ORIGINAL ARTICLE ASIAN JOURNAL OF MEDICAL SCIENCES

A retrospective observational study analyzing the clinical presentation, complications, and outcome of Melioidosis in a tertiary healthcare center in South India

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Submission: 12-05-2025 Revision: 30-06-2025 Publication: 01-07-2025

ABSTRACT

Background: Melioidosis is caused by a saprophytic environmental Gram-negative bacterium *Burkholderia pseudomallei*. It is widespread in Northern Australia and South-east Asia and has shown an increasing trend in India. There are limited studies done in South India analyzing the clinical profile of melioidosis patients, hence the need for this study. **Aims and Objectives:** To analyze the demographic data, clinical presentation, investigations, treatment, complications, and outcomes in patients with melioidosis. **Materials and Methods:** A retrospective observational study was done on 35 patients who were admitted to a tertiary health care centre in South India from January 2017 to March 2025, who had culture-proven melioidosis. The spectrum of clinical profiles was analyzed. **Results:** 35 patients were studied, 68.6% were male, 71.5% were in the age group of 45–65 years, clustering of cases was seen around the rainy months, fever and cough were the most common symptoms (94.3% and 42.9%, respectively), diabetes mellitus was the most common risk factor. The most common presentation was abscess (45.71%) and pneumonia (37.1%). 42.9% required intensive care, and 2 out of 35 patients died. **Conclusion:** Melioidosis is an acute infection that may lead to sepsis and multi-organ dysfunction. It is often misdiagnosed due to variable clinical presentation and a lack of awareness among clinicians. Diabetes is the most common risk factor. Pneumonia, abscesses, and hepatosplenomegaly should raise suspicion of melioidosis. Blood cultures are positive in almost all cases and respond well to carbapenems/ceftazidime with cotrimoxazole. Early diagnosis and prompt treatment are paramount in improving patient outcomes.

Key words: Melioidosis; *Burkholderia pseudomallei*; Whitmore's disease

Access this article online

Website: https://ajmsjournal.info/index.php/AJMS/index

DOI: 10.71152/ajms.v16i7.4612

E-ISSN: 2091-0576

P-ISSN: 2467-9100

INTRODUCTION

Melioidosis, also known as Whitmore's disease, is a potentially fatal infectious disease caused by the Gram-negative bacterium *Burkholderia pseudomallei*, resulting in about 89,000 deaths/year. Melioidosis is predominantly a tropical disease, with the Indian subcontinent accounting for 44% of the global disease burden.[1] It is classified as a rare disease and often missed due to its similarity to tuberculosis (TB), and its diverse clinical symptoms, coupled with a lack of awareness among clinicians and a dearth of proper testing facilities.[2]

Melioidosis is endemic to Southeast Asia, Northern Australia, most parts of India, Southern China, Hong Kong, and Taiwan.[3,4] Within South Asia, India is estimated to have between 20,000 and 52,000 new cases annually and an estimated mortality rate of 32,000/year.[5] India has

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suitable climatic conditions for melioidosis and is known to be the diabetes capital of the world.[6,7] A literature search revealed that many cases in India were reported in southern and eastern India.[7] Sporadic case reports have been reported in India, from regions such as Vellore, Manipal, Pune, and North India.[8-11] Tropical climate, wet weather, increased rainfall, wind, temperature, and loose soil create favourable conditions for the disease.[12] The pathogen infects both humans and animals through direct contact with contaminated soil and water and can be naturally acquired through skin abrasion, ingestion, or inhalation.[13] Diabetes mellitus is a major risk factor along with chronic kidney disease, pulmonary, and coronary diseases.[2] The mean incubation period of *B. pseudomallei* in humans is 9 days, but can vary from days (acute) to years (chronic).[14]

The clinical spectrum of melioidosis can be wide and categorised into four types. The acute septicaemic type, the subacute type, the chronic type, and the latent or asymptomatic type.[15,16] Acute melioidosis manifests as pneumonia, multiorgan abscesses, and fulminant septicemia, whereas the chronic infection presents as symptoms mimicking TB and multiorgan abscesses with occasional neurological involvement.[17]

