

Editorial:**Discovery of “Aligarh Super Bug” and Widespread variants of NDM1: A concern in antimicrobial resistance**Rahman SZ¹, Mishra A²

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In clinical and non-clinical settings, bacteria are increasingly becoming resistant to prevalent antibiotics. Previously, this concern was for Gram-positive bacteria, particularly methicillin-resistant *Staphylococcus aureus* and vancomycin-resistant *Enterococcus* spp. These days, however, multidrug-resistant Gram-negative bacteria pose the greatest risk to public wellbeing. Not only are the Gram-negative bacteria developing resistance faster than Gram-positive bacteria, but also there are few antibiotics active against Gram-negative bacteria^{1, 2} and drug development programs are moving at much slower pace, insufficient to provide therapeutic cover in coming years. The resistance of Gram-negative bacteria is primarily because of mobile genes (plasmids) that can readily propagate through bacterial populations. Unprecedented human migration and travels allow bacterial plasmids to be transported rapidly across continents³.

Carbapenems are a class of beta-lactam antibiotics that are capable of killing most bacteria by inhibiting the synthesis of one of their cell wall layers. The carbapenems were developed to overcome antibiotic resistance mediated by bacterial beta-lactamase enzymes. However, a new type of carbapenem resistance gene, termed as *bla*_{NDM-1} was reported in 2009 by D Yong et al.⁴ The *bla*_{NDM-1} gene forms NDM-1, which is a carbapenemase beta-lactamase-enzyme that inactivates carbapenem antibiotics. Detection of NDM-1 gene is based upon the phenotypic determination of enzyme activity³. These enzymes are zinc dependent and are termed

as metallo-beta-lactamase. NDM-1 was first detected in a *Klebsiella pneumoniae* and *Escherichia coli* with *bla*_{NDM-1} on plasmids from an *in vitro* isolate of a Swedish patient of Indian origin in 2008 after hospital admission in New Delhi, India⁵. Hence got the name, “New Delhi Metallo-beta-lactamase-1 (NDM-1), an enzyme that makes bacteria resistant to a broad range of beta-lactam antibiotics and is readily transferred between bacterial strains. NDM-1 β-lactamase was later detected in Pakistan, Canada, United Kingdom, United States of America and Balkans. A total of 17 different variants of NDM1 have been identified, having variations at different site of their primary protein structure. These variants have varying catalytic activity against carbapenem.

From our municipal city Aligarh, a team of scientists led by Asad U Khan et al., reported a NDM-4-producing *Escherichia coli* in the sewage of Jawaharlal Nehru Medical College Hospital (JNMCH)⁶. They also reported NDM-1-producing *C. lapagei* in a preterm baby admitted to the Intensive Care Unit of JNMCH, Aligarh, India⁷. The editor of *The Lancet*, apologized that naming a superbug after New Delhi was wrong. Following this, Ajai R. Singh, editor of *Mens Sana Monographs*, proposed changing NDM-1 to PCM (plasmid-encoding carbapenem-resistant metallo-beta-lactamase)⁸. Similarly, “Aligarh Super Bug” would come under PCM.

Present strategies of combating the emergence and spread of multi drug resistance depends on the discovery of newer agents⁹, reduction in antibiotic induced bacterial mutation¹⁰, use of combinations

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therapy¹¹⁻¹², early intensive (frontline) therapy¹³, and lately, surveillance of hypermutable organisms¹⁴ and targeting regulating functions necessary for infection¹⁵. The selective use of probiotics and prebiotics and the deliberate refocus on narrow-spectrum as opposed to broad-spectrum antibiotics in clinical practice can also help in the current scenario. Antibiotic resistance is continuously evolving to attain higher antibiotic resistance exhibiting elevated bacterial genetic evolution. The preventive measures are proving increasingly inadequate in the existing global scenario of MDR.

Conclusion:

The “superbugs” have attained the status of community acquired pathogens. The capability for wider international spread and for NDM-1-encoding plasmids to become an endemic pathogen worldwide, are very much there and frightening. Because of the significant lag time between the discovery and introduction of new anti-infective agents and the need for new discovery of alternative solutions, all physicians should refocus on the appropriate and judicious use of antibiotics in any clinical settings¹⁵.

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