

Myriad Presentations of Melioidosis in Sri Lanka: A Review

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Abstract: *Melioidosis, caused by the bacterium Burkholderia pseudomallei, is a tropical infectious disease with a wide range of clinical presentations. In Sri Lanka, the disease is increasingly diagnosed, with diabetes and agricultural practices being the most common risk factors. This review explores the diverse manifestations of melioidosis in Sri Lanka, categorizing them by organ systems. Additionally, it discusses diagnostic and therapeutic strategies specific to the region. This study aims to improve clinician awareness of melioidosis in tropical countries and enhance diagnostic accuracy and treatment outcomes.*

Keywords: Melioidosis, Burkholderia pseudomallei, Sri Lanka, infectious diseases, tropical diseases

1. Introduction

Gaining the interest of many researchers in the recent past, a notorious disease has gained widespread attention. Melioidosis, often referred to as the great mimicker, has a wide range of symptoms that of life-threatening potential, has acquired this designation due to its protean range of non-specific symptoms and signs across multiple organ systems, often leading to misconceptions and misdiagnoses [1–4].

Melioidosis is an infectious disease caused by *Burkholderia pseudomallei*, a saprophytic, aerobic, non-spore-forming, non-fermenting, environmental, Gram-negative bacillus commonly found in the rhizosphere and superficial groundwater sources of tropical and subtropical regions [2,4–7]. Factors such as high levels of rainfall, extreme weather events like floods and storms, and occupational exposure during paddy field cultivation contribute to its increasing occurrence [1–5,7].

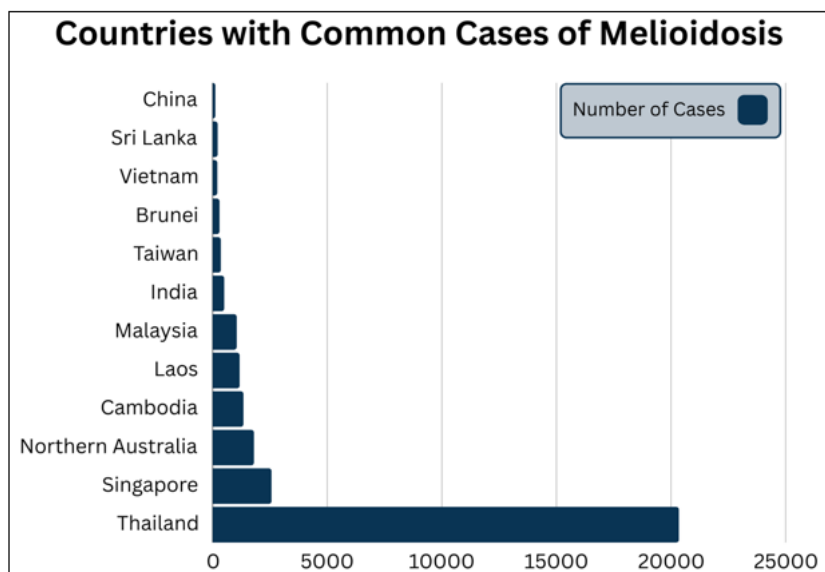


Figure 1: Countries with the most common cases of Melioidosis (with a sum number of cases reported to be ≥ 100 as of 2022) [8,9]

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Researchers have reported individuals being affected over a wide age range (2-92 years), with a greater number of patients anchored in rural areas and being male [1,5,6]. Additionally, investigations revealed that different population groups (based on occupation and exposure) were involved and found to be infected [2,5,6]. This helps link the prevalent lifestyle practices of the country to the dissemination of the microorganism; most influentially, the ‘outdoor, agricultural, barefoot’ way of life exposing them to the aforementioned conditions, allowing penetration through broken skin, ingestion of untreated water, and amusingly even inhalation of dust containing *B. pseudomallei* [2,4–6]. Moreover, in addition to diabetes mellitus being the most common risk factor, other conditions have also been found to increase susceptibility (refer Table 1) [1,3–7].

