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Unearthing the burden of melioidosis in North India – an emerging threat in a non-endemic region

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ABSTRACT

Burkholderia pseudomallei (B. pseudomallei) is the causative agent of the high-mortality disease called melioidosis. It is a severe infection that can be misdiagnosed due to variable presentation and low awareness among clinicians of the disease. It is endemic in India and well-described in southern and eastern coastal states. In the last decade, sporadic cases of melioidosis have been diagnosed in North Indian states, predominantly Rajasthan and Gujarat. The reported cases highlight the many risk factors for infection in this region that was not previously recognised as being endemic for melioidosis, including high prevalence of diabetes mellitus, alcoholism, and large rural population engaged in paddy cultivation. Climate change results in frequent flooding and waterlogging in urban areas, leading to exposure of soil harbouring *B. pseudomallei,* thus a contributing factor to the rise in cases in cities. As North India has not previously been considered an endemic region for melioidosis, wider awareness amongst clinicians and laboratorians is essential for early identification of symptoms, testing for *B. pseudomallei* in microbiology laboratories, and timely management of the disease to save lives lost to misdiagnosis. The present article describes various aspects of melioidosis in North India including diverse clinical manifestations, risk factors, and possible reasons for misdiagnosis and underreporting.

1. Introduction

Melioidosis is a potentially fatal tropical infection caused by the environmental intracellular gram- negative bacterium, *Burkholderia pseudomallei*. The infection has the potential to persist for many years before becoming apparent (Mays and Ricketts, 1975) or may recrudesce after inadequate treatment. (Sullivan et al., 2020) Melioidosis is endemic in Southeast Asia, Northern Australia, much of the Indian subcontinent, Southern China, Hong Kong, and Taiwan. (Currie et al., 2015; Meumann et al., 2024) South Asia, is estimated to have the highest burden of the disease (44 % of all cases), as suggested by a recent modelling study-attributed to its large population living in areas with soil harbouring *B. pseudomallei*. (Limmathurotsakul et al., 2016) Within South Asia, India has the largest population, and is estimated to have between 20,000 and 52,000 new cases annually and an estimated mortality rate of 32,000 per year attributed to melioidosis. Sero-surveillance studies conducted in Udupi, South India, revealed an asymptomatic sero-positivity rate of 29 % among adults aged 18–65 years, indicating that exposure to *B. pseudomallei* is relatively common. (Vandana et al., 2016)

India has suitable climatic conditions for melioidosis and is known to be the diabetes capital of the world. (Pandey and Sharma, 2018; Mukhopadhyay et al., 2018). Since most of the Indian population lives in rural areas, they can easily contract infections through direct contact with soil and water, especially workers in paddy fields (Limmathurotsakul et al., 2013b).

A literature search revealed that many cases in India were reported southern and eastern India. (Mukhopadhyay et al., 2018) These states have large coastal areas and hot and humid climates which are ideal for melioidosis. Cases reported from Southwest India also strongly correlate with periods of heavy rainfall and humidity. (Vidyalakshmi et al., 2008; Mukhopadhyay et al., 2018; Suputtamongkol et al., 1994; Cheng and

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Table 1
Case reports/series of melioidosis from North India published in last decade (2014–2024).

S. No.	Reference	No. of Cases	Age	Risk Factor	Site of Infection	Reported from
1	Shah et al, 2024	1	32	Diabetes mellitus	Bloodstream	Gujarat
2	Dubey DK et al, 2023	4	Median Age-32	Diabetes mellitus	Lungs, Liver, Brain	Lucknow, Uttar Pradesh
3	Kumar et al, 2023	1	37	Diabetes mellitus, Chronic Alcoholic	Spleen	Rajasthan
4	Singhal et al, 2023	1	68	Diabetes mellitus	Joints	Delhi
5	Patel et al, 2021	11	Median Age 48	Diabetes mellitus	Blood, lungs, musculoskeletal, skin and soft tissue	Gujarat
6	Mishra et al, 2021	1	28	None	Brain	Rajasthan
7	Savaj et al, 2020	1	67	None	Bloodstream	Gujarat
8	Goel et al, 2016	1	36	Diabetes mellitus	Bloodstream	Delhi
9	(Garg et al., 2015)	2	Median Age 35	Diabetes mellitus	Liver, Brain	Delhi
10	Sood et al, 2014	1	49	None	Lungs and Bloodstream	Rajasthan

Currie, 2005) Further, greater awareness and diagnostic capacity in these states may also be responsible for the detection of a higher number of cases in South India.

