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ABSTRACT
Q150
POSTER

ISAAR 2026
15th International Symposium on Antimicrobial Agents and Resistance
Hong Kong, China | June 12-14, 2026

Prevalence and Molecular Epidemiology of NDM-Producing Enterobacterales in Gulf Cooperation Council Countries: A Literature Review

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BACKGROUND

WHO Critical Priority Pathogen: Carbapenem-resistant Enterobacterales (CRE) are classified as the highest-priority pathogens requiring urgent intervention worldwide.

New Delhi metallo-β-lactamase (NDM) was first identified in 2008 in *Klebsiella pneumoniae* from a Swedish patient treated in New Delhi, India. It rapidly disseminated globally, with multiple NDM variants (NDM-1 to NDM-30+) now identified.

NDM belongs to Ambler Class B metallo-β-lactamases and confers resistance to **all β-lactam antibiotics** except aztreonam. It is **not inhibited** by conventional β-lactamase inhibitors (clavulanate, tazobactam, sulbactam).

GCC Region: The Gulf Cooperation Council countries (Saudi Arabia, UAE, Kuwait, Qatar, Bahrain & Oman) represent a unique epidemiological nexus due to high population mobility, large expatriate workforces, and intensive healthcare utilization.

Despite the Middle East being recognized as an NDM epicenter, comprehensive regional data synthesis across GCC countries had not been previously performed.

METHODS

Database Search
PubMed, Scopus & Web of Science searched systematically (2010–2024)

Search Terms
"NDM" OR "carbapenem resistance" AND "Saudi Arabia" OR "UAE" OR "Kuwait" OR "Qatar" OR "Bahrain" OR "Oman" OR "GCC"

Inclusion Criteria
GCC-based studies; Enterobacterales only; molecular confirmation of NDM; peer-reviewed; English language

Exclusion Criteria
Non-Enterobacterales; single case reports; conference abstracts without full-text; no molecular confirmation

Data Extraction
Prevalence, species, NDM variants, sequence types, plasmid types, co-resistance, transmission data

Synthesis
Narrative synthesis due to methodological heterogeneity; no meta-analysis performed

KEY STATISTICS

46.5%
NDM prevalence among CRE isolates (2015 GCC study, n=200)

26%
NDM prevalence in 2018 GCC-wide study (n=62 isolates)

56.8%
NDM cases with NO foreign travel or hospitalization history

8.9%
Co-production of NDM + OXA-48 (all from UAE)

0%
KPC carbapenemases detected — ARGENT from all GCC countries

>90%
NDM-producing isolates carrying NDM-1 variant (dominant)

CARBAPENEMASE DISTRIBUTION

Carbapenem-Resistant Enterobacterales (n=200, Four GCC Countries, 2015)

- **NDM-1 (blaNDM-1)** — 46.5% (93/200)
- **OXA-48-like** — 32.5% (65/200)
- **NDM + OXA-48 co-producers** — 8.9% (18/200)
- **KPC-type** — 0% — Not Detected

Distinct Regional Pattern: Complete absence of KPC carbapenemases distinguishes GCC from North America & Europe where KPC-producing ST258 *K. pneumoniae* predominates.

MOLECULAR EPIDEMIOLOGY

Country	Dominant Clone	Plasmid Type	Key Feature
SA Saudi Arabia	ST152	IncHI1b	NDM + OXA-48 co-producers
AE UAE	ST14	IncHI1b (>170kb)	Highest dual carbapenemase rate
OM Oman	ST147	IncHI1b (>170kb)	Similar plasmid to UAE strains
KW Kuwait	Diverse	IncX3	NDM-7 rare variant detected
QA Qatar	Diverse	Various	No clonal relationship to others
BH Bahrain	Diverse	Various	Limited published data

Dominant Species: *Klebsiella pneumoniae* accounts for ~70–80% of all NDM-producing isolates across the GCC region

- NDM-7 variant (IncX3 plasmids) identified in Kuwait, Oman & UAE — highly mobile plasmids with efficient conjugation
- IncHI1b plasmids carrying blaNDM are >170kb and shared between UAE (ST14) and Oman (ST147)
- Both clonal spread AND horizontal gene transfer operating simultaneously in the GCC

TRANSMISSION DYNAMICS

AUTOCHTHONOUS TRANSMISSION (NO FOREIGN EXPOSURE)

56.8%
NDM-positive cases with **no documented** foreign travel or hospitalization

75.7%
OXA-48-like cases with **no documented** foreign travel or hospitalization

- **Established endemicity:** NDM is no longer merely an imported pathogen — it is endemic in GCC healthcare facilities
- **Hospital-associated:** ~84% of NDM CRE cases are healthcare-associated; 16% community-onset
- **Risk factors:** ICU admission, prolonged hospitalization, invasive devices, and prior antibiotic exposure
- **Environmental reservoirs:** Hospital water systems (sinks, drains) implicated in some outbreak clusters
- **Foreign exposure:** 78.6% of patients with prior foreign healthcare carried NDM, demonstrating importation pathway still active

