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Review Article

MDR Sepsis in Critically Ill Patient: Global Trend and Specific Challenges for Bangladesh

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Abstract:

Multidrug-resistant (MDR) sepsis poses an escalating global health threat, particularly in intensive care units (ICUs) where vulnerable patient populations are at heightened risk due to frequent invasive procedures, immunosuppression, and prolonged hospitalization. This review explores the global burden and rising prevalence of MDR sepsis among ICU patient population, with a specific focus on challenges and implications in Bangladesh. Ventilator-associated pneumonia (VAP), catheter-associated urinary tract infections (CAUTIs), and central-line-associated bloodstream infections (CLABSIs) are identified as the predominant ICU-acquired infections contributing to MDR sepsis. This review highlights alarming rates of antimicrobial resistance (AMR) among Gram-negative and Gram-positive pathogens, with Bangladesh reporting disproportionately higher resistance levels compared to global trends. Inadequate antimicrobial stewardship, poor infection prevention and control (IPC) practices, and lack of robust regulatory oversight exacerbate the crisis in resource-limited settings like Bangladesh. Furthermore, the review emphasizes the importance of adopting a multidisciplinary and One Health approach, strengthening surveillance systems, enhancing IPC infrastructure, reforming medical education, and raising public and political awareness. Addressing MDR sepsis in Bangladesh demands urgent policy-level interventions, international collaboration, and sustainable investment in healthcare capacity building to mitigate this silent yet deadly epidemic.

Keyword: *AMR, VAP, CLABSI, CAUTI, ICU acquired infection, MDR, MDR sepsis, MDR global trends, Sepsis.*

Introduction:

Across the globe, healthcare systems grapple with the challenges posed by sepsis, a life-threatening condition resulting from a dysregulated host response to infection. Sepsis claims the lives of 11 million individuals annually and leaves millions more incapacitated.[1] When this infection caused by a multi-drug resistant (MDR) organism that adds an extra layer of complexity on sepsis, rendering conventional treatments ineffective and exacerbating the already critical condition of patients.[2] Patients infected with MDR bacteria exhibited notably higher mortality.[3] MDR sepsis was associated with worse clinical outcomes, prolonged hospital stays and nearly twice the hospitalization costs in contrast to the non-MDR group[4]. The European Union estimated that over 35,000 individuals succumb annually due to infections caused by antibiotic-resistant bacteria.[5] The global prevalence of MDR sepsis raised over time.[6,7]

We know that globally ICU patient population is more vulnerable to hospital-acquired infection(HAI) due to the high prevalence of invasive procedures and devices, induced immunosuppression, comorbidity, frailty and increased age, moreover HAIs in ICU patient population exhibit high mortality and morbidity.[8] Intensive care units (ICUs), particularly in tertiary care facilities, tend to exhibit a higher frequency of infections caused by multidrug-resistant organisms (MDROs) compared to settings outside the ICU.[9] So the invisible threat of multidrug-resistant (MDR) sepsis among ICUs poses a significant challenge for healthcare facilities that needs immediate attention.

The purpose of this review is to understand the global MDR sepsis load among the ICU patient population, comparison of the findings with Bangladeshi ICU patient population, specific challenges for Bangladesh in combating this health threat and potential solutions.

Dimension of MDR Sepsis: Global perspective

Ventilator associated pneumonia (VAP), Catheter associated urinary tract infection (CA-UTI) and Central-line-associated bloodstream infections (CLABSIs) are the most common HAI in ICU.

VAP is the most frequent ICU acquired infection. The prevalence of VAP varies among different countries; the highest VAP prevalence rate (116 per thousand ventilator days) was reported from India.[10] Gram-negative organisms, such as Acinetobacter spp., Pseudomonas aeruginosa, and Klebsiella pneumoniae, and Gram-positive organisms, such as Staphylococcus aureus, were frequently found in the tracheal aspirate samples of VAP patients.[11-14] Among this organism responsible for VAP, the burden of MDR pathogen is very high; the frequency varies between healthcare centers. One study from India reported that, VAP is associated with 43.65% MDR pathogens where Late-onset VAP was predominantly caused by MDR pathogens (77.27%).[15] MDR gram negative

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bacterial (GNB) pathogen load was 48.52% reported from Vietnam, where they sub categorized GNB resistance as 10.6% MDR, 63.6% extensively drug-resistant (XDR), and 25.8% pan drug-resistant (PDR), this study also report colistin resistance about 2.8–20%.[16]

When reported by the specific organism species- Most of isolated A. baumannii (97%) and S. aureus (88%) were multidrug resistant.[11] The combined prevalence of MDR among P. aeruginosa causing VAP was 33%, where Iran reported the highest prevalence at 87.5%, while the USA had the lowest at 19.7%. The prevalence appears to be steeply increasing over times.[17] According to the 2019 data from the European Antimicrobial Resistance Surveillance Network (EARS-Net), more than a third of the K. pneumoniae (36.6%) identified in the EU/EEA showed resistance to at least one antibiotic group monitored, with multiple resistance to various antimicrobial groups being common.

