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Editorial ***Open Access***

Impact of Carbapenem Resistance Enterobacterales (CRE) on Human Health: Bangladesh Perspective

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Carbapenems are widely considered as last-resort antibiotics for the treatment of infections caused by multidrug-resistant Gram-negative bacteria[1]. With the increasing use of carbapenems in clinical settings, the emergence of carbapenem-resistant pathogens has become a grave threat to public health. The clinical consequences of carbapenem-resistant Enterobacterales (CRE) infections are severe, with reported mortality rates ranging from 30% to 75% in patients with severe infections[2]. Mortality rates above 50% have been reported in patients with CRE bloodstream infections[3], and a study has shown an excess mortality of 27% in patients with pneumonia or bloodstream infection caused by carbapenem-resistant *K. pneumoniae*[4]. The high mortality that has been associated with CRE is likely attributable to the lack of effective treatment options.

Carbapenem-resistant Enterobacterales (CRE) are ranked among the top tier of the WHO list of antibiotic-resistant "priority pathogens" that pose the greatest threat to human health[5].

The spread of CRE varies geographically, with different carbapenemase-producing strains predominating in various regions. For example, the Indian subcontinent has seen widespread emergence of NDM (New Delhi Metallo-beta-lactamase) CRE, while *KPC* (Klebsiella pneumoniae carbapenemase) CRE is most prevalent in the USA, Israel, Greece, and Italy. In contrast, *OXA-48* CRE has been notably identified in Turkey and North Africa[6]. This geographical variation highlights CRE's complexity and diversity, posing significant challenges for controlling its spread. In the Asia-Pacific region, a study by Kayoko Hayakawa et al. reported a concerning 30% prevalence rate of CRE among patients in tertiary hospitals[7].

In Bangladesh, the spread of *NDM-1*-producing organisms is of growing concern, with studies revealing a high prevalence of these resistant bacteria in wastewater samples collected from areas adjacent to hospitals[8]. One study found that approximately 3.5% of Gram-negative clinical isolates were *NDM-1*-producing[9] highlighting the increasing burden of this resistance mechanism in clinical settings. Particularly concerning is the high prevalence of carbapenemase producers among urinary isolates, with a significant proportion carrying the bla_{NDM-1} gene[10].

The rapidly increasing prevalence of antibiotic-resistant bacterial strains in Bangladesh's agriculture and farm animals is also a threat, largely fueled by the excessive and inappropriate use of antibiotics in agriculture[11]. It is speculated that flies available in poultry houses may be responsible for the spread of antibiotic-resistant bacteria from infected poultry to other animals and poultry[12]. The improper disposal of farm waste and sewage further exacerbates the situation. Resistant bacteria can enter nearby water sources through contaminated sewage systems, creating a pathway for spreading AMR into the broader environment[13].

The treatment of carbapenem-resistant Enterobacterales (CRE) depends on accurate gene detection to identify the specific carbapenemase-producing mechanisms responsible for resistance. Several novel techniques have emerged for detecting CRE, such as the modified carbapenem inactivation method (mCIM), Carba NP-direct test, immunochromatographic methods (lateral flow assays), matrix-assisted laser desorption ionization-time of flight mass spectrometry (MALDI-TOF MS), PCR, whole genome sequencing, and others. While some of these methods cannot distinguish between carbapenemase types, others have not gained widespread adoption in clinical laboratories or require

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additional steps beyond routine procedures. Among these, the immunochromatographic assay, such as the NG-Test CARBA 5 (NG CARBA 5; NG Biotech, Guipry, France), has been validated and offers the advantage of a short turnaround time. Conversely, the BD Phoenix CPO(Carbapenemase-producing organisms) detection test has the benefit of simultaneous testing alongside standard antimicrobial susceptibility testing[14].

Several antimicrobial drugs have been tested for effective treatment of CRE. These are Fosfomycin[15] Colistin, amikacin, tigecycline and gentamycin[16].

Ahmed and colleagues highlighted current antibiotic resistance scenarios in Bangladesh; notably, this study found that inadequate surveillance data on antimicrobial resistance from 58 out of the 64 districts of Bangladesh fails to accurately represent the country's current situation concerning antimicrobial resistance. Studies have shown that in Bangladesh, 83% of prescriptions in the community setting are made without clinical justification for prescribing an antibiotic[17], and in many cases, physicians irrationally prescribe antibiotics to their patients without following any recommended guideline[18]. unfortunately, studies have rarely focused on the use of carbapenems and their resistance mechanisms in Bangladesh[19,20].

The threat of CRE in Bangladesh requires a coordinated national response supported by evidence-based research and surveillance systems. Strengthening stewardship programs, infection control measures, and addressing the overuse of antibiotics in both healthcare and agriculture are critical steps. In parallel, the country needs to prioritize research on the prevalence and outcomes of CRE infections to make informed decisions and establish a national antimicrobial resistance surveillance network to track and respond to the spread of CRE. Only through concerted, multi-sectoral efforts involving healthcare providers, researchers, policymakers, and the public can Bangladesh mitigate the impact of CRE and preserve the effectiveness of antibiotics for future generations.

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