COUNTRY-SPECIFIC NDM FINDINGS ACROSS GCC

SA
Saudi Arabia
Dominant Clone: ST152
Largest GCC country; highest number of reported cases; NDM + OXA-48 co-production in some centers; major healthcare hub for Hajj/Umrah pilgrims

AE
United Arab Emirates
Dominant Clone: ST14
Highest rate of dual carbapenemase producers (NDM + OXA-48); >85% expatriate population; major international travel hub; IncHI1b plasmids >170kb

OM
Oman
Dominant Clone: ST147
ST147 carrying IncHI1b plasmids similar to UAE strains; NDM-7 rare variant detected; limited published surveillance; plasmid sharing with UAE suggests regional spread

KW
Kuwait
Clonally Diverse
NDM-7 on IncX3 plasmids confirmed; IncX3 plasmids known for high conjugation frequency; limited longitudinal surveillance data published

QA
Qatar
Clonally Diverse
NDM-positive isolates show no clonal relationship to other GCC strains; suggests independent introduction or horizontal plasmid transfer; limited published data

BH
Bahrain
Limited Data
NDM presence confirmed in multi-country studies; most underrepresented in published literature; national surveillance system needed; small geographic area, high healthcare utilization

ANTIMICROBIAL SUSCEPTIBILITY

Resistance Rates in NDM-Producing Isolates:

- **Carbapenems** — ~100% Resistant
- **Fluoroquinolones** — >85% Resistant
- **Aminoglycosides** — >75% Resistant
- **Colistin (susceptible)** — >70% Susceptible
- **Tigecycline (susceptible)** — 60–80% Susceptible

Treatment Challenge: Ceftazidime-avibactam is NOT active against MBLs including NDM. Aztreonam-avibactam shows promise but was unavailable in GCC during the study period.

DISCUSSION

- **NDM as dominant carbapenemase:** At 26–46.5%, NDM is the most prevalent carbapenemase in the GCC, reflecting strong epidemiological links to the Indian subcontinent
- **Endemicity established:** With over half of NDM cases arising without foreign exposure, GCC healthcare facilities can no longer rely solely on screening international travelers
- **Dual mechanism spread:** Both clonal dissemination (country-specific STs) and horizontal plasmid transfer (shared IncHI1b plasmids between UAE and Oman) operating concurrently
- **High-risk clones:** ST152, ST14, and ST147 are globally recognized pandemic lineages with enhanced fitness for nosocomial survival and transmission
- **Regional divergence:** Absence of KPC and predominance of NDM/OXA-48 distinguishes GCC from Western resistance patterns, reflecting distinct importation pressures
- **Temporal increase:** Middle East-Africa surveillance (ATLAS 2018-2022) showed CRE doubling from 5.7% to 10.4%, suggesting GCC burden is increasing

PUBLIC HEALTH RECOMMENDATIONS

- **Enhanced screening:** Active surveillance for CRE carriage in ICU, transplant, oncology and post-surgical wards
- **Contact precautions:** Strict implementation for all confirmed or suspected CRE-positive patients
- **Environmental controls:** Systematic sampling of hospital water systems; UV disinfection and hydrogen peroxide vapor in outbreak settings
- **Antimicrobial stewardship:** Carbapenem-sparing strategies and formulary restrictions with stewardship review
- **Regional surveillance:** Harmonized GCC-wide surveillance platform with standardized methods and real-time data sharing
- **Whole-genome sequencing:** Expand WGS-based transmission reconstruction to identify and interrupt nosocomial spread
- **Antibiotic policy:** Regulation of over-the-counter antibiotic availability across GCC member states

CONCLUSIONS

Endemic Threat
NDM-producing Enterobacterales are firmly established across all GCC countries, with autochthonous transmission accounting for 56.8% of cases — confirming endemicity beyond importation

Diverse Clonality
Country-specific high-risk clones (ST152, ST14, ST147) and shared IncHI1b plasmids >170kb indicate both clonal spread and horizontal gene transfer driving regional dissemination

Unique Profile
Complete absence of KPC-type carbapenemases across all GCC countries distinguishes the regional resistance landscape from North America and Europe, reflecting unique importation pressures

Urgent Action
Coordinated GCC-wide surveillance, enhanced infection prevention, harmonized antimicrobial stewardship programs, and expanded molecular epidemiology are urgently needed

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No conflicts of interest declared
Abstract ID: Q150 | ISAAR 2026 | Hong Kong