

## Correspondence

### Clinical correlates of New Delhi metallo-beta lactamase isolates - a survey of published literature

Sir,

Recent articles on New Delhi metallo-beta lactamase-1 (NDM-1) have raised alarm among clinicians worldwide on a potential pan-resistant pathogen which is said to be a global threat<sup>1,2</sup>. However, a clinician will be interested to know the actual impact this pathogen has produced in terms of clinical illness, susceptible patients, treatment choice, community spread, hospital expenditure, morbidity and mortality.

The present attempt was made to analyse details of patient characteristics, foci of sepsis, culture specimen, drug used to treat the NDM-1 isolate and patients' outcome in published reports on NDM-1 isolates from January 2008 to October 20, 2011. A PubMed search with the keyword "New Delhi metallo-beta lactamase" was made from October 1 to October 20, 2011 to identify citations related to NDM-1 which yielded 106 reports; from which 33 reports which discussed at least one NDM-1 isolate, were selected for the review<sup>1-33</sup>. Six reports discussed five or more NDM-1 isolates and 27 reported less than 5 isolates (23 reported a single isolate). Commentaries on published clinical reports on NDM-1 and *in vitro* reports studying bacterial virulence, clonality and transmission of resistance were excluded. Full texts of all these articles were obtained.

A total of 327 NDM-1 isolates were reported from 22 countries (Sweden, India, United Kingdom, USA, Pakistan, Belgium, Germany, Netherlands, Denmark, Singapore, France, Oman, Taiwan, Australia, Austria, Kenya, Hong Kong, Italy, China, Serbia, Canada and Japan). *Klebsiella pneumoniae* (n=172) was the most frequent NDM-1 isolate followed by *E. coli* (n=91). Table I shows the type of pathogen, country of origin and clinical details in studies reporting at least five isolates. In 10 reports it was mentioned that the NDM-1 isolate was a colonizer. Nineteen reports

mentioned about the presence of foci of sepsis and 23 mentioned about culture specimen, though not for all samples. Table II shows summary of seven reports which provided treatment details and patients' outcome. Of the 327 isolates, 219 (67%) were from patients admitted to hospitals in the Indian subcontinent largely due 180 isolates reported by Kumarasamy *et al*<sup>2</sup> which did have gross inadequacies as highlighted in a recent editorial<sup>34</sup>. Seven patients had no history of travel to the Indian subcontinent and details of travel were not mentioned in 53 cases.

Given the fact that NDM-1 is a resistant pathogen, every attempt should have been made by the authors to document all relevant clinical details including treatment and patient outcome. The best description of patients' characteristics was observed in a report by Kus *et al*<sup>23</sup> which describes the patients' characteristics in detail including events on follow up. It may be interesting to note that this report highlights the fact that NDM-1 though a resistant pathogen can remain as a colonizer for 3 to 5 months without producing clinical infection despite presence of multiple co-morbidities in the patient<sup>23</sup>. It may be premature to think that NDM-1 is a resistant but a less virulent pathogen, although a few clinical facts point towards this possibility<sup>21,23</sup>. The present attempt has made it obvious that most published data about NDM-1 are incomplete from a clinicians perspective.

A better understanding of the pathogen is possible only if epidemiological and clinical data are available about the isolates published so far. It will be a worthwhile effort if these details are collected in retrospect to the best extent possible since it may help us view a larger picture especially when it has been said that NDM-1 has a pandemic potential.

**Table I.** Summary of NDM-1 isolates, country where isolated, and the clinical correlates in studies reporting at least five isolates

S. No.	Report	Number and type of NDM-1 isolates	Country where specimen was obtained	Patients' characteristics	Foci of sepsis	Culture specimen	Treatment details	Patient outcome
1	Health Protection Report <sup>4</sup>	22 isolates 14- <i>Klebsiella</i> 4- <i>E. coli</i> 4 - others	UK	One had haematological malignancy and suffered blood stream infection due to NDM-1 <i>E. coli</i> . Second underwent cosmetic surgery which was complicated with wound infection due to NDM-1 positive <i>Klebsiella</i> .  Seven had renal or liver transplantation and one had cosmetic surgery but details of infection not mentioned. Details of remaining 12 patients not mentioned. Nine patients had recent hospitalization in India or Pakistan.	One blood stream infection One skin infection 20 - not mentioned	1-blood 1-wound sample  20-not mentioned	Not mentioned	Not mentioned
2	Deshpande <i>et al</i> <sup>5</sup>	22 isolates 10 - <i>Klebsiella</i> 9 - <i>E. coli</i> 3 - others	India	All 22 hospitalized in India. Further clinical details not mentioned.	Not mentioned	11-urine 4-sputum 3-blood 2-tracheal 1-swab 1-pus 1-BAL 1-stool	Not mentioned	Not mentioned