2. Geography and climatic conditions in North India

The epidemiology of melioidosis is vulnerable to climate change due to both direct and indirect impacts on human interactions with the

Table 2
Clinical and demographic details of cases reported from 2014–2024.

Reference	State	Month/Year of publication	Age/Sex	Risk Factor	Occupation	Site of Infection	Mode of Diagnosis	Treatment	Outcome
Shah et al.	Ahmedabad, Gujarat	March, 2024	32/M	DM-2	Unknown	Sepsis	Blood culture	Ceftazidime and Cotrimoxazole	Recovered
Dubey et al.	Lucknow, Uttar Pradesh	July 2023	28/M	DM-2	Unknown	Pneumonia	Blood culture	Meropenem and Cotrimoxazole	Recovered
Dubey et al.	Lucknow, Uttar Pradesh	July 2023	33/M	DM-2	Unknown	Liver Abscess	Pus culture	Meropenem and Cotrimoxazole	Recovered
Dubey et al.	Lucknow, Uttar Pradesh	July 2023	53/M	DM-2, Alcohol	Unknown	Liver Abscess	Pus culture	Ceftazidime and Cotrimoxazole	Recovered
Dubey et al.	Lucknow, Uttar Pradesh	July 2023	22/M	Alcohol	Unknown	Brain Granuloma and Abscess	Tissue culture	Ceftazidime and Cotrimoxazole	Recovered
Kumar et al.	Jodhpur, Rajasthan	March, 2023	37/M	DM-2, Alcohol	Unknown	Splenic abscess	Pus culture	Ceftazidime and Cotrimoxazole	Recovered
Singhal et al.	New Delhi	December, 2022	68/M	DM-2, Alcohol	Army Personal	Oligo-arthritis	Pus culture	Meropenem and Ceftazidime	Recovered
Mishra et al.	Rajasthan	January, 2021	28/F	None	Unknown	Brain Abscess	Pus culture	Meropenem and Ceftazidime	Recovered
Savaj et al.	Munpur, Gujarat	June, 2020	67/M	None	Farmer	Sepsis and Pneumonia	Blood culture	Meropenem	Died
Patel et al.	Ahmedabad, Gujarat	September, 2020	40/M	DM-2, HTN	Business	Sepsis	Blood culture	Meropenem and Cotrimoxazole	Died
Patel et al.	Udaipur, Rajasthan	September, 2020	49/M	DM-2	Farmer	Pneumonia, Osteomyelitis	Pus culture	Meropenem and Cotrimoxazole	Recovered
Patel et al.	Udaipur, Rajasthan	September, 2020	61/M	DM-2	Not known	Pneumonia	BAL culture	Meropenem and Cotrimoxazole	Recovered
Patel et al.	Vapi, Gujarat	September, 2019	70/F	None	Farmer	Skin and soft tissue infection	Pus culture	Meropenem and Cotrimoxazole	Recovered
Patel et al.	Ankleshwar, Gujarat	September, 2019	70/M	None	Farmer	Pneumonia	Blood culture	Meropenem and Cotrimoxazole	Recovered
Patel et al.	Amalsad, Gujarat	December, 2019	65/M	None	Teacher	Lung empyema	Pus culture	Meropenem and Cotrimoxazole	Recovered
Patel et al.	Jaipur, Rajasthan	September, 2019	21/M	None	Service	Osteomyelitis	Pus culture	Meropenem and Cotrimoxazole	Recovered
Patel et al.	Amreli, Gujarat	November. 2019	33/M	None	Farmer	Sepsis	Blood culture	Ceftazidime and Cotrimoxazole	Recovered
Patel et al.	Surat, Gujarat	August, 2018	48/M	DM-2, Alcohol	Business	Pneumonia	Blood culture	Meropenem and Cotrimoxazole	Recovered
Patel et al.	Mahisagar, Gujarat	October, 2018	67/M	COPD	Farmer	Pneumonia and Sepsis	Blood culture	Meropenem	Died
Patel et al.	Ankleshwar, Gujarat	December, 2018	57/M	DM-2	Farmer	Skin and soft tissue infection	Pus culture	Meropenem and Cotrimoxazole	Recovered
Goel et al.	New Delhi	June, 2016	36/M	DM-2	Farmer	Sepsis	Blood culture	Ceftazidime and Cotrimoxazole	Recovered
Garg et al.	New Delhi	June,2015	24/M	DM-2	Unknown	Liver Abscess	Pus culture	Piperacillin +Tazobactam and Cotrimoxazole	Recovered
Garg et al.	New Delhi	June,2015	47/M	DM-2	Unknown	Brain Abscess	Pus culture	Meropenem and Cotrimoxazole	Recovered
Sood et al.	Jaipur, Rajasthan	December, 2014	49/M	None	Unknown	Pneumonia and Sepsis	Blood culture	Meropenem and Cotrimoxazole	Died

