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Rising Threat of Carbapenem-Resistant Enterobacterales in Bangladesh: Challenges and Future Directions

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Abstract

Carbapenem-resistant Enterobacterales (CRE) represent a rapidly escalating threat in Bangladesh, posing significant challenges to public health within both hospital and community settings. Recent studies report alarmingly high CRE colonization rates of up to 37% among hospitalized patients, with community prevalence, albeit comparatively reduced, underscores the risk of extensive dissemination. The rise of CRE is driven by the proliferation of carbapenemase genes such as New Delhi metallo-β-lactamase (NDM), often facilitated by antibiotic misuse, inadequate infection control, and poor sanitation. Although surveillance and diagnostic capacities are evolving, their consistent deployment at the national scale remains limited. Current responses focus on infection prevention programs, antimicrobial stewardship, and public awareness efforts, yet these require greater coordination and investment in capacity building and research to address molecular trends and resistance profiles. Moving forward, Bangladesh faces an urgent need to enforce stronger regulatory frameworks, expand surveillance, and prioritize education and targeted interventions to contain CRE and safeguard the efficacy of available antibiotics. [*Bangladesh Journal of Infectious Diseases, December 2025;12(2):306-311*]

Keywords: Carbapenem-resistant Enterobacterales; antimicrobial resistance; Bangladesh epidemiology; infection control challenges; public health threats; future interventions

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Introduction

Antimicrobial resistance (AMR), particularly among Gram-negative bacteria like Enterobacterales, has reached critical levels in low- and middle-income countries (LMICs) , including Bangladesh[1]. Prevalence of Carbapenem-resistant Enterobacterales (CRE) in Bangladesh has evolved from a relatively minimal problem in the early 2000s into a major public health threat over the last two decades[2,3]. Carbapenems, classified as 'Reserve' agents in the World Health Organization's (WHO) AWaRe system, have historically provided effective treatment for Enterobacterales infections, including those caused by common pathogens such as *Klebsiella pneumoniae* and *Escherichia coli*[4]. However, the emergence of CRE poses a significant and rising menace due to its high prevalence in both

hospital and community settings[5]. They represent a grave public health threat and are designated as critical pathogens on the WHO's priority pathogens list[6]. Of particular note, critical pathogens are defined as antibiotic-resistant bacteria presenting the highest public health threat, driven by limited therapeutic options, high morbidity, frequent treatment failures, rapid transmissibility, substantial healthcare costs, and a dearth of effective new antibiotics in the pipeline[7]. Suboptimal diagnostic microbiology infrastructure, surveillance deficits yielding data gaps, restricted antibiotic therapeutic alternatives, and insufficient infection prevention and control (IPC) practices represent pivotal drivers facilitating the emergence and dissemination of AMR bacteria[8]. CRE are characterized as members of the Enterobacterales order demonstrating resistance to at least one carbapenem agent or expressing carbapenemase enzymes.

The principal mechanism of carbapenem resistance entails carbapenemase production, an enzyme that hydrolyzes this critical antibiotic, thereby severely curtailing therapeutic efficacy and posing formidable challenges for clinicians and policymakers[9]. Moreover, carbapenemase-producing Enterobacterales (CPE) dissemination transcends healthcare environments, manifesting in non-clinical reservoirs including sewage, livestock, retail foodstuffs, and feces from asymptomatic carriers, as corroborated by their circulation in community settings across designated regions[10]. The accelerated dissemination of these pathogens across healthcare settings and beyond poses an urgent challenge, demanding integrated strategies to bolster antimicrobial stewardship, robust infection prevention and control measures, and augmented diagnostic-surveillance frameworks[11].

Current Epidemiology of CRE in Bangladesh

Carbapenem-resistant Enterobacterales (CRE) have become endemic in Bangladesh, with an alarming increase in prevalence across both healthcare and community settings. Recent surveillance reports from leading research institutions indicate a concerning expansion of CRE infections, particularly among hospitalized patient populations. The following are important recent epidemiological extracts related to CRE in Bangladesh.

Current study conducted by icddr,b identified a notably high prevalence of CRE colonization among hospitalized patients in Bangladesh, with rates approaching 37%. In contrast, the community setting exhibited a substantially lower CRE prevalence, estimated at approximately 9%. Elevated CRE prevalence was evident in intensive care units (ICUs), burns units, and surgical wards, where patient exposure to broad-spectrum antibiotics, prior healthcare contact, and ICU admission represent key risk factors driving CRE colonization and subsequent bloodstream infections[12].