Clinical clues include presentation during the monsoon months, a history of soil exposure, and risk factors such as diabetes mellitus and chronic renal disease. Nearly 20% of community-acquired bacteraemia is attributed to melioidosis.[18]

Non-specific laboratory findings include raised C-reactive protein (CRP) and anemia. In common with other Gram-negative bacteremias, neutrophilic leukocytosis may be absent. Others are hepatic and renal derangements, hypoglycemia, and acidosis.[8]

Radiological imaging often reveals multifocal nodular lesions, patchy consolidation with cavitary lesions in the lungs.[19] Abscesses in organs may be seen, especially the liver and spleen. In patients with neuronal involvement, a magnetic resonance imaging scan of the brain often shows ring-enhancing lesions with hyperintense changes.[20]

B. pseudomallei can be detected in blood, throat and rectal swabs, sputum, and pus from abscesses, but their presence in clinical samples is limited. Melioidosis can be confirmed by culturing biological specimens. However, care must be taken not to misinterpret results as *Pseudomonas*, *Burkholderia cepacia*, or *Bacillus* species.[17] Under light microscopy, *B. pseudomallei* appears as safety-pin-shaped bacilli, which can be confirmed by immunofluorescence microscopy.[21] The diagnosis is often overlooked because of culture's low diagnostic sensitivity (nearly 60%). Therefore, nearly 40% of diagnoses are missed initially.[17] It is advisable to take specimens for culture from as many sites as possible, because of wide haematogenous dissemination and even one positive culture is diagnostic.[22]

The treatment of melioidosis comprises an intravenous intensive phase and an eradication phase.[22,23] The aim of the intensive phase is to achieve stabilization, resolution of fever, and reduce inflammatory markers. A parenteral antibiotic is given for 2–4 weeks and is usually ceftazidime or carbapenems. In the acute septicaemic and subacute types, since microbiological diagnosis is not immediately available and the differential diagnosis is wide, a carbapenem is the frequent choice. In the other types, since antibiotic treatment is often commenced after microbiological diagnosis, ceftazidime can be the choice; it is combined with oral cotrimoxazole if there are significant deep-seated foci. The intensive phase needs to be continued until the patient is afebrile, any abscesses have significantly resolved, or CRP is reduced to near-normal levels. This often requires 2–4 weeks. Next is the eradication phase, which is used to prevent recurrence of the disease. Here, two oral antibiotics are recommended, and these are usually cotrimoxazole, doxycycline, coamoxiclav, or chloramphenicol.[23]

Melioidosis can be treated without difficulty if diagnosed at an early stage. The fatality of melioidosis is due to delay in diagnosis and due to challenges in the laboratory identification of *B. pseudomallei*.[24] Because of low sensitivity (60.2%) of the culture of melioidosis,[17] and delay in diagnosis, case fatality may be seen in up to 50% of cases.[25] The actual mortality rates vary across regions from 9% to 70%.[26] With early diagnosis, appropriate antibiotic administration, and advanced intensive care, mortality can be decreased to <10%.[27]

Multimodal approach for prevention of melioidosis includes avoiding contact with contaminated soil and water, wearing proper footwear, access to safe drinking water, adequate glycemic control, control of other risk factors, along with increasing public awareness. Of these, glycemic control is the most effective strategy.[28]

Melioidosis has been prevalent in many parts of South Asia for more than five decades but remains an underdiagnosed and under-reported disease.[29] There has also been a steady increase in the number of melioidosis cases reported from India.[7,30,31] The increase in number could be attributed to awareness among clinicians, correct diagnosis, and improved diagnostic facilities.

Due to a myriad of clinical presentations, a lack of awareness of the disease among clinicians and microbiologists, and close similarity to other tropical

infections like TB or bacterial pneumonia, the diagnosis of melioidosis is often missed or delayed. This study aims to analyze the clinical presentations and outcomes observed in patients with melioidosis in a tertiary care setting, thereby helping the clinician to make an early diagnosis and initiate treatment.

Aims and objectives

To analyze the demographic data, clinical presentation, investigations, treatment, complications, and outcomes in patients with melioidosis.