Table 1: Categorized Risk Factors Associated with Melioidosis

Risk Factors
Age-Related
Age > 45 years
Lifestyle
Increased consumption of alcohol
Medical Conditions
Organ diseases (Liver, Lung, Kidney)
Thalassemia
Prolonged steroid use
Immunosuppression
Sri Lanka Specific
Dengue hemorrhagic fever
IgA nephropathy
Lepromatous leprosy
Prednisolone administration during SLE

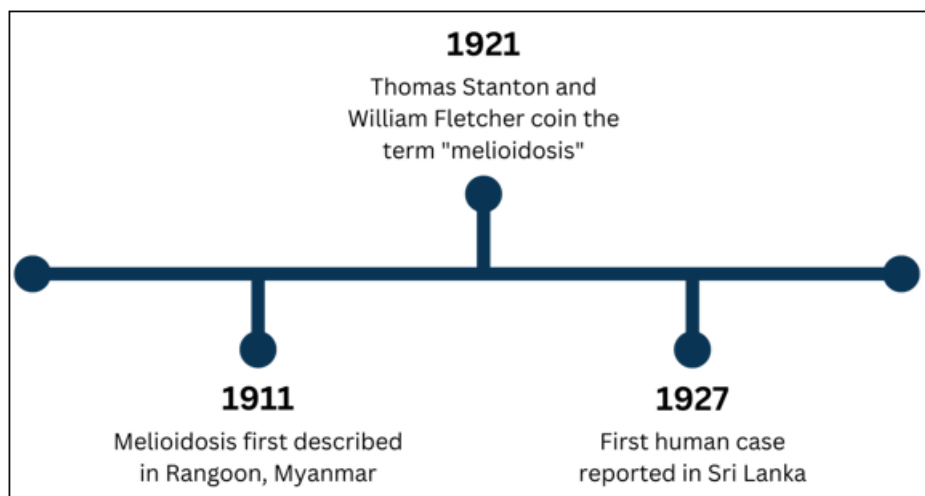


Figure 2: Timeline illustrating key events in the history of melioidosis in relation to Sri Lanka [4,5,10]

Sri Lanka has been significantly affected by this disease, particularly in its rice-growing areas. Nevertheless, *B. pseudomallei* is rarely detected in tea and rubber plantations due to lower temperatures, soil conditions and agricultural

practices (refer Figure 3) [6]. Conversely, the microorganism showcases impressive resilience in diverse settings, including water, sand, soil lacking in nutrients, and extreme ranges of pH and temperature [1,4].

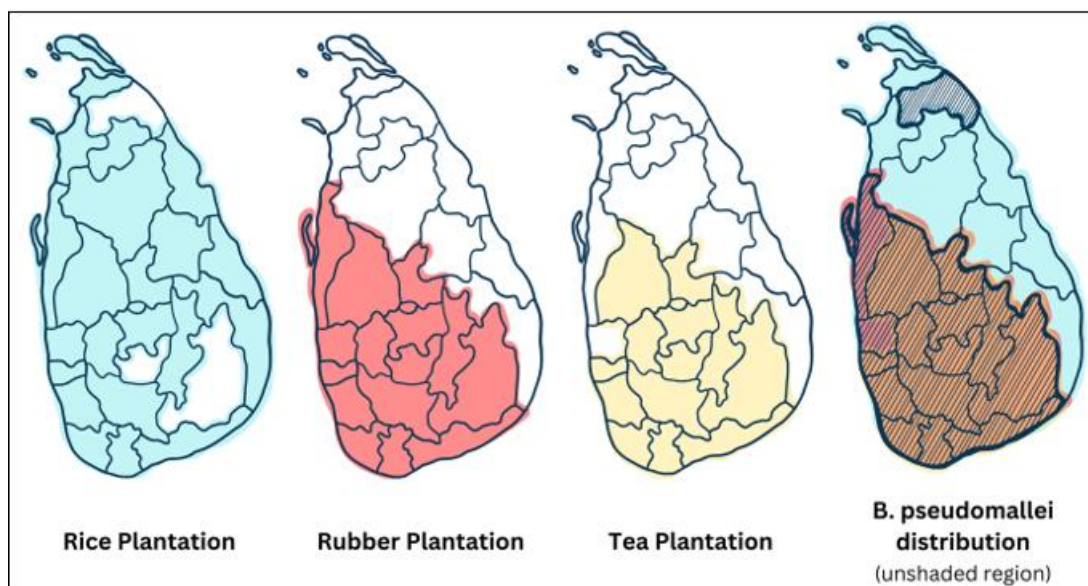


Figure 3: The agricultural landscape of Sri Lanka alongside the geographical distribution of *B. pseudomallei* [11–13]