Community colonization reaches 9.0% (vs. 37.0% to 82.0% in hospitals), fueling endemic spread via *bla*NDM/ *bla*OXA-48 plasmids in high-risk clones like *K. pneumoniae* ST15. This burdens an already strained system, exacerbated by fragmented surveillance and rising healthcare-associated infections (HAIs), escalating costs from prolonged stays, and necessitating urgent stewardship. 2026 nationwide studies confirm ongoing trends, underscoring the need for enhanced diagnostics and IPC[13].

Carbapenemase-producing Enterobacterales (CPE), especially *Escherichia coli* and *Klebsiella pneumoniae* carrying enzymes such as *bla*NDM-5, have been detected in community samples, including retail foods, sewage, and fecal specimens from apparently healthy individuals. These findings indicate that CPE are circulating beyond hospitals, functioning as a reservoir for transmission and dissemination in urban and peri-urban environments[14].

Molecular epidemiological analyses from tertiary care hospitals in Bangladesh reveal a predominance of carbapenemase-encoding genes, principally *bla*NDM and *bla*OXA-48-like (oxacillinase, a type of beta-lactamase enzyme), underlying high-level carbapenem resistance and multidrug-resistant phenotypes among clinical Enterobacterales isolates[15].

Epidemiological assessments across Asia, including Bangladesh, have documented a progressive rise in carbapenem resistance among Enterobacterales from 2000 to 2012, with resistance rates increasing from around 0.5% to over 1% in selected regions. Although data specific to Bangladesh are largely based on limited case reports embedded within broader Asian studies, they nonetheless underscore the emergence of carbapenem resistance as a growing public health threat in the country[16].

Risk factors associated with CRE colonization and infection include prior hospitalization, non-prescription antibiotic use, inadequate sanitation, and healthcare-associated exposure. These drivers collectively foster an environment

highly conducive to the proliferation and transmission of CRE[17].

Current surveillance analyses have underscored the critical urgency of reinforcing diagnostic capacity and instituting robust, nationwide antimicrobial stewardship programs to curb the dissemination of CRE[18].

Thus, current studies consistently document a concerning increase in CRE prevalence in Bangladesh, particularly within hospital settings where carbapenemase-producing Enterobacterales predominate. Although community CRE colonization rates are lower than those reported in healthcare facilities, the community nonetheless serves as an important reservoir for transmission, especially in settings characterized by antibiotic misuse and inadequate sanitation. Multiple investigations have shown that CRE colonization is significantly associated with recent hospitalization, use of shared or unimproved sanitation facilities, and suboptimal hygiene practices[19].

Carbapenemase Genes

The principal mechanism of carbapenem resistance is the production of carbapenemase, an enzyme that hydrolyzes this potent antibiotic and thereby inactivates its antimicrobial activity. Carbapenem resistance genes, including *bla*NDM, *bla*KPC (*Klebsiella pneumoniae* carbapenemase), and *bla*OXA-48-like, are frequently located on conjugative plasmids, enabling rapid interspecies dissemination of this resistance mechanism[20]. Studies indicate that *bla*NDM and *bla*OXA-48-like are the two most common carbapenemases driving resistance in Enterobacterales globally and in regions including South Asia[21].

In South Asia, including Bangladesh, the *bla*NDM gene has exhibited a sharp rise in prevalence, consistent with its regional origin and rapid dissemination. Similarly, *bla*OXA-48-like genes, while more prevalent in parts of Europe and the Middle East, have also shown increasing frequency across South Asia in recent years. This regional heterogeneity mirrors global trends, whereby distinct carbapenemase determinants predominate in different settings, shaped by local selective pressures and pathogen transmission dynamics[22].

Notably, the prevalence of the *bla*NDM carbapenemase among *Escherichia coli* and *Klebsiella pneumoniae* isolates has shown a steady upward trend, thereby substantially amplifying the burden of resistance. In contrast, the *bla*OXA-48-like carbapenemase gene is frequently reported as the predominant or co-dominant variant. For instance, certain investigations have detected *bla*OXA-48-like in over 70-80% of carbapenem-resistant isolates, either alone or co-occurring with *bla*NDM. Other carbapenemase genes, such as *bla*KPC, have exhibited variable trajectories with regional declines or rebounds, yet *bla*NDM and *bla*OXA-48-like persist as the predominant, ascending variants. The co-occurrence of multiple carbapenemase genes within individual strains, such as dual carriage of *bla*KPC and *bla*NDM has risen markedly in recent years, further complicating resistance profiles[23,24].

Regional genetic analyses reveal that population-specific selective pressures and demographic factors underpin the observed geographic heterogeneity in resistance gene frequencies. Accordingly, the escalating prevalence of carbapenemase genes such as *bla*NDM and *bla*OXA-48-like in Bangladesh corresponds to the prevailing South Asian regional pattern, driven by geographic and environmental determinants of gene dissemination[21]. Nevertheless, *bla*NDM and *bla*OXA-48-like genes represent the predominant carbapenemases exhibiting year-on-year increases, substantially propelling both the rising prevalence and escalating complexity of CRE globally and within Bangladesh[25].