causative agent. Tropical climate, wet weather, increased rainfall, wind, temperature, and loose soil create favourable conditions for the disease. In addition, the organism can also survive in harsh and even desert environments outside the wet tropics. (Yip et al., 2015). Heavy rains, floods, storms, and cyclones contribute to the clustering of melioidosis cases, especially with the occurrence of the La Niña phenomenon leading to flooding in rural as well as highly urbanized areas.

North India includes parts of the Indo-Gangetic plain, spanning the states and union territories of Chandigarh, Delhi, Punjab, Haryana, Uttar Pradesh, the Himalayas and sub-Himalayan belt, Uttarakhand, Himachal Pradesh, Jammu & Kashmir in the North up to the Thar desert [Rajasthan and Gujarat]. Climate in North India is semi-arid with 400–800 mm annual rainfall, land is gently sloping to saucer-shaped, soils are alluvial and alkaline soils in pockets. (Gajbhiye and Mandal, 2006)

Some states of North India receive a heavy and extended rainfall till September. Western disturbances in the last few years have led to frequent floods and rainfall in these states. The bacteria responsible for melioidosis typically reside in the soil, and during the rainy season, increased soil porosity facilitates the movement of bacteria from deeper layers to the surface, promoting their multiplication. (Limmathurotsakul et al., 2013a) Cloud cover levels are also related to soil moisture, which creates favourable conditions for bacterial survival. (Kaestli et al., 2012) Additionally, dense cloud cover may protect against UV radiation from sunlight, as previously observed in studies on the UV sensitivity of *B. pseudomallei*.

Over the last decade, North India has experienced significant impacts of climate change, including rising temperatures leading to hotter summers and milder winters. There has been a shift in rainfall patterns because of rapid urbanization, reduced green cover and increased impervious surfaces. This limits natural water absorption and increases runoff, exacerbating flooding with some areas experiencing heavier monsoon rains leading to flooding. A few examples are the devastating floods and landslides of 2013 in Uttarakhand, resulting in the country's worst natural disaster since the 2004 tsunami. Another major landslide hit the same area in 2023. Floods were also recorded in Delhi following unprecedented rainfall in July 2023. In 2024, parts of Gujarat and Rajasthan were devastated by extreme and untimely rains and floods (Times of India 2024a).

Climate change and uneven rains often result in the mixing of soil and water, and average city dwellers are exposed to soil contaminated with *B. pseudomallei*. Kannan et al demonstrated the presence of *B. pseudomallei* in a 3–4 feet deep pipeline repair pit with a rusted iron pipeline in a busy market area in Kotla, South Delhi. (Kannan et al., 2023) This example highlights the effect of rapid concretization and increased chances of exposure in urban population, where traditionally melioidosis is not considered a disease of the city dwellers.