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S. No.	Report	Number and type of NDM-1 isolates	Country where specimen was obtained	Patients' characteristics	Foci of sepsis	Culture specimen	Treatment details	Patient outcome
3	Kumarasamy <i>et al</i> <sup>2</sup>	180 isolates 36 - <i>E. coli</i> 111 - <i>Klebsiella</i> 33 - others	India Pakistan UK	Reasons for admission in UK were renal or bone marrow transplantation, dialysis, cerebral infarction, chronic obstructive pulmonary disease, pregnancy, burns, road traffic accidents, and cosmetic surgery (clinical correlation not mentioned). The mean age of UK patients was 60 yr (17-male, 12-female). 17 UK patients had a history of travelling to India or Pakistan. Of them, 14 were hospitalized in India or Pakistan. Number of study patients from Asian hospitals not mentioned	Community acquired urinary tract infections, pneumonia and blood-stream infections in isolates from India and Pakistan. No mention made about foci of sepsis in UK isolates	UK-specimens: no.26 15- urine 3-blood 4-burn or wound swab 2-sputum 1-central line tip 1-throat swab. Details of Indian and Pakistan specimens not mentioned	Not mentioned	Not mentioned
4	Poirel <i>et al</i> <sup>9</sup>	7 - <i>Klebsiella</i>	Kenya	Not mentioned	Not mentioned	Urine	Not mentioned	Not mentioned
5	Bogaerts <i>et al</i> <sup>18</sup>	2 - <i>E. coli</i> 1 - <i>Klebsiella</i> 1 - <i>Morganella</i> 1 - <i>Enterobacter</i>	Belgium	Patient 1: diabetic with wound infection Patient 2: epileptic with pneumonia Patient 3: SLE with leg wound	Soft tissue Lung Soft tissue	Rectal swab, wound swab and sputum (patient specific specimen source not mentioned)	Not mentioned	Patient 1 died. Others recovered
6	Seema <i>et al</i> <sup>33</sup>	30 - <i>E. coli</i> 12 - <i>Klebsiella</i> 12 - <i>Citrobacter</i>	India	32 male, 22 female, age ranged from 1 day to 85 yr	Not mentioned	26-Urine	Not mentioned	Not mentioned

Table II. Summary of 7 reports mentioning treatment details and patient outcome

S.No.	Report	Number and type of NDM-1 isolates	Country where specimen was obtained	Patient characteristics	Foci of sepsis	Culture specimen	Treatment details	Patient outcome
1	Chan <i>et al</i> <sup>19</sup>	1 - <i>E. coli</i>	Singapore	46 year old woman suffering from ALL	Lungs	Blood	Polymyxin	Died
2	Chen <i>et al</i> <sup>1</sup>	1 - <i>Klebsiella</i>	China	Asymptomatic	None	Stool	Not treated	Spontaneously eradicated
3	Kus <i>et al</i> <sup>3</sup>	1 - <i>Morganella</i>	Canada	86 year male with h/o stroke, diabetes, hypertension, atrial fibrillation, CA-colon and prostate	Asymptomatic	Urine	Not treated	Persistent bacteriuria at 5 month. Patient asymptomatic
4	Mochon <i>et al</i> <sup>24</sup>	1 - <i>Proteus</i>	United States	71 year female suffering from multiple sclerosis and neurogenic bladder on catheter	Asymptomatic	Urine	Not treated	Persistent bacteriuria at 3 months. Patient asymptomatic
5	Mulvey <i>et al</i> <sup>25</sup>	1 - <i>Klebsiella</i>	Canada	13 year old boy with 3 day fever, cough and wheeze. h/o bronchial asthma and developmental delay	Lung	Urine, nasal wash and sputum	colistin	Recovered
6	Pfeifer <i>et al</i> <sup>28</sup>	1 - <i>E. coli</i>	Germany	76 year old women with diarrhoea and impaired mentation	Urinary tract	Urine, rectal swab	Colistin and chloramphenicol	Died
7	Poirrel <i>et al</i> <sup>29</sup>	1 - <i>Klebsiella</i>	France	70 year male with acute appendicitis and paralytic ileus	Not related to isolate	Tracheal aspirate	Not treated since no respiratory symptoms	Discharged. Follow up not mentioned
				22 year old Iraqi with shoulder injury	None	Rectal swab	Not treated	Discharged. Follow up not mentioned

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