

Editorial

Superbug – the so-called NDM-1

The recent paper on the *emergence of a new antibiotic resistance mechanism in India, Pakistan and the UK*¹ may have sounded yet another wake-up call to counter the global menace of antibiotic resistance. Curiously, the paper with little credible scientific evidence makes sweeping generalizations and conclusions by offering ‘strong advice’ against surgery for people opting for such treatment in India. Multi drug-resistant pathogens exist in India as they do in *different forms* globally including the western world with a death toll of over 2500 in the USA alone (more than the deaths due to AIDS) and some 2500 deaths in Europe every year². Does it mean that the whole of Europe is “unsafe for medical treatment”, and that all such notorious pathogens originated in Europe? *Klebsiella pneumoniae* clone with KPC carbapenemase for example, is a major problem in the US, Israel, Greece and other parts of Europe; and plasmids encoding Verona integron-encoded metallo- β -lactamase (VIM) metallo-carbapenemase have disseminated among *K. pneumoniae* in Greece^{3,4}. As Nordman, Director, Institut national de la santé et de la recherche médicale (INSERM) Unit of Emergent & Multi-resistant Bacteria put it “..... for the moment there is no indicator that the multi-resistant stems are more virulent than the other”⁴.

The war between drugs and bugs has been on since the time of Alexander Fleming. It is known that the *frequent-flow* of genetic material across the whole bacterial species is an inevitable phenomenon that keeps happening in nature as part of natural selection. This evolutionary process does not respect geographical boundaries, countries or continents. It could just happen anywhere and anytime.

It is in this context that this paper¹ attracts some glaring discrepancies against the principles

of truth and science that need to be addressed. The authors themselves admit that *there was no statistically significant strain relatedness between the Indian and UK isolates* which raises doubts about the alleged origin of so-called NDM-1 from India. Mere fact that some of the study patients (shown to possess NDM-1) had visited India for some kind of surgery during preceding years is not adequate proof to claim huge epidemiological link as claimed in the paper¹. The authors could link only 17 of 37 UK patients to Indian subcontinent. Disclosing clinical details and outcome of each of the patients harboring NDM-1 and absence of such details is hardly helpful. Had the authors included isolates from other geographic regions as well, their claim regarding origin of NDM-1 would have looked convincing. Since no pre-screening of the patients was done before their visit to India, it would be wrong to conclude that the ‘bug’ had its origin in India.

NDM-1 shares very little identity with other metallo beta-lactamases (MBLs). With a molecular mass of 28kD, NDM-1 possesses unique residues near the active site, with an additional insert between positions 162 and 166, which is not present in other MBLs⁵. Sequence-based DNA signature studies may be essential to pin-point such changes and also to augment claims relating to the origin route(s) of transmission of NDM-1 from India. Interpretation of results by the authors despite non-typability of plasmids from over 50 per cent isolates from Haryana (northern India) is equally intriguing. Even while the authors have admitted that there was no statistical proof of strain relatedness between Indian and the UK isolates, the Journal chose to publish the paper¹ *cautioning global community to refrain*

from undergoing surgery in India. The concluding remarks of the authors are clearly biased. Despite these gross inadequacies, the paper has certainly raised some very critical issues on antimicrobial resistance that the global community needs to address.

The WHO, SEARO recently have highlighted four areas which will need attention of national authorities which pertains to governance, regulatory mechanisms, building national capacity in antimicrobial surveillance area, and mobilizing active participation of communities. A governance mechanism comprising establishment of a national alliance against AMR, designation of national focal point and establishment of a multi-sectoral National Steering Committee to guide national efforts⁶, has been put in place.

In a recently published editorial⁷ it has been stated that “*It is high time that we put in place practices and institutions that regulate antibiotic therapy. Essentially, the practices should aim at diminishing environmental antibiotic levels and inhibiting the spread of resistance factors this has also been addressed.*”

It is well known that antimicrobial resistance in pathogens causing important communicable diseases has become a matter of great public health concern globally including our country. Resistance has emerged even to newer, more potent antimicrobial agents like carbapenems. The factors responsible for this are widespread use and availability of practically all the antimicrobials across the counter meant for human, animal and industrial consumption. There are definite policies/guidelines for appropriate use of antimicrobials at national level in specific national health programmes being run in the country *e.g.*, Revised National Tuberculosis Control Programme (RNTCP), National AIDS Control Programme. For other pathogens of public health importance like enteric fever, diarrhoeal disease, respiratory infections *etc.*, the individual hospitals are following their own antimicrobial policies and hospital infection control guidelines. In order to devise uniform guidelines for use of antimicrobials in the country like India, it is essential to have a comprehensive collated data on antimicrobial resistance. To monitor antimicrobial resistance it is also necessary to have regulations for use and misuse of antibiotics in the country, creation of national surveillance system for antibiotic resistance, mechanism of monitoring prescription audits, regulatory provision for monitoring use of antibiotics in human, veterinary and industrial sectors

and identification of specific intervention measures for rationale use of antibiotics.

In this regard a Task Force has been constituted by Government of India to review the current situation regarding manufacture, use and misuse of antibiotics in the country and to recommend the design for creation of a National Surveillance System for Antibiotic Resistance. The Task Force is expected to finalize the policy on following issues:

1. Studies documenting prescription patterns and establishing a Monitoring system.
2. Enforce and enhance regulatory provisions for use of antibiotics in human and veterinary and industrial use.
3. Rationale use of antibiotics and antibiotic policies in hospitals.

The Task Force has already formulated the antibiotic policy which is under finalization for implementation.

The apology from the Editor of The Lancet regarding naming it as NDM-1 came too late and serves little purpose as the paper has dealt a serious blow to the credibility of health care system in India. The Government of India is making all efforts to prioritize all actions to have surveillance of AMR and promote rationale use of antibiotics in the country.

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