3. Occupational predilection

The North Indian states of UP and Punjab have seen increasing paddy cultivation and currently rank as the second and third-highest rice producers in India. (Times of India 2024b) Bacteria, this upward trend in paddy farming is one of the major risk factors for melioidosis in rural North India. In a study by Chantratita et al., 61.9 % of melioidosis patients were farmers (Chantratita et al., 2023). Construction site workers have also been known to be exposed to contaminated soil and water. (Behera et al., 2019) Other occupations with a high risk of melioidosis include military personnel, fishing and forestry. (National Centre for Disease Control, 2019)

4. Genomic instability

B. pseudomallei has a relatively large genome (approximately 7.2 Mbp) which exhibits significant plasticity. (Bzdyl et al., 2022) This allows the bacterium to adapt quickly to environmental changes and host defences resulting in diverse clinical presentations, (Holden et al., 2004) ranging from acute septicaemia to chronic granulomatous disease. This can further lead to diagnostic dilemmas with other infections endemic in India like tuberculosis. (Vidyalakshmi et al., 2008) Genomic instability also results from the presence of mobile genetic elements, potentially creating antibiotic resistance hotspots or the spread of resistance genes within bacterial populations and the evolution of virulence factors. It can also impact the persistence of the bacteria in the host, contributing to chronic infection and the potential relapse after treatment. (Partridge et al., 2018)

5. Literature review of melioidosis cases from North India (2014–2024)

Currently, the only available data on melioidosis in the South Asian region comes from published case reports and case series, which are likely to represent just a small fraction of the actual cases (Mukhopadhyay et al., 2018). PubMed and Google scholar databases were searched with keywords "Melioidosis", "*Burkholderia pseudomallei*" and "North India" for publications in the last ten years (2014–2024). A further search with inclusion of each of the states and union territories of North India was performed. A total of ten articles with twenty-four cases have been reported from 2014 to 2024 are detailed in Tables 1 and 2.

The median age at the time of presentation was 56 years [Range 22 to 67 years]. Twenty-two cases were males and only two cases were female patients. This was also noted by Vidyalakshmi et al. (Vidyalakshmi et al., 2012) who concluded that as women are less exposed to gardening and other minor agricultural tasks with subsequent exposure to low inoculum of bacteria, fewer women were infected with melioidosis than men. This hypothesis may be further supported by an increased incidence of melioidosis during the monsoonal season when individuals have prolonged and intense contact with soil and surface water at a higher inoculum of bacteria.

Diabetes mellitus (DM-2) was the most common risk factor associated with the infection, present in fourteen out of twenty-four patients. Diabetes was associated with melioidosis in 76 % of cases in a previous study from India. (Vidyalakshmi et al., 2012) Reports from different countries have also shown that melioidosis was commonly detected in patients with Diabetes mellitus. (Lo et al., 2009; Limmathurotsakul et al., 2010) An estimated 17 % of the North Indian population suffers from Diabetes mellitus. (Coronary Artery Disease in Asian Indians, 2021) Therefore, clinicians should consider melioidosis as a possible cause of Infections in diabetics even in areas of North India that were previously considered non-endemic. Amongst other risk factors, alcoholism was noted in five patients as the second most common. (Araúz et al., 2020) Binge alcohol exposure suppresses the uptake of bacteria by alveolar macrophages which leads to enhanced intracellular survival in activated macrophages and increased biofilm formation. (Jimenez et al., 2017). In terms of occupation, eight patients were engaged in farming, two were businessmen, two were servicepersons and one was in the army. There was no evidence of travel history observed in any of these cases.

Central nervous system melioidosis was reported in three cases: one alcoholic, one diabetic patient, and one patient with no predisposing factors. Brain infections have been reported in 1.5 % to 10 % of all melioidosis cases, with a high mortality rate of up to 60 %. (Mannam et al., 2021, Shobhana et al., 2022) Radiologically and histopathologically, CNS melioidosis resembles tuberculosis, and is therefore often erroneously diagnosed and treated as tuberculosis.