Drivers and Mechanisms of CRE in Bangladesh

The primary drivers of CRE emergence in Bangladesh include widespread misuse and overuse of antibiotics in both healthcare and agriculture, inadequate infection prevention and control, and insufficient surveillance systems. Antibiotics are commonly prescribed in the community without adequate clinical indication, and patients frequently receive inappropriate regimens in hospital settings, both of which contribute to the accelerated emergence and spread of antimicrobial resistance.

Environmental factors such as untreated waste from hospitals and farms, poor sanitation infrastructure, and contamination of water sources also play a significant role in the dissemination of resistant bacteria[2]. At the molecular level, the principal mechanisms underlying CRE in Bangladesh involve plasmids harboring resistance genes such as *bla*NDM and *bla*OXA-48-like, which facilitate the rapid horizontal transfer of carbapenem resistance determinants among diverse bacterial species (Figure I).

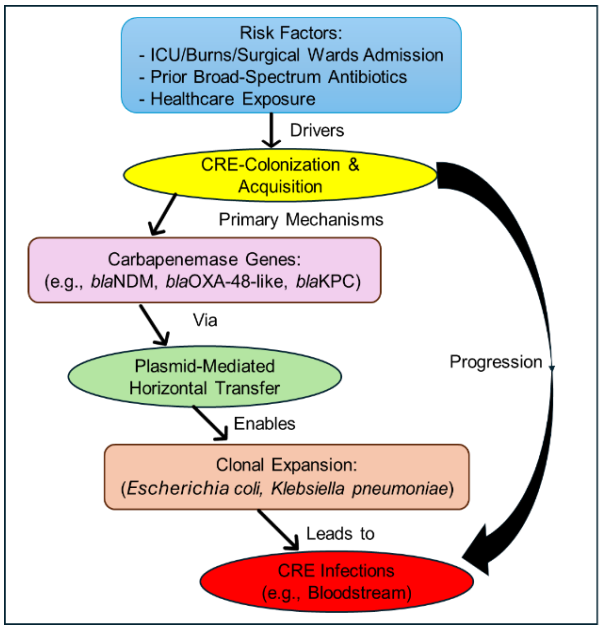

Figure I: Flow diagram depicting the drivers, mechanisms, and progression of carbapenem-resistant Enterobacterales infections in Bangladesh healthcare settings[26]. Key risk factors (ICU/burns/surgical ward admission, prior broad-spectrum antibiotic exposure, and healthcare contact) drive CRE colonization and acquisition (yellow). Primary resistance mechanisms involve carbapenemase genes (*bla*NDM, *bla*OXA-48-like, *bla*KPC; pink), disseminated via plasmid-mediated horizontal transfer (light green, e.g., IncFII/IncX3 plasmids), enabling clonal expansion of high-risk strains such as *Escherichia coli* ST167 and *Klebsiella pneumoniae* ST15/ST23 (orange). This cascade progresses to severe CRE infections, particularly bloodstream infections (red). Arrows denote causal relationships and progression pathways, informed by recent genomic surveillance data from Bangladeshi.

Clinical and Public Health Implications of CRE Infections

Enterobacterales are common pathogens causing a variety of severe infections, including bloodstream infections (BSIs), community-acquired pneumonia (CAP), hospital-acquired pneumonia (HAP), ventilator-associated pneumonia (VAP), complicated urinary tract infections (cUTIs), and complicated intra-abdominal infections (cIAIs). CRE infections in Bangladesh drive high morbidity, mortality, and healthcare strain, with recent nationwide surveillance showing 12.5% prevalence among 146,960 Enterobacterales isolates from clinical samples[27]. Additionally, CRE disproportionately affects vulnerable groups: males (16.75%) vs. females (9.55%), the elderly ≥60 years (14.56%), and infants <1 year (18.23%). These infections commonly originate from respiratory (57.8% tracheal aspirates) and wound sources (21.2%). Associated with healthcare-acquired infections (18.6% indoor vs. 9% outdoor samples), CRE leads to limited treatment options (high colistin/tigecycline susceptibility but multidrug resistance in 91% carbapenemase producers) and mortality rates approaching 48% in comparable regional settings[28]. Management of CRE infections presents substantial clinical challenges, as these organisms frequently exhibit multidrug-resistant phenotypes, often leaving clinicians with severely limited or no effective therapeutic options. CRE infections are associated with substantially elevated morbidity and mortality rates, while prolonged hospitalizations impose a considerable and often unsustainable economic and operational burden on patients and healthcare systems alike[29].