MATERIALS AND METHODS

A retrospective observational study was done on 35 patients who were admitted to a tertiary health care centre in Mangalore in South India from January 2017 to March 2025, who were culture proven to have melioidosis. Approval was obtained from Institutional Ethics Committee under the letter having reference number FMIEC/CCM/296/2024 dated April 16, 2024. Electronic case records of 35 patients were reviewed. Demographic data, clinical presentation, investigations, treatment, complications, and outcomes were analyzed. Descriptive statistics were used to summarize the data. Categorical variables were described using frequencies and percentages. The mean and standard deviation were used to interpret the data. A p-value≤0.05 was considered statistically significant.

Inclusion criteria

Patients aged >18 years and who were culture-proven to have melioidosis were included.

Exclusion criteria

Patients with other coexistent acute febrile illness such as dengue, leptospirosis, and malaria were excluded.

RESULTS

In our study, 35 patients were analyzed, of whom 68.6% of patients were male. 71.5% of patients were in the age group of 45–65 years, followed by 20% in the age group 35–44 years, and 8.6% were >65 years. Median age of presentation was 53 years.

There was a seasonal distribution noted with a clustering of cases seen around the rainy months, with most patients presenting between July and December(74.3%) and a smaller cluster around the month of January(17.1%) (Figure 1). 45.8% of patients were from North Kerala (Kannur and Kasargod), followed by regions in and around Mangalore (43%).

Majority of patients had a symptom duration of 7–14 days (45.7%). Short duration of <7 days was seen in 25.7% of patients, while 17.1% had symptom duration of >21 days. The mean duration of symptoms was 15.3 days and the median was 8 days.

Fever and cough were the most common presenting symptoms (94.3% and 42.9%, respectively). Pain in the abdomen was seen in 20% and breathlessness was also seen in 20%. Other less common symptoms were headache, joint pain, vomiting, weight loss, altered sensorium chest pain, myalgia, fatigue, vomiting, decreased urine output, hematuria, jaundice, B/L neck swelling (due to lymphadenopathy), B/L hip and thigh pain (due to femoral osteomyelitis with septic arthritis) (Figure 2).

Among the risk factors studied for melioidosis, diabetes mellitus was the most common, which was seen in 80% and was statistically significant. Alcohol use was seen in 17.1%, chronic steroid use in 14.3%, and ischemic heart disease in 11.4%. Among the seven patients who did not have diabetes, the risk factors noted were chronic steroid use (3 patients), chronic liver disease (CLD)-secondary to