B. pseudomallei infection can present as acute in the majority of cases (85%), with a minority experiencing chronic or latent

forms [4]. Recurrent infections affect 5-28% of acute cases [4]. The bacterium employs a series of steps to establish

infection (refer Figure 4) [1,4]. These strategies collectively enable *B. pseudomallei* to persist and spread effectively, posing challenges for treatment and containment efforts.

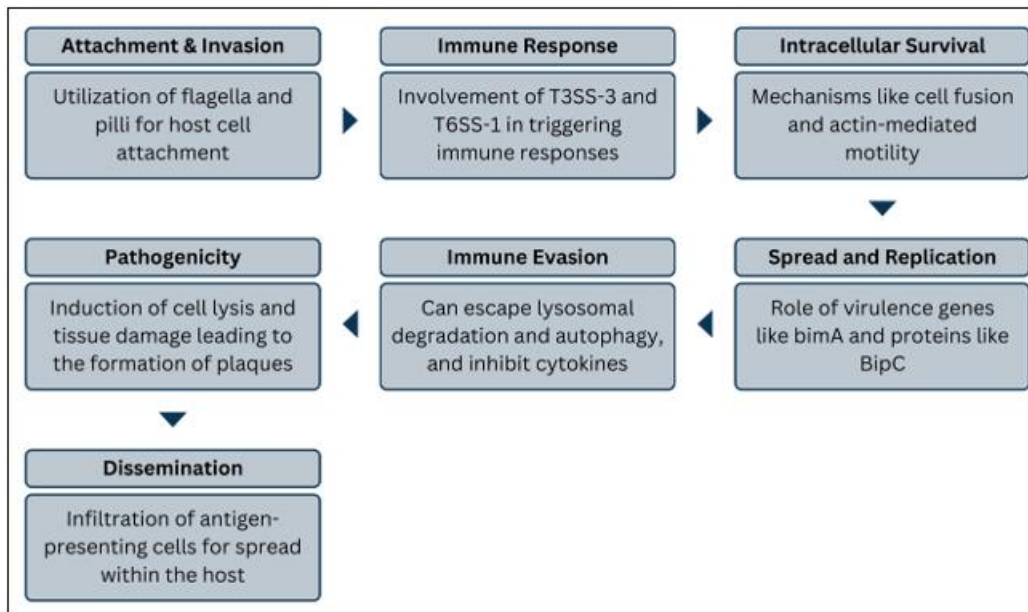


Figure 4: Flowchart depicting the pathophysiology and mechanisms of action of *B. pseudomallei*

Classified as a tier 1 select agent (high-risk entities with potential for significant harm) by the US Centers for Disease Control (CDC) and a hazard group 3 pathogen (biological agents with severe health risks, warranting careful management), suspected cases must be immediately reported to the hospital laboratory to ensure all necessary precautions

are followed [1,3,4]. However, reaching that diagnosis is not easy in the first place [5]. The time required for incubation is typically around 1-21 days [4]. Yet, if the microorganism is inhaled or aspirated, a severe form of the illness could unfold with a shorter period [4].

Table 2: Spectrum of *B. pseudomallei* Infection manifestations [4,7]

Presentation of Melioidosis	
Central Nervous System	
	Meningitis
	Subdural Empyema
	Cerebral Abscess
	Brain-Stem Encephalitis
	Transverse Myelitis
	Guillain-Barré Syndrome
	Status Epilepticus
Musculoskeletal	
	Septic Arthritis
	Muscles Abscesses
	Osteomyelitis
Gastrointestinal	
	Liver Abscesses
	Splenic Abscesses
	Psoas Muscle Abscesses
Integumentary	
	Skin and Soft Tissue Abscesses
	Cutaneous Symptoms
Genitourinary	
	Urinary Tract Infections
	Prostatitis
Lymphatic and Salivary Glands	
	Infections
Cardiovascular	
	Pericardial Effusion
	Endocarditis
Other	
	Bacteremia
	Sepsis