Intensive Care Unit acquired infection is an independent predictor for poor prognosis, and VAP caused by MDR and XDR strains is very challenging to cure.[18] ICU-acquired pneumonia caused by highly antimicrobial-resistant (HAMR) bacteria was linked to higher rates of mortality, prolonged ICU stays, and extended periods of mechanical ventilation.[19]

Catheter associated urinary tract infection (CA-UTI) is one of the most common ICU acquired infection and sepsis. Among Hospital acquired infection 29% are CUATI.[20] The CA-UTI incidence density was 9.6/1000 catheter days.[21] Several study stated that Escherichia coli is the most common responsible organism for CAUTI followed by Pseudomonas species, Klebsiella species and Enterococcus species, which were the dominant bacterial isolates. Candida also an important causative organism for CAUTI. One study from Addis Ababa, Ethiopia, showed that the overall prevalence of candiduria was 19%, where bacteriuria was 21%. A significant proportion of this organism is MDR.[20] The fungus exhibit resistance to multiple classes of antifungal drugs is known MDR fungal pathogen, Candida auris is an alarming example of an emerging MDR fungal pathogen.[23] The drug resistance pattern was varied with study area and population . In recent studies across different regions, on rates of multi-drug resistant (MDR) uropathogens have been documented. Mohamed et al.[24] highlighted a substantial 47% prevalence of MDR uropathogens in Mogadishu, Somalia. Similarly, research by Obaid et al.[25] revealed a significant antibiotic redistence rate of 19.67% among uropathogens in saudi Arabia. Meanwhile findings from Bizuayehu et al. [26] reported an overall 65.8% of these pathogens were resistance to multiple antibiotics in Addis Ababa, Ethiopia. Along with alarming rates of antibiotic resistance Bizuayehu et al.[26] reported the resistance rates among specific isolates: 86.7% of Acinetobacter isolates, 100% of Klebsiella species isolates, and all E. coli isolates (100%) exhibited resistance to multiple antibiotics. The global scenario of Candida resistance is concerning. Candida auris, a newer species, is particularly resistant to antifungal drugs and can spread quickly in healthcare settings.[27] CAUTIs are also associated with increased morbidity, mortality, healthcare costs and ICU length of stay.[28]

Central-line-associated bloodstream infections (CLABSIs) are serious healthcare-associated infections and very common among ICU patient populations with substantial morbidity and hospital costs. The incidence rates of CLABSI varied across different settings. According to the World Health Organization's systematic review and meta-analysis of published data, CLABSI rates were found to be significantly higher in low- and middle-income countries (LMICs) compared to high-income countries. Specifically, the rate was reported as 12.24 CLABSIs per 1,000 central line-days in LMICs, whereas in high-income countries, it was documented as 3.5 .[29] However The CLABSI rate can be significantly reduced over time by CLABSI prevention bundle's reinforcement.[30,31] Gram-negative bacteria (59.3%) were main microorganisms of CLABSIs.[32] The most frequently implicated pathogens included Acinetobacter baumannii, Klebsiella pneumoniae, Pseudomonas aeruginosa, Staphylococcus Species. and Enterococcus. The predominant organism varied across different healthcare settings.[30,31,33,34]However, each study consistently highlighted a significant prevalence of multidrug-resistant (MDR) pathogens.[34] from Athens, Greece, reported a CLABSI incidence rate of 4.80 per 1000 catheter-days, where MDR organisms accounting for 2.62 per 1000 catheter-days.[31] in New Delhi, India, found that 81.6% of CLABSIs were caused by MDROs, including 18.4% that were pan-drug resistant. Similarly, Al-Khawaja et al[30] that MDR organisms contributed to 56% of CLABSIs in their study in Bahrain.

MDR Sepsis: Bangladesh perspective

In Bangladesh, the organisms causing ventilator-associated pneumonia (VAP) are similar to global trends, but their resistance patterns are notably higher. Apart from Staphylococcus aureus, nearly 90% of the predominant bacterial strains exhibited resistance to multiple antibiotics, with approximately 60% of Acinetobacter spp. and Pseudomonas spp. categorized as extensively drug-resistant[12].

Available research data on prevalence of CAUTI) among ICU patients in Bangladesh are limited. Some study on hospital admitted catheterized patient have been carried out, which revealed that 30% of catheterized patient developed bacteriuria or urinary tract infection with catheter. E.coli, Klebsiella, Proteas and Pseudomonas aeroginosa are the common organism.