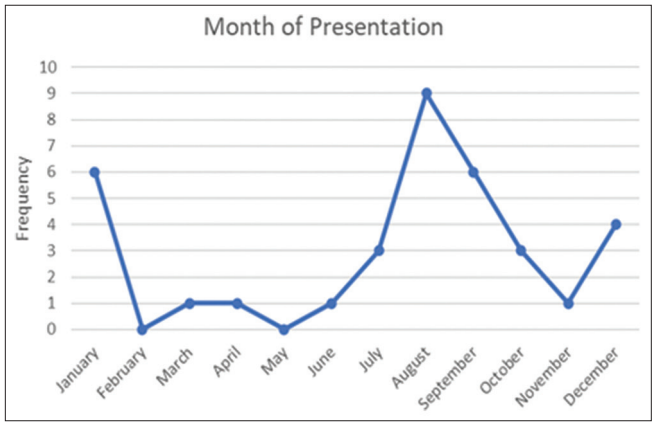

Figure 1: Pattern of case distribution during the year

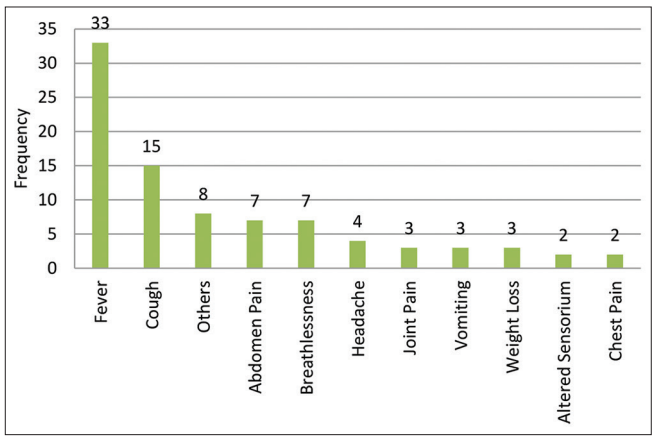

Figure 2: Symptoms of melioidosis

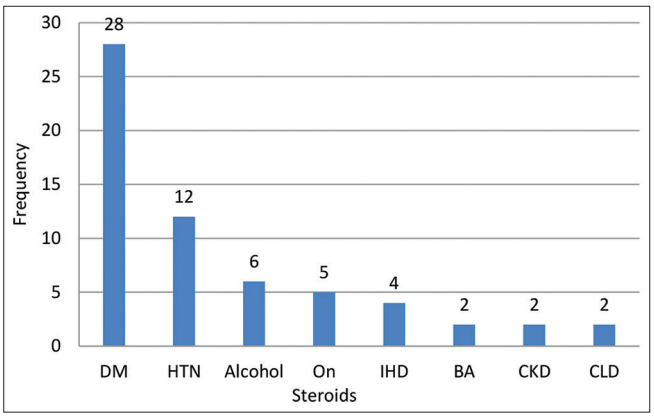

Figure 3: Risk factors of melioidosis

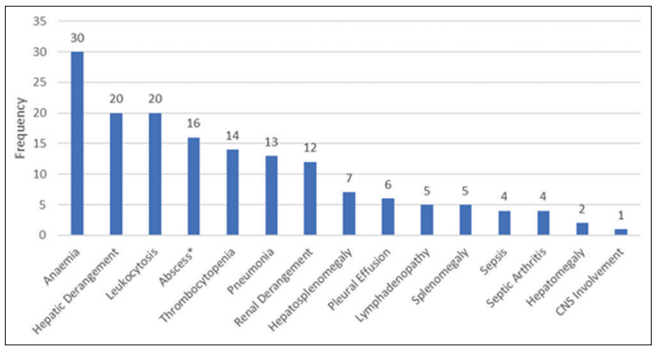

Figure 4: Summary of clinical presentations and lab investigations. *Sites of abscess noted were hepatic, splenic, intramuscular, lung, paratracheal, abdominal wall, scrotal and lymph node

alcohol use (1 patient). However, three patients did not have any risk factors. Some patients had more than one risk factor (Figure 3).

Among the hematological abnormalities, the most common noted were anaemia (85.7%), leukocytosis (57%), thrombocytopenia (40%), and elevated erythrocyte sedimentation rate (74.3%). Among the patients who had thrombocytopenia, 57.14% had mild thrombocytopenia, 28.57% had moderate thrombocytopenia, and 14.28% had severe thrombocytopenia.

Elevated bilirubin levels (40.6%), aspartate aminotransferase and alanine aminotransferase levels (37.5% and 43.8%, respectively) were the most consistently noted biochemical abnormalities. Renal dysfunction was noted in 25.7% of the patients. Patients with diabetes as a comorbidity had poorly controlled blood sugars, with 54.3% presenting with a glycosylated hemoglobin (HbA1c) >9% and 17.1% with HbA1c of 6.5–9%.

Ultrasound (USG) of abdomen revealed hepatosplenomegaly in 7 patients (20%), hepatic and splenic abscess in 5 patients (14.3%), splenomegaly alone in 5 patients (14.3%), hepatomegaly alone in 2 patients (5.7%), hepatic abscess alone in 3 patients (8.6%), splenic abscess alone in 2 patients (5.7%), ascites in 1 patient (2.9%) and normal USG in 10 patients (28.6%). Chest X-ray showed pneumonia in 13 patients (37.1%), pleural effusion in 6 patients (17.1%), and other less common findings seen were collapse and acute respiratory distress syndrome. Normal chest X-ray was in 17 patients (48.6%).