But clinical signs and symptoms alone do not suffice for a final say; microbiological culture remains the backbone [3,4,7]. However, it is worth mentioning that there are specific identification steps that aid in differentiating *B. pseudomallei* (refer Table 3) [1,3–5,7,14]. While *B. pseudomallei* may be able to grow on most routine media, the untrained eye, due to the bacteria's unspecificity, can dismiss it as a contaminant, or altogether misidentify it as another microorganism [1,4,14]. Due to this disease's diverse clinical presentations, it can often be misdiagnosed. This review article emphasizes presenting all these manifestations in one place, thematically arranged according to the organ system. The aim is to enhance clinician awareness by providing a compilation of cases specific to Sri Lanka.

Table 3: Diagnostic Strategies for *B. pseudomallei* Infection

Diagnostic Methods	
Colony Characteristics	
	Small gram-negative bacilli
	Bipolar staining (safety pin appearance)
	Metallic appearance
	Sweet earthy smell
	Positive oxidase reaction
Drug Interactions	
	Resistant to colistin and gentamicin
	Sensitive to co-amoxiclav
Sample Collection	
	Blood, throat, or rectal swabs
	Urine deposits
	Pus
	Sputum
Growth Media	
	Selective media like Ashdown's agar and broth
Molecular Approaches*	
	16S rDNA sequencing
	Specific PCRs
	Disc diffusion antibiotic sensitivity tests
	Antigen detection
	Nucleic acid amplification tests
	Indirect hemagglutination assay
	16S rDNA sequencing

* Novel tests may not be cost-effective in resource-limited settings

2. Methodology

This review article synthesizes available literature to provide a comprehensive overview of melioidosis manifestation in the specific geographical context of Sri Lanka.

A thorough literature search was conducted using databases such as PubMed, Google Scholar, Cochrane Library, and Scopus. The search focused on articles published in English without date restrictions. Keywords used included "Melioidosis", "Sri Lanka", "Clinical presentations", "Integumentary", "Musculoskeletal", "Reproductive", "Gastrointestinal", "Lymphatic", "Sepsis", "Neurological", "Genitourinary", "Cardiovascular", and "Pulmonary systems."

Inclusion Criteria

Studies were included if they provided insights into the clinical manifestations of melioidosis in human populations within Sri Lanka across all ages. This includes studies that

represent epidemiological data, laboratory investigations, treatment, and outcomes in the country.

Exclusion Criteria

Articles on melioidosis cases outside of Sri Lanka, non-human studies, and other infectious diseases, were all excluded.

Data Extraction and Analysis

A total of 5,659 articles were screened and 5,588 were excluded from this review due to not meeting the inclusion criteria, such as data not being from Sri Lanka, multiple duplicates of the same study across different databases, or melioidosis-like diseases.

Information from the selected articles was recorded on two online spreadsheets. One with columns for: article title, study type, year of publication, date of search, and type of clinical manifestation. The second sheet had columns for data extracted: patient demographics, prevalence in Sri Lanka, specific signs and symptoms reported, frequency, duration, and severity of symptoms, risk factors, diagnostic measures, treatment administered, and outcome (morbidity/mortality).

The spreadsheet was a standardized template that was used by all reviewers and at the end of the data extraction, two reviewers re-checked all the collected data for accuracy, redundancies, and language errors. The data was then organized in this article with clinical presentation being the common theme.

Limitations

This review article may have missed some papers from the literature due to human error when screening; this was minimized to the best by two separate reviews of the data. This review only used papers published in English; however, it can be considered to have less impact since most Sri Lankan journals are in the English language.

3. Funding

There was no funding obtained for this review.

Clinical Presentations Across Organ Systems

Integumentary Melioidosis

In melioidosis, cutaneous signs are apparent in 60% of children and 13% of adults. This is often linked with other symptoms and seldom presents as an isolated problem¹⁵.

