid, Chloramphenicol.[11]

Conclusions

We conclude from our study that gram positive organisms have emerged as the common organisms isolated from the burn wounds in the first week of burn admission in 2016 and 2017 as compared to previous years. From the second week, the gram-negative organisms are the more prevalent organisms. Their presence in the burn wound and their antibiotic

resistance keeps progressively increasing as time passes.

Overall, Non-fermenting gram-negative bacilli, *Pseudomonas aeruginosa* and *Staphylococci* are the most commonly isolated organisms over the last 5 years. The patients with a rapid progression of sepsis with burn wound infected with *Pseudomonas* and non-fermenting gram-negative bacilli will benefit from starting of Colistinat an early stage. Similarly, those with *Staphylococci* (MRSA) growing in the burn wounds will benefit from Linezolid, Chloramphenicol. [12]

Microbial flora of the burn wound and its antibiotic profile is an ever-changing entity. Constant evaluation and analysis of the wound cultures will help the treating physicians to keep abreast with the pathogens and give the patient a fighting chance in this battle for survival. Each burn centre should have its own system of audit and should review its burn wounds cultures periodically, as the results will change for different centres depending on location, population served and the type of injury sustained. Antimicrobial susceptibility difference are also to be followed as different for different centres.[13]

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