A study of bloodstream infections (BSI) in Bangladesh revealed that initially, Gram-negative bacteria were predominant. Among these, Salmonella Typhi was identified as the most common pathogen. Over time, there was a general rise in the presence of Gram-positive bacteria. Despite this shift, both Gram-positive and Gram-negative bacteria exhibited significant resistance to commonly prescribed antibiotics, highlighting the increasing difficulty in managing antimicrobial resistance in BSI cases in Bangladesh.[35] Patients with CLABSI infected with multidrug-resistant organisms had a statistically significant association with worse prognosis.[33]

Global Initiatives for Combating this Health Issue

Addressing antimicrobial resistance (AMR) as a critical global health threat., emphasizing the importance of international cooperation, data transparency, and evidence-based strategies to combat antimicrobial resistance effectively, In 2019, the World Health Organization (WHO) declared antimicrobial resistance as one of the top 10 global public health threats. The EU adopted a One Health approach to address AMR, recognizing its multifaceted impact on human health, animal health, and the environment.[36] By July 2022, the EU Commission, working closely with its Member States, prioritized AMR as one of the top three health concerns .To enhance understanding and inform policy decisions, WHO established the Global Antimicrobial Resistance Surveillance System (GLASS), with the aims to improve the quality and quantity of data on AMR epidemiology, enabling better monitoring of trends and providing reliable, comparable information for guiding antimicrobial treatment strategies.[1]

Challenges of MDR sepsis in Bangladesh and Possible Way Out:

Managing MDR Sepsis requires a multidisciplinary approach, including antimicrobial stewardship, infection control measures, and the development of new treatment strategies to combat antibiotic resistance. In resource limited setting like Bangladesh there are a lot of challenge for combating this burning issue.

Introducing antimicrobial stewardship programs (ASPs) poses greater challenges in low- and middle-income countries (LMICs) like Bangladesh due to numerous implementation hurdles. Antimicrobial drugs are readily accessible without prescription in Bangladesh through unregulated retail outlets (‘drug shops’).[35,37] This problem is worsened by pharmaceutical companies' aggressive and unethical marketing tactics aimed at increasing sales, particularly targeting drug shop attendants and other informal providers [38]. Furthermore, Bangladesh's regulatory framework lacks sufficient human, technical, and logistical capacity to effectively oversee this expansive market.[35] Physicians in low- and middle-income countries may have limited awareness of ASPs compared to those in higher-income nations.[39,40] In Bangladesh, people living below the poverty line often lack of health education about the proper use of antibiotics. Consequently, they frequently use antibiotics without consulting doctors and do not complete the antibiotic course.[41] Infection prevention and control (IPC) is an important component to reduce the AMR. Similar to many LMICs, IPC practices in Bangladesh have been impeded by overcrowding, understaffing, inadequate environmental cleaning, limited availability of hand washing stations, low adherence to recommended hand hygiene practices, inadequate ventilation, and insufficient IPC training.[42,43] The majority of tertiary care hospitals of Bangladesh show insufficient IPC level to guarantee the safety of healthcare workers, patients, and visitors. The median score on “The Infection Prevention and Control Assessment Framework (IPCAF)” across these hospitals was 355.0 out of a total of 800.[44] Due to low budget and shortage of manpower monitoring and evaluation activities and surveillance is very poor at Bangladesh. Though some activities and surveillance had been going on, those were primarily small in scale, uncoordinated, and lacking in a feedback mechanism.[45] There is very little medical research that examines the prevalence of hospital-acquired infections (HAIs) and their impact on prolonged hospital stays and costs. In Bangladesh, guidelines or protocols regarding the management of antimicrobial resistance (AMR) and the use of antibiotics were absent from the medical and allied health education curricula. A very few institutions like Bangladesh Medical University (BMC) and Chittagong Medical College rely on their own institutional guidelines for patient treatment.[45] One Health approach is also mandatory for combating the complex issue, MDR sepsis. But in Bangladesh, its application remains in rudimentary stage, particularly in addressing AMR issues in veterinary contexts, as noted by.[46] Unfortunately environmental sectors are far behind from the initiatives of implementation of One Health approach.[45]

Bangladesh badly needs to develop trained healthcare providers, enforcing guidelines for antibiotic administration, and closely monitoring both antibiotic consumption and resistance trends to ensure effective AMPs. Like other LMICs, in Bangladesh, effective implementation of water, sanitation, and hygiene (WASH) initiatives plays a crucial role in basic infection prevention and control (IPC) by preventing transmission of resistant strains in the environment. It is also very important to raising awareness among policymakers to facilitate, updating medical and allied health sciences curricula to promote the rational use of antimicrobials, developing rapid diagnostic facility, engaging mass media for raising community awareness and ensuring sufficient resources for implementing this activities as well as for Research and Innovation. High level political commitment, intra and inter-ministerial coordination among relevant sectors, and enforcement of regulatory regime are urgently warranted for a successful One Health approach.

Last of all as a developing nation, Bangladesh faces significant challenges in tackling MDR sepsis. It requires collaboration and partnerships with international organizations to share resources, exchange knowledge, and coordinate efforts to address this silent pandemic.

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