The first case was a 53-year-old lady who did not have any contact to infected water or soil. She had fever, oral ulcers, and bilateral blepharitis, with a discharging sinus over the submental region. Inspection showed multiple tender papules, targetoid lesions, and subcutaneous nodules. However, primarily considered suggestive of sweet syndrome, the lymph node aspirate confirmed it as *Burkholderia pseudomallei*. She was treated with meropenem, after which she recovered¹⁶.

The second case was an 11-year-old girl with recent history of exposure to paddy fields. She was diagnosed with melioidosis based on fever, sore throat, and erythematous

nodules on the lower limbs, initially misidentifying erythema nodosum for streptococcal pharyngitis. There was no improvement in her condition with penicillin, but after further tests confirmed melioidosis, she improved remarkably after the administration of antibiotics¹⁷.

The third case was a 42-year-old diabetic male who had pyrexia of unknown origin, periorbital cellulitis, rhinosinusitis, and leg abscesses. The diagnosis at presentation was invasive fungal sinusitis; however, *B. pseudomallei* was finally cultured from the blood, and the patient responded to treatment with antibiotics¹⁸.

Musculoskeletal Melioidosis

Musculoskeletal infections by melioidosis are sporadic, happening in only 4% of cases, with 11 cases documented in Sri Lanka¹⁵. It is more frequently seen amongst males, farmers, and diabetics between 45 and 60 years old, with septic arthritis mostly due to a barefoot lifestyle¹⁹.

Out of the 11 cases, 6 had septic arthritis, and 5 affected the knee joint; all patients were diabetics with constitutional symptoms. The first case was a female with severe bilateral septic arthritis, who died from septic shock despite treatment with ceftazidime and cotrimoxazole, and had an antibody titre of 5,120. The remaining cases were unilateral septic arthritis. One male patient with knee arthritis developed multiple skin abscesses and required ventilatory support after septic shock^{20,21}. Another male farmer, initially misdiagnosed with pneumonia, was found to have *B. pseudomallei* after knee aspiration. Two other patients with right knee pain developed hepatic abscesses and were treated successfully. The sixth case involved a female gardener with autoimmune hepatitis, who developed left hip pain and had an antibody titre of 10,240.^{22,23}

A diabetic woman with sacroiliitis and melioidosis-proven intramuscular abscesses recovered after intensive antibiotic treatment. Two male diabetic farmers presented with right thigh myositis, confirmed via biopsy and ultrasound, and both recovered on antibiotics. The final three cases were of osteomyelitis in male farmers, each with a history of abscesses or prior injuries. All had high antibody titres and achieved full recovery with antibiotics.²⁶⁻³⁰

Reproductive Melioidosis

Reproductive system manifestations of melioidosis have only been documented in a few publications, with one mainly from Sri Lanka. These conditions, though, suggest while reproductive involvement is likely, it is rare in melioidosis.

The first case is a 38 years old female patient there was an ovarian teratoma and gliomatosis peritonei associated with melioidosis. She had constitutional symptoms and had lost at least 10kg of weight due to the other normal activities weight loss and abdominal swelling. Examination of the genitalia indicated a tender bulge in the lower abdomen more specifically a 20-week pregnant uterus. This was after a trip to India and North Central Province in Sri Lanka where she participated in water sports. Imaging showed the presence of ovarian teratoma. The titre of the melioidosis antibody was positive. This was performed due to the high suspicion of an infection. She underwent left salpingo-oophorectomy and

omentectomy due to the presence of infection and was on antibiotics which improved her condition.³¹

The other two cases involved melioidosis related prostatic abscesses. The patients were between 45 and 60 years of age and were fine on antibiotics. The first case was a 73 year old man with a 4 year history of hypertension, prostatitis, and acute urinary retention with acute kidney injury, who received so called standard treatment in case of severe Euroaganistic syndrome. He was treated for urosepsis and septic shock.³² The prostate was found to have an abscess that was detected by Transrectal ultrasound and underwent drainage. There were cultures that have also grown *Burkholderia pseudomallei*, the patient underwent eradication therapy that was included in the treatment given to him which comprised folic acid. The second patient was a diabetic farmer who presented with nephrolithiasis with low abdominal and low back pain, dysuria, and diarrhea. Digital rectal examination revealed enlarged prostate. Ultrasound revealed multiple prostate abscesses, which resolved following a course of antibiotics and he was adequately recuperated.³³

Genitourinary Melioidosis

Genitourinary illnesses of melioidosis are rare, accounting for a mere 4% of the reported cases in Sri Lanka. These usual presentations are bladder infection and prostatitis⁶ with only four literature reviewing diseases of the urogenital system involving *Burkholderia pseudomallei*.

