**Background**

Melioidosis is caused by the Gram-negative bacterium *Burkholderia pseudomallei*. This organism is present in the environment in a defined geographic distribution including much of South-east Asia and Northern Australia, where infection is thought to be acquired after bacterial inoculation, ingestion or inhalation.\(^1\)\(^2\) The clinical presentation is highly variable and ranges from a mild localised infection to acute fulminant sepsis with widespread bacterial dissemination. Diagnostic confirmation relies on culture of *B. pseudomallei*; lack of accurate microbiological services in many tropical countries may result in under-reporting of cases and an under-estimate of the global burden of this infection. Melioidosis has been increasingly reported in India in recent years.\(^3\)\(^4\) This study aimed to determine the epidemiologic profile, clinical characteristics and final outcomes of culture confirmed melioidosis in India.

**Material and Methods**

Our centre is a 600 bed tertiary care referral hospital to which patients from many parts of India, especially South India and North-east India are referred. Cases were patients with culture proven melioidosis who were admitted between January 2005 and December 2010. They were classified as having bacteraemic or nonbacteraemic melioidosis, depending on whether their blood cultures were positive or negative, respectively, for *B. pseudomallei*.

The patients’ records were reviewed with respect to age, gender, area of residence, suspected risk factors for melioidosis,
sample(s) positive for *B. pseudomallei*, known sites of organ involvement, clinical features, results of laboratory and radiological investigations, antimicrobial treatment, outcome at hospital discharge and details of follow-up. Sites of infection were established based on history and examination findings in the medical notes together with investigation reports and procedure notes.

### Microbiologic Methods

For blood culture, at least 10 ml of blood was collected aseptically and inoculated into BacT ALERT (Biomerieux, Inc. Durham, NC 27704) blood culture bottles and incubated in the BACTEC™ automated blood culture system. Pus and tissue were plated on blood, chocolate and Mckonkey agar media. *B. pseudomallei* was identified by growth of silver white colonies on blood agar (as shown in Figures 1 and 2). The organism is a motile gram-negative, oxidase positive bacterium that produces a neutral-alkaline reaction on triple sugar iron, grows at 42°C and is colistin resistant. Isolate identification was also confirmed by API NE system (Bio Merieux, France).

### Treatment Regimen

Patients with severe or bacteraemic melioidosis were treated either with ceftazidime alone or ceftazidime plus co-trimoxazole for at least 14 days. They were then switched to oral treatment with a combination of oral co-trimoxazole and doxycycline for a total duration of 24 weeks.

### Statistical analysis and ethical clearance

Results were expressed in terms of the number and percentages or the mean ± standard deviation. The study was examined and cleared by the ethics committee of the hospital.

### Results

Thirty two cases of culture-proven melioidosis were identified during the study period. No case clustering was observed, and cases were distributed throughout the study period. Summary data for the 32 cases are shown in Table 1. Median age was 42.5 years (range = 4 - 60 years), of which twenty four (75%) patients were male. Overall 25 patients (78.12%) were from rural areas of India. State of origin is as shown in Table 1. Seventy five percent (24/32) had an underlying risk factor. Diabetes mellitus (14 patients (43.75%)) was the single commonest risk factor, the other common underlying conditions being alcoholism (7 patients (21.87%)) trauma (2 patients (6.25%)) and pregnancy (1 patient) respectively.

Infection was defined as localised in 14 patients (43.75%) and disseminated in 18 (56.25%) patients. The disseminated infection group included 16 patients with *B. pseudomallei* bacteraemia. Two with respiratory secretions positive for *B. pseudomallei* but negative cultures or other foci of infection were also classified as having disseminated infection based on their severity of illness.

Of the 14 localised infections, 6 had septic arthritis, 2 had pneumonia, 2 had prostatic abscess (as shown in Figure 3), 1 had a splenic abscess (as shown in Figure 4), 1 had a parotid abscess, 1 had suppurative lymphadenitis and 1 had a scrotal abscess.

Duration of presenting symptoms ranged from 7 days to as long as 6 months (average 2.34 months). Fever was the commonest presenting symptom of melioidosis in this study (65% - 22 patients). On follow up review 24 patients out of 32 (75%) were considered to have been treated successfully with cure.
Discussion

Our study is the largest case series of melioidosis from India although sporadic cases have been reported in the literature from different parts of India.3,4,13-17 There was no specific age group at risk, with the youngest case being a four year old boy and the oldest one being 60 years old. Patients were encountered from South and North-east India as well as the Andaman Islands.

As in other studies on melioidosis men were predominantly affected, perhaps due to more frequent exposure to soil and water or greater incidence of alcoholism.3 The disease has been shown to mimic tuberculosis as well.10 In contrast to children, adults tend to have at least one risk factor that affects host immunity and predispose to melioidosis. In our series three-fourth of our patients had an underlying risk factor with diabetes being the commonest, similar to the findings of others.4,6-8 Alcoholism was the second commonest risk factor for melioidosis. The importance of excessive alcohol intake as a risk factor for melioidosis was recognised in an earlier study from the Northern Territory of Australia and also in a study from north Queensland9. The predisposition to melioidosis in individuals with diabetes and those with excessive alcohol intake appears to be related primarily to impaired neutrophil function, such as mobilisation, delivery, adherence, and ingestion.10,11

Fever was the most common clinical presentation; however, absence of fever on presentation was observed in nine patients. Our finding that about half of our patients had localised disease is consistent with the published literature from Asia.4,5 The wide diversity of local syndromes in our series such as septic arthritis, pneumonia and focal abscess is well known in melioidosis. Prostatic abscesses seen in two of our patients is also a typical manifestation.

Despite disseminated disease in more than half of our patients, three-fourths of our patients were treated successfully, in contrast to other studies which reported high mortality.13,14,17 A high index of suspicion for the infection, starting ceftazidime early in illness, good supportive care and prolonging the consolidation phase to 24 weeks all may have contributed to the good outcome seen in our series.

The exact reasons for the increased incidence of melioidosis in India in recent years remain unclear.13,18-20 We speculate that increased detection in our study was due to considering the diagnosis in all patients with severe sepsis / abscess / septic arthritis /severe pneumonia and routinely speciating all non-fermenters grown in culture. In addition diabetes is increasing in the Indian population and may be driving an increase in incidence of the disease. It is also possible that increased awareness among clinicians and microbiologists and routine speciation of Gram negative bacteria are resulting in better recognition and reporting, rather than a truly increasing incidence of the disease.

Conclusion

Melioidosis is a treatable emerging infection in India and needs to be considered in the differential diagnosis of sepsis syndromes and focal abscesses, especially in diabetics. To facilitate diagnosis, all non-fermenting gram negative bacteria grown in clinical specimens should be speciated. A combination of a high index of suspicion, culture confirmation, prompt therapy with parenteral ceftazidime followed by cotrimoxazole and doxycycline for 24 weeks results in an excellent outcome in the majority of patients.

References