Evidence of expanding geographic distribution of melioidosis in Bangladesh: reports of three cases
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ABSTRACT
Melioidosis is an emerging infectious disease in Bangladesh. Reported cases are mostly diagnosed among inhabitants of central and north-east zone of the country. We report three cases of melioidosis occurring among patients with diabetes mellitus and chronic kidney disease from not well-known endemic areas within the country. Patients presented with fever, anorexia and weight loss. Laboratory reports confirmed growth of Burkholderia pseudomallei from blood and urine. These cases are reported to increase awareness among physicians regarding melioidosis occurring beyond the so-called hot spots in Bangladesh.

Key words: Burkholderia pseudomallei, chronic kidney disease, diabetes mellitus, endemicity, melioidosis.

INTRODUCTION
Melioidosis is caused by \textit{Burkholderia pseudomallei}, a Gram-negative, environmental saprophytic bacterium found in wet soil, mud and pooled surface water in the tropics and subtropics.\textsuperscript{1} Patients with diabetes mellitus (DM) and chronic kidney disease (CKD) are at increased risk for melioidosis.\textsuperscript{1,2} Patients may present with fever, pneumonia, septicemia and visceral abscess and there is high mortality. In spite of being an endemic disease, melioidosis has not been reported frequently in Bangladesh, may be due to lack of awareness among physicians and microbiologists and inadequate diagnostic facilities.\textsuperscript{3} Reported autochthonous cases are mostly diagnosed among inhabitants of central and north-east zone of Bangladesh.\textsuperscript{4-6} We report three cases of melioidosis having DM and CKD hailing from not well-known endemic areas within the country.

METHODS
Patients’ clinical and laboratory data were recorded in case record forms after obtaining informed written consent from patients or attendants. In-hospital treatment and outcomes were also recorded.

CASE REPORTS
Three male patients, aged between 50 and 75 years from Rajshahi (patient 1), Chattogram (patient 2) and Munshigonj (patient 3) districts, presented with fever, anorexia and weight loss (Table I, Figure 1) for variable duration. They were initially evaluated locally and received treatment including antibiotics (ciprofloxacin and ceftriaxone) without any benefit. One of them had abdominal pain. They were known to be suffering from DM and CKD. They had neutrophilic leukocytosis, high erythrocyte sedimentation rate (ESR), C-reactive protein (CRP) and
Raised serum creatinine (Table I). All had uncontrolled diabetes (HbA1c 8-9%) (Table I). Ultrasonography showed splenomegaly in one case (patient 3), prostatic abscess in another and all had contracted echogenic kidneys. Chest X-ray appeared normal in all three cases. Blood culture grew *B. pseudomallei* in all cases and urine culture confirmed *B. pseudomallei* in one of them. Unfortunately, the patient (patient 2) with prostatic abscess died before receiving blood culture report.

Patients were treated initially with ceftazidime and meropenem (dose adjusted for kidney function) for 4 weeks and in eradication phase co-amoxiclav or co-trimoxazole and doxycycline combination. One patient required 4 sessions of hemodialysis and intensive care unit support initially. Other medications included paracetamol and blood transfusion. Patients were discharged with stable renal function.

| Parameters                  | Patient 1 | Patient 2 | Patient 3 |
|-----------------------------|-----------|-----------|-----------|
| **Demographic**             |           |           |           |
| Age (years)                 | 50        | 57        | 75        |
| Sex                         | male      | male      | male      |
| Address                     | Chottogram (urban) | Rajshahi (rural) | Munshiganj (urban) |
| Occupation                  | businessman | farmer    | businessman |
| **Clinical presentation**   |           |           |           |
| Fever                       | (2 weeks) | (3 weeks) | (6 weeks) |
| Vomiting                    |           |           |           |
| Altered conscious level     |           |           |           |
| Weight loss                 |           |           |           |
| Dehydration                 |           |           |           |
| Suprapubic abdominal pain   |           |           |           |
| Dehydration                 |           |           |           |
| Tenderness                  |           |           |           |
| Abdominal pain              |           |           |           |
| **Biochemical**             |           |           |           |
| Random blood glucose (mmol/L) | 10   | 12        | 8         |
| HbA1c (%)                   | 9         | 9         | 8         |
| Hb (gm/dl)                  | 10.3      | 9.0       | 7.0       |
| Total WBC                   | 37.370×10⁹/L | 16350×10⁹/L | 15,830×10⁹/L |
| Platelet count              | 364×10⁹/L | 160×10⁹/L | 138×10⁹/L |
| ESR                         | 70 mm/hour | 70 mm/hour | 90 mm/hour |
| CRP                         | 207 mg/L  | 207 mg/L  | 125 mg/L  |
| Serum creatinine            | 8.1 mg/dl | 7.7 mg/dl | 4.5 mg/dl |
| **Microbiological**         |           |           |           |
| Blood culture               | Growth of *B. pseudomallei* | Growth of *B. pseudomallei* | Growth of *B. pseudomallei* |
| Urine culture               | -         | Growth of *B. pseudomallei* | - |
| **Radiological**            |           |           |           |
| Abdominal sonography        | bilateral echogenic kidney | prostatitis with abscess formation | splenic abscess |
Figure 1 Districts of Bangladesh reported to have melioidosis cases (new cases – red, new and previously reported cases – orange and previously reported cases – yellow)
DISCUSSION
Melioidosis is now recognized as a major cause of fatal septicaemia in endemic tropical regions. Patients with DM, CKD, chronic lung disease and excess alcohol intake were associated with increased risk for melioidosis.1,7 Patients with *B. pseudomallei* infection may present with fever, pneumonia, cutaneous and visceral abscess.3 CKD itself is a risk factor for melioidosis by impairing host immune response due to impaired chemotaxis of neutrophils, reduced phagocytic ability, decreased generation of reactive oxygen intermediates during oxidative burst and significant elevation of resting levels of cytosolic calcium and reduction in adenosine triphosphate of the phagocytic cells.8,9 In an Australian prospective study, 39% of patients with melioidosis had DM and 12% had CKD and in 20% cases there was no identifiable risk factor.7

In Bangladesh, there is paucity of incidence data of melioidosis cases among risk group population; sporadic cases with DM, CKD and steroid intake were reported.2-5,10,11 In Bangladesh, most endemic melioidosis cases were reported from Tangail, Mymensingh, Gazipur, Jamalpur and Sylhet districts (Figure 1) along with imported cases.4,5,12 Cases beyond this geographic distribution have rarely been reported; our reported cases draw attention that melioidosis can occur beyond the so-called hot spots of the country and physicians should have a high index of clinical suspicion in appropriate clinical settings.

Further attention is sought to the fact that, most melioidosis cases in Bangladesh were identified in microbiology laboratory of Bangladesh Institute of Research and Rehabilitation in Diabetes, Endocrine and Metabolic Disorders (BIRDEM) General Hospital in Dhaka, Bangladesh, one of the tertiary care center in Bangladesh. It is understandable that, it was possible for only those patients who could manage to come and get admitted in BIRDEM General Hospital or tested from there. It is likely that most patients remain beyond these facilities and so inappropriately evaluated. Capacity building efforts especially for microbiology facility is emphasized.

Authors’ contribution: SKS, TS, WMMH managed cases. SKS drafted the manuscript. All authors read and reviewed the final manuscript before submission.

Conflicts of interest: Nothing to declare.

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