The first case of this disease is a postpartum 33-year-old woman who developed a fever that improved but came back showing signs of pneumonia. Imaging shows bilateral pyelonephritis with multiple abscess collections. There were raised levels of serum lactate dehydrogenase, serum creatinine and titers of specific antibodies suggesting melioidosis infection. As treatment was initiated, her condition improved, and she was discharged without any complications³⁴.

The second case encompassed a 54-year-old male farms worker who came with a painful screaming leg with septicemia and an open cut. His progress was short lived as he developed acute kidney dysfunction and septicemia. Even with all the treatment including the use of antibiotics and infections, he went into multi-organ failure within a short time and died³⁵.

The third case was a 29-year-old soldier with a history of IgA nephropathy, who presented with flank pain and constitutional symptoms. Imaging showed pyelonephritis, and blood cultures confirmed melioidosis. After treatment with meropenem, he was discharged on co-trimoxazole and ciprofloxacin, leading to a complete recovery³⁶.

Common factors in these cases included exposure to paddy fields and surface water, alongside conditions like IgA nephropathy or substance use, which could increase the risk of infection^{1,4-6}. The final case was a 60-year-old man with prostatitis, dysuria, and urinary retention. Imaging identified a prostate abscess¹⁴, confirmed to be due to *B. pseudomallei*. He was treated with antibiotics and folic acid, resulting in full recovery³².

Cardiovascular presentation of melioidosis is an infrequent occurrence and the incidence is about 1%³⁷. Of this, 95% occur in males with pericarditis being the most common manifestation of the disease followed by endocarditis and myocarditis³⁸. It has reported four cases of cardiovascular involvement in Sri Lanka; three of which were cases of infective endocarditis (IE) and one mycotic aneurysm³⁹.

The 66-year-old male aneurysm case has no risk factors. He complains of dull and severe pain in the right iliac fossa which spreads to the upper thigh. On examination, a pulsatile mass was palpable in the same region. A CT scan was also performed with a leaking saccular aneurysm in the common iliac artery.³⁷ Though he developed septic shock and had to undergo emergency surgery, he had a complete recovery with antibiotic therapy.

Two of the three cases of IE were part of invasive melioidosis. One is a 60-year-old diabetic, alcoholic, former farmer and smoker. which came with pneumonia and a herb was found on the mitral valve. The second case is a 53-year-old diabetic worker with diabetes. Chronic fever and joint pain. The echo reveals healthy flora over the mitral valve. Both were diagnosed through blood cultures and cured with antibiotic treatment⁴⁰.

The third case of IE is a 73-year-old farmer with chronic obstructive pulmonary disease. He came in with a fever and difficulty breathing. The echo shows vegetation on the aortic valve. Early misdiagnosis His symptoms improved after switching to melioidosis-specific antibiotics. This was confirmed by PCR⁴¹. Such cases suggest that doctors suspect melioidosis in infected patients from endemic areas, high-risk occupations, or those with compromised immune systems. Due to early diagnosis and treatment, it will be useful.

Pulmonary melioidosis

Lung involvement is common in melioidosis. This accounts for approximately 50%⁴² of all cases. The large number of cases in Sri Lanka highlights the importance of lung symptoms. Pneumonia and lung abscesses are often found. Especially with diabetes or other chronic diseases. Bleeding in both lungs was found in a 59-year-old farmer with coinfection with leptospirosis. She was initially treated for leptospirosis before receiving melioidosis-specific antibiotics. This resulted in recovery⁴³. Other cases⁴⁵⁻⁵⁰ reported pneumonia with typical symptoms such as coughing and crackling on auscultation. Chest x-ray and priapism confirmed. Specifically, a 33-year-old woman developed dyspnea and pneumonia after a cesarean section. Along with neurological symptoms due to thrombotic purpura (TTP)³⁴