Summary of clinical presentations and lab investigations is depicted in Figure 4. Other less common clinical presentations noted were epididymo-orchitis, myositis, femoral osteomyelitis, and pericardial effusion.

Blood culture was positive for *B. pseudomallei* in 85.7% of patients. Other specimens positive for *Burkholderia* (14.3%) included pleural fluid, bronchoalveolar lavage fluid (BAL), cerebrospinal fluid (CSF), pericardial fluid, or pus. Cultures in all patients were sensitive to amoxicillin clavulanate, ceftazidime, cotrimoxazole, and carbapenems. All patients were treated with ceftazidime/carbapenem and cotrimoxazole.

It is important to note that three patients were misdiagnosed at initial presentation. One patient was treated for suspected leptospirosis and 2 patients for suspected TB.

Majority of patients (40%) required in-hospital stay ranging from 2 to 3 weeks and 25.7% required 1–2 weeks. The median length of stay in the hospital was 14 days and the mean was 14.71 days. Of the patients admitted with melioidosis, 42.9% of patients required admission to the ICU. Out of these, 60% required more than 1 week of stay in ICU. Out of 35 patients, 2 patients died. They were aged >50 years, had sepsis with septic shock, required ventilatory support and inotropes, and also had comorbidities (One patient had CLD, the other patient was on steroids).

DISCUSSION

In our study, majority of patients were males (68.6%). 71.5% of patients were of the age group between 45 and 65 years, with the median age of presentation being 53 years. A study of 24 cases done by Raina et al.,[32] in North India, found the median age of presentation to be 56 years and the majority (91.6%) were males. In a study by Chantratita et al.,[33] the median age was found to be 55 years, 72% were males and 53.6% of patients were of the age group between 51 and 70 years.

Similar observations were made in studies done by Ganesan et al.,[34] Saravu et al.,[35] and Easow et al.[36] Increased incidence in males and the age distribution noted could be attributed to increased outdoor activities.

In our study, 74.3% of patients presented during the monsoon season and after (July to December). Similar observations were made in studies done by Raina et al.,[32] Ganesan et al.,[34] Saravu et al.[35] In our study, majority of patients had a symptom duration of 7–14 days (45.7%) and some had an even shorter history of <7 days (25.7%). Fever and cough were among the most common presenting symptoms (94.3% and 42.9%, respectively), followed by pain abdomen in 20% and breathlessness in 20% of patients. In a study done by Yadav et al.,[37] 57.14% of patients had symptom duration between 10 and 15 days and 42.8% of patients had been symptomatic for 2–3 months. Fever was the universal symptom, followed by respiratory/abdominal symptoms (57.14%). In a study done by Easow et al.,[36] 80% of patients presented with symptom duration between 7 and 14 days. Fever was a presenting complaint in 80% of patients, followed by abdominal and respiratory symptoms (60% and 40%, respectively).

Among the risk factors analyzed in our study, diabetes mellitus was the most common (80%) and this was statistically significant (P<0.001). Alcohol use was the second most common risk factor (17.1%). 3 patients (8.5%) did not have any risk factors. In the Indian Subcontinent, about 80% of melioidosis cases are seen in diabetics.[38-40] Raina et al.,[32] found 58.3% of melioidosis patients had diabetes, 20.8% of patients had alcohol use as a risk factor, while 33.3% of patients did not have any risk factors. The study done by Yadav et al.,[37] found all patients to have diabetes. In the study by Chantratita et al.,[33] 70.3% had diabetes, 5% had alcohol use, while 13% did not have any risk factors. Ganesan et al.,[34] also noted that all patients had diabetes and 42.8% of patients had alcohol use. In a study done by Saravu et al.,[35] 85.71% had diabetes, 71.42% had alcohol use. In a study by Easow et al.,[36] 60% of patients had diabetes.