Detection technologies for CRE in Bangladesh are advancing, with multiplex PCR, whole-genome sequencing, and rapid diagnostic assays becoming increasingly available; however, access to these tools remains inconsistent nationwide. These technological methods have markedly enhanced the ability to detect carbapenemase-producing strains and inform targeted clinical management. However, comprehensive national implementation and universal access remain elusive[30]. Targeted infection control interventions including enhanced hand hygiene compliance, antimicrobial stewardship programs, and rigorous environmental decontamination protocols have demonstrated substantial efficacy in curtailing CRE transmission within healthcare facilities. However, their success hinges on systematic, sustained implementation with rigorous oversight and multidisciplinary coordination across diverse clinical settings[2].

Mitigation Recommendations

To effectively mitigate CRE in Bangladesh, it is crucial to implement a multi-faceted approach that includes several interlinked strategies (Figure II). Policy and legislative actions should enforce stringent regulations around antibiotic sales, usage, and disposal, with penalties for non-compliance to curb misuse and environmental contamination. Within the healthcare system, universal infection prevention and control programs should be implemented in hospitals, complemented by routine CRE screening of high-risk patient populations to enable prompt identification and isolation of infected or colonized individuals. Substantial investment in research is required to monitor evolving molecular epidemiology and resistance patterns, thereby facilitating the local identification and optimization of targeted interventions against carbapenem-resistant pathogens. Strengthening

laboratory capacity through training of personnel in rapid diagnostic technologies such as multiplex PCR and phenotypic assays and ensuring equitable nationwide access to these tools is critical for timely detection, characterization, and containment of carbapenem-resistant pathogens. Finally, community engagement must be prioritized through multifaceted grassroots education initiatives that foster behavioral change toward improved personal and environmental hygiene, judicious antibiotic stewardship, and sustainable environmental protection measures. These efforts aim to diminish key ecological reservoirs of CRE, thereby curtailing transmission risks and supporting broader AMR mitigation strategies[7,31].

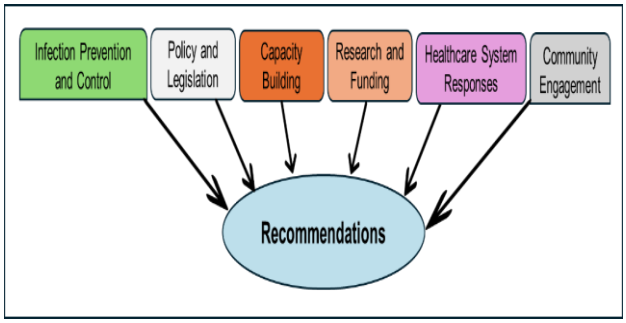

Figure II: Schematic representation of recommendations for combating carbapenem-resistant Enterobacterales in Bangladesh. The central node illustrates integrated "Recommendations," supported by six strategic pillars: (i) *Infection Prevention and Control* (enhanced hand hygiene, contact precautions, environmental decontamination); (ii) *Policy and Legislation* (national AMR action plans, antimicrobial stewardship regulations); (iii) *Capacity Building* (laboratory training in rapid diagnostics, healthcare worker education); (iv) *Research and Funding* (genomic surveillance, intervention trials); (v) *Healthcare System Responses* (antibiotic audits, cohorting of CRE patients); and (vi) *Community Engagement* (public awareness campaigns, rational antibiotic use promotion). Arrows indicate directional support toward comprehensive CRE control strategies.

Conclusion

The emergence and spread of carbapenem resistance underscore the urgent need for the development of novel antimicrobial agents, alongside the rigorous implementation of antibiotic stewardship programs to preserve the efficacy of existing therapeutic options. The One Health approach has emerged as a comprehensive framework for addressing antimicrobial resistance, including CRE, by explicitly recognizing the interconnectedness of human, animal, and environmental health domains. This approach emphasizes the necessity for coordinated cross-sectoral collaboration to address the complex and multifactorial challenges posed by AMR. The current situation surrounding CRE in Bangladesh represents an urgent public health challenge. Without coordinated, cross-sectoral interventions addressing both clinical management and broader societal drivers of resistance, CRE will continue to compromise patient outcomes and erode Bangladesh's health security infrastructure. The need for decisive action in surveillance, antimicrobial stewardship, and policy is immediate, in order to safeguard the effectiveness of life-saving antibiotics for future generations.

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Conflict of Interest
The author has declared no conflict of interest in this work.

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Authors' contributions
Md. Abdus Salam (MAS) was responsible for conceptualization, writing original draft, reviewing and editing of the manuscript.

Data Availability
Any inquiries regarding supporting data availability of this study should be directed to the corresponding author and are available from the corresponding author on reasonable request.

Ethics Approval and Consent to Participate
Not Applicable

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