Neurological Melioidosis

Neuromelioidosis which involves the central nervous system (CNS), occurs in approximately 4% of cases and is associated with high morbidity and mortality⁵¹. In Sri Lanka, 14 cases of neurological involvement have been recorded, with the majority affecting the central nervous system (CNS). central nervous system A notable case involved a 21-year-old farmer who had spinal cord inflammation and multiple abscesses extending all the way to his spine. He presented with sudden weakness in both limbs and was unable to urinate. despite

receiving treatment and every patient has some residual symptoms. Brain abscesses are a common symptom in neurological cases. It affects both young and elderly patients. Often presenting with headaches, confusion, and in some cases seizures. A 15-year-old girl who had multiple bilateral brain abscesses. Full recovery is possible after appropriate antibiotic treatment⁵²⁻⁶⁰.

Gastrointestinal melioidosis

Gastrointestinal involvement is prominent in melioidosis in Sri Lanka, with 16% of cases showing symptoms^{6,61}. Patients often experience abdominal pain, splenomegaly in the liver, and sometimes gastritis. A typical case is a 61-year-old diabetic woman with fever, chills, and splenomegaly in the liver⁶². Imaging confirmed multiple liver abscesses and mild pancreatitis. Cases of gastritis have been observed. Especially in children who come into contact with soil and water. Causes swelling in the mouth and in some cases, oral paralysis⁶³. In general, antibiotic treatment is effective. But there was one death in a 58-year-old woman who had liver abscess and melioidosis⁶⁴⁻⁶⁶.

Lymphatic melioidosis

Lymph node involvement is rare in melioidosis. and is often found in conjunction with other systemic symptoms A notable case involved a 54-year-old diabetic man with lymphadenitis in the groin and a splenic abscess⁶⁷. It presents with multiple episodes of lymphadenopathy and sinus drainage due to noncompliance with antibiotic therapy. Many other cases of diabetes that present with abscesses and lymph nodes occur in the neck and groin. Treatment typically involves a combination of antibiotics, including co-amoxiclav and doxycycline, with mixed results regarding Recovering and remaining symptoms⁶⁸.

Sepsis melioidosis

Infections associated with melioidosis remain a major concern because of their high mortality rate. This accounts for more than half of all melioidosis cases⁶⁹. In Sri Lanka, cases of sepsis usually result from lung infections or skin lesions from contact with soil. The first laboratory-confirmed case in Sri Lanka is of diabetes with fatal septicemia. It emphasizes the serious consequences of melioidosis infection. A recent report of 54-year-old farmer suffering injuries in his rice fields led to multiple organ failure and death³⁵. Emphasize the importance of Targeted antibiotic detection and treatment Clinical practice guidelines recommend suspicion of melioidosis in cases of sepsis. Especially in people who come into contact with soil through occupation or in people with impaired immune systems⁷⁰⁻⁷⁴.

Management and Prevention

Table 4: Management and Prevention Strategies for Melioidosis [3–5,7]

Treatment Stage*	Aim	Therapy	Duration
Initial Therapy	Resolution of current illness	Intravenous ceftazidime or meropenem	Minimum 10-14 days (as long as needed)
Eradication Therapy	Prevention of recurrence	Trimethoprim-sulfamethoxazole (preferred)	3-6 months
		Co-amoxiclav or doxycycline (second line)	
Non-Pharmacological	Management	Inspection for abscesses, drainage, and oral therapy	-

* Following international guidelines

4. Conclusion

This review emphasizes the clinical spectrum of melioidosis in Sri Lanka, highlighting its varied manifestations across multiple organ systems with considerable overlap within systems as well. Of note, meropenem and co-trimoxazole were the drugs of choice used in combination for complicated infections. Diagnosis was often confirmed by positive titers for *B. pseudomallei* following a positive occupational history. Pulmonary infection was the most common presentation of melioidosis in Sri Lanka with diabetes as the leading risk factor. Considering the disease's complexity and consequences of delayed treatment, healthcare professionals from endemic regions like Sri Lanka must be aware of the multitude of melioidosis presentations.

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