In our study, the most common presentations were abscesses (45.71%) and pneumonia (37.1%). Others were septic arthritis (11.4%) and neuromelioidosis (2.9%). Raina et al.,[32] noted neuromelioidosis in 12.5% of patients. In a study done by Yadav et al.,[37] 85.7% had pneumonia, 57.14% had abscesses, and all patients had joint involvement, while none had neuromelioidosis. In the study done by Chantratita et al.,[33] 41.8% were found to have lung infection, 8% had septic arthritis, 0.8% had osteomyelitis, and 0.8% had neuromelioidosis. In the study done by Ganesan et al.,[34] abscesses were seen in 42.8%, septic arthritis in 42.8%, and cellulitis in 28.57%. Saravu et al.,[35] noted abscesses in 42.8%, pleural effusion (42.8%), and pneumonia (14.2%). Easow et al.,[36] found that 60% presented with pneumonia and 20% had neuro melioidosis. As per literature, Central nervous system infections accounted for 1.5–10% of all melioidosis cases.[41,42]

In our study, the most common hematological abnormalities were anemia (85.7%), leucocytosis (57%) and thrombocytopenia (40%). Hepatic and renal dysfunction were seen in 57.14% and 25.7%, respectively. In the study done by Yadav et al.,[37] 57.14% of patients had anemia and 57.14% had leukocytosis. In a study done by Ganesan et al.,[34] all patients had anemia, and leukocytosis was seen in 85.71%. 57.14% and 28.57% had renal and hepatic dysfunction, respectively. In the study done by Saravu et al.,[35] 42.85% had anemia, and 71.42% had leukocytosis.

In our study, blood culture was positive for *B. pseudomallei* in 85.7% of patients and all isolates were sensitive to amoxicillin-clavulanate, ceftazidime, cotrimoxazole, and carbapenems. All our patients were treated with ceftazidime/carbapenem and cotrimoxazole.

In a study done by Raina et al.,[32] 41.6% had positive blood culture and 50% of patients had positive pus culture for *B. pseudomallei*. All patients were treated with ceftazidime/carbapenem and cotrimoxazole. In study done by Yadav et al.,[37] 57.14% had positive blood culture and 57.14% had positive pus culture for *B. pseudomallei* and all isolates were sensitive to carbapenems. Chantratita et al.,[33] and Ganesan et al.,[34] found positive blood cultures in 77.1% and 42.85% respectively, and all isolates were sensitive to ceftazidime, carbapenems, and cotrimoxazole.

In our study, the median length of hospital stay was 14 days. Similar findings were noted by Chantratita et al.,[33] where the median length of stay in the hospital was 13 days (interquartile range 8–19). In our study, 42.9% of patients required ICU care and 2 out of 35 patients died (5.7%). In studies done by Raina et al.,[32] Saravu et al.,[35] and Ganesan et al.,[34] the mortality was 16.6%, 28.57%, and 42.85%, respectively. In a study done by Chantratita et al.,[33] 28% required ICU care, 24.9% died within 1 month, and 33.9% died within 1 year. The improved outcomes in our study may be attributed to early presentation to the hospital and early initiation of therapy.

Limitations of the study

This was a retrospective observational study that was conducted in a single medical centre. A larger number of study patients would help in further analysis. Follow-up of patients would have given additional information on long-term outcomes.

CONCLUSION

Melioidosis is an acute infection that may lead to sepsis and multi-organ dysfunction with high mortality if treatment is not commenced early. Due to its similarity to other tropical

infections, a high index of clinical suspicion is required, especially during the monsoon months and after. Prompt investigation, early diagnosis and initiation of treatment are paramount in improving patient outcomes. Diabetes is the most common risk factor seen, followed by alcohol use. Pneumonia, abscesses, hepatosplenomegaly should point toward melioidosis. Blood cultures are positive in almost all cases. Other specimens such as pus, pleural fluid, BAL, and CSF can also yield positive cultures. Almost all patients respond well to carbapenems/ceftazidime with cotrimoxazole during the acute septicemic phase. Increasing awareness of this disease among clinicians and microbiologists, the availability of rapid diagnostic tests, and early treatment have to be prioritized.

ACKNOWLEDGMENT

The authors acknowledge Miss. Kripa Rasquinha, statistician, FMRC, Mangalore, for helping us with the statistical analysis of the data.

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Authors' Contributions:
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Source of Support: Nil, **Conflicts of Interest:** None declared.