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Letter to the Editor

Response to "New Delhi Metallo-β-lactamase (NDM-1): an emerging Threat Among *Enterobacteriaceae*"

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To the Editor,

We compliment Professor Hsueh on the meticulous dissertation on emergence and dissemination of the New Delhi metallo-β-lactamase (NDM-1) gene.[1]

In all probability, there has already been extensive cryptic dissemination of NDM-1 in several cities in the Indian subcontinent. Of the 100 samples collected from sewers across Delhi, isolates that carried NDM-1 were detected in 11 samples.[2] No standardized phenotypic test is available for NDM-1 detection and molecular methods such as real-time polymerase chain reaction (PCR) are necessary. Non-availability of a phenotypic test for detection of NDM-1 is a major obstacle towards any therapeutic or preventive interventions against NDM-1 carriage and dissemination.

A standardized phenotypic test is essential for poor countries where laboratory services are a neglected component with little appreciation of their role in patient care and management, disease control, public health, and disease surveillance.[3] In developing countries, a large number of laboratories, even in large cities, lack a high level of competence.[4] The majority of diagnostic laboratories would probably not be able to identify any NDM-1 carriage in their premises, and real-time PCR of NDM-1-specific genes would by no means be feasible. NDM-1 diagnosis would only be achieved through simpler test versions that are not contingent on costly equipment and trained personnel.

Phenotypic diagnosis of isolates that carry metallo-β-lactamases (MBLs) has been performed using the modified Hodge test, MBL Etest, or Imipenem-DETA Double Synergy Test.[5] None of these tests is specific for NDM-1. Furthermore, a turbidity meter and the standard reference stain *Escherichia coli* ATCC 25922 are essential for carrying out the modified Hodge test, and false-positive results are known with some isolates that do not produce carbapenemases.[5] Any positive result requires confirmation by real-time PCR.

Simpler assay formats have been useful to monitor antimicrobial resistance in staphylococci and *Mycobacterium tuberculosis*. For example, 30 μg cefoxitin disks are useful to screen methicillin-resistant *Staphylococcus aureus* (MRSA) in routine laboratories and have been popular in healthcare centers at various locations.[4,6] Cefoxitin screening

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combined with PCR for the *mec*A gene have emerged as the best phenotypic assay among the four MRSA detection phenotypic tests.[7] A highly sensitive and simple-to-use system to detect *M. tuberculosis* and rifampin resistance directly from sputum has been evaluated in the field in Uganda and Vietnam. The Cepheid Gene Xpert System's MTB/RIF (*M. tuberculosis*/resistance to rifampicin) assay, which is an integrated hands-free sputum-processing and real-time PCR system with rapid on-demand, near-patient technology, has shown great potential to simultaneously detect *M. tuberculosis* and rifampin resistance. *M. tuberculosis* could be detected from sputum in < 2 hours. Furthermore, all the 23 different commonly occurring rifampin resistance mutations were identified as rifampin resistant.[8]

Philanthropic organizations including international organizations like the World Health Organization should spare funds towards development and standardization of point-of-care assay procedures, which resemble those that monitor methicillin resistance in staphylococci and rifampin resistance in *M. tuberculosis*, for NDM-1 detection in routine clinical laboratories.

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