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. 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. 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 which did have gross inadequacies as highlighted in a recent editorial. 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 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. 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. 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 so far. It will help us view a larger picture especially when it has been said that NDM-1 has a pandemic potential.

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<table>
<thead>
<tr>
<th>S. No.</th>
<th>Report</th>
<th>Number and type of NDM-1 isolates</th>
<th>Country where specimen was obtained</th>
<th>Patients’ characteristics</th>
<th>Foci of sepsis</th>
<th>Culture specimen</th>
<th>Treatment details</th>
<th>Patient outcome</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Health Protection Report¹</td>
<td>22 isolates</td>
<td>UK</td>
<td>One had haematological malignancy and suffered blood stream infection due to NDM-1 <em>E. coli</em>. Second underwent cosmetic surgery which was complicated with wound infection due to NDM-1 positive <em>Klebsiella.</em> 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.</td>
<td>One blood stream infection One skin infection 20 - not mentioned</td>
<td>1-blood 1-wound sample 20-not mentioned</td>
<td>Not mentioned</td>
<td>Not mentioned</td>
</tr>
<tr>
<td>2</td>
<td>Deshpande et al⁵</td>
<td>22 isolates</td>
<td>India</td>
<td>All 22 hospitalized in India. Further clinical details not mentioned.</td>
<td>Not mentioned</td>
<td>11-urine 4-sputum 3-blood 2-tracheal 1-swab 1-pus 1-BAL 1-stool</td>
<td>Not mentioned</td>
<td>Not mentioned</td>
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<tr>
<td>3</td>
<td>Kumarasamy et al</td>
<td>180 isolates</td>
<td>India</td>
<td></td>
<td></td>
<td>Community acquired urinary tract infections, pneumonia and bloodstream infections in isolates from India and Pakistan. No mention made about foci of sepsis in UK isolates</td>
<td>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</td>
<td>Not mentioned</td>
</tr>
<tr>
<td>4</td>
<td>Poirel et al</td>
<td>7 – Klebsiella</td>
<td>Kenya</td>
<td></td>
<td></td>
<td>Not mentioned</td>
<td>Urine</td>
<td>Not mentioned</td>
</tr>
<tr>
<td>5</td>
<td>Bogaerts et al</td>
<td>2 – E. coli</td>
<td>Belgium</td>
<td>Patient 1: diabetic with wound infection</td>
<td>Soft tissue</td>
<td>Rectal swab, wound swab and sputum (patient specific specimen source not mentioned)</td>
<td>Patient 1 died. Others recovered</td>
<td>Patient 1 died. Others recovered</td>
</tr>
<tr>
<td>6</td>
<td>Seema et al</td>
<td>30 – E. coli</td>
<td>India</td>
<td>32 male, 22 female, age ranged from 1 day to 85 yr</td>
<td>Not mentioned</td>
<td>26-Urine</td>
<td>Not mentioned</td>
<td>Not mentioned</td>
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Table II. Summary of 7 reports mentioning treatment details and patient outcome

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<tr>
<td>1</td>
<td>Chan et al (19)</td>
<td>1 - E. coli</td>
<td>Singapore</td>
<td>46 year old woman suffering from ALL</td>
<td>Lungs</td>
<td>Blood</td>
<td>Polymyxin</td>
<td>Died</td>
</tr>
<tr>
<td>2</td>
<td>Chen et al (21)</td>
<td>1 - Klebsiella</td>
<td>China</td>
<td>Asymptomatic</td>
<td>None</td>
<td>Stool</td>
<td>Not treated</td>
<td>Spontaneously eradicated</td>
</tr>
<tr>
<td>3</td>
<td>Kus et al (23)</td>
<td>1 - Morganella</td>
<td>Canada</td>
<td>86 year male with history of stroke, diabetes, hypertension, atrial fibrillation, CA- colon and prostrate</td>
<td>Asymptomatic</td>
<td>Urine</td>
<td>Not treated</td>
<td>Persistent bacteriuria at 5 months. Patient asymptomatic</td>
</tr>
<tr>
<td></td>
<td></td>
<td>1- Proteus</td>
<td></td>
<td>71 year female suffering from multiple sclerosis and neurogenic bladder on catheter</td>
<td>Asymptomatic</td>
<td>Urine</td>
<td>Not treated</td>
<td>Persistent bacteriuria at 3 months. Patient asymptomatic</td>
</tr>
<tr>
<td>4</td>
<td>Mochon et al (24)</td>
<td>1 - Klebsiella</td>
<td>United States</td>
<td>13 year old boy with 3 day fever, cough and wheeze. history of bronchial asthma and developmental delay</td>
<td>Lung</td>
<td>Urine, nasal wash and sputum</td>
<td>colistin</td>
<td>Recovered</td>
</tr>
<tr>
<td>5</td>
<td>Mulvey et al (25)</td>
<td>1 - Klebsiella</td>
<td>Canada</td>
<td>76 year old women with diarrhoea and impaired mentation</td>
<td>Urinary tract</td>
<td>Urine, rectal swab</td>
<td>Colistin and chloramphenical</td>
<td>Died</td>
</tr>
<tr>
<td>6</td>
<td>Pfeifer et al (28)</td>
<td>1 - E. coli</td>
<td>Germany</td>
<td>70 year male with acute appendicitis and paralytic ileus</td>
<td>Not related to isolate</td>
<td>Tracheal aspirate</td>
<td>Not treated since no respiratory symptoms</td>
<td>Discharged. Follow up not mentioned</td>
</tr>
<tr>
<td>7</td>
<td>Poirel et al (29)</td>
<td>1 - Klebsiella</td>
<td>France</td>
<td>22 year old Iraqi with shoulder injury</td>
<td>None</td>
<td>Rectal swab</td>
<td>Not treated</td>
<td>Discharged. Follow up not mentioned</td>
</tr>
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References