6. Present challenges in diagnosis and management and the way forward

In this case series, melioidosis infections were primarily diagnosed through blood and pus cultures, with sensitivity testing guiding appropriate antimicrobial therapy. Often wrinkled colonies of *B. pseudomallei* are mistaken for aerobic spore-bearing bacteria, which are common environmental contaminants. Additionally, any oxidase-positive, non-lactose fermenting Gram-negative bacillus is likely to be categorized as a 'pseudomonad' or '*Pseudomonas spp*.,' without further identification to the species level. The diagnosis is often overlooked because of low diagnostic sensitivity (approximately 60 %) of blood or tissue cultures, meaning that approximately nearly 40 % of cases are initially missed. Wiersinga et al., 2018) The usual culture report of 'Pseudomonas like organisms resistant to aminoglycosides, polymyxin or colistin' in a patient unresponsive to conventional treatment should be considered a suspect. (Wiersinga et al., 2012)

Even commercial identification kits and modern automated systems (such as API 20NE, VITEK 2, and MALDI-TOF) are not fully reliable for identifying *B. pseudomallei*. Hospitals can employ point-of-care tests for antigen detection to offer rapid diagnosis in health care facilities. A lateral flow immunoassay (LFIA) that identifies *B. pseudomallei* capsular polysaccharide (CPS) using a monoclonal antibody is becoming increasingly popular as a point-of-care (POC) testing option. (Houghton et al., 2014) However, it is yet unlicensed and is currently only a research tool.

The Darwin guidelines are the 'gold standard' for patient management in melioidosis. (Currie et al., 2023) Clinicians and microbiologists must be aware that *B. pseudomallei* is inherently resistant to many antibiotics when planning treatment. In recent years, there has been increasing recognition and concern regarding adverse effects arising during the required prolonged use of trimethoprim+sulfamethoxazole for melioidosis therapy. (Martin et al., 2025) The 2024 revision of the Darwin Melioidosis Treatment Guidelines further refines the dosing and duration of antibiotics. It presents a new graded introduction of therapy with trimethoprim+sulfamethoxazole and provides new comprehensive guidance on monitoring for and management of adverse effects from trimethoprim+ sulfamethoxazole.

Notably, meropenem and cotrimoxazole were more commonly used in most of the cases we reviewed. However, the outcomes reveal a concerning mortality rate, particularly among patients with pneumonia and sepsis, highlighting the critical need for early diagnosis and prompt treatment. The recovery rates among patients receiving appropriate therapy underscore the importance of timely intervention.

A shift has been observed in recent years, with numerous cases of melioidosis being reported from North India in the last decade. In India, we are at a very early stage of determining the disease's epidemiology and dynamics. It is difficult to say whether the rise in reported cases in North India is a result of improvement in ascertainment due to better diagnostics, an extension of the normal endemic zone, or a genuine increase in incidence. In 2021, Indian council of Medical Research (ICMR) recognised the potential public health threat of melioidosis in India and a taskforce project was funded. This is a multi-centric capacity building initiative to strengthen the clinical and laboratory detection of melioidosis in India with special focus on North Eastern states. Fifteen sites were identified across the country to carry out the project with two sites in North India, one in Delhi and one in Jodhpur, Rajasthan. The objectives are training and laboratory strengthening for improved detection of melioidosis cases in potential hotspots of India, estimation of the prevalence of melioidosis among the hospitalized patients in the network hospitals, molecular epidemiology and phylogenetic analysis of *B. pseudomallei* strains isolated from different parts of India.

Expected outcomes of the project are that it will help build capacity across the nation on local, state and national levels. On local level, the initiative has built awareness through training which will further help develop customized diagnostic algorithms for high-risk locations and patients in critical conditions. Through the project, awareness programmes have been conducted at primary, secondary and tertiary care healthcare facilities. The project sites have built a referral system for these facilities to accelerate the diagnosis and treatment of suspected melioidosis cases. This has resulted in identification of six new cases over last one year (unpublished). All cases were treated successfully.

The early successes indicate that the task force will help determine a region and state-wise incidence of melioidosis. The phylogenetic analysis will lead to determination of the extent of genetic variation of *B. pseudomallei* strains between indigenous and global gene pools as well as any diversity within different regions of India. It will also enable identification of the effects of spatiotemporal factors of melioidosis. The taskforce also expects that the generated database of Indian *B. pseudomallei* strains will act as a reference collection of genetic information that would be used to understand genotypic determinants of antibiotic resistance as well as to virulence. The data generated will be submitted to Government of India to make policy decisions regarding disease notification and further capacity building. Correlating inferences obtained from sequence analysis to clinical presentations and the phenotypic virulence of *B. pseudomallei*, would aid in developing scoring algorithms for effective diagnosis, and deciding therapeutic interventions.

7. Conclusion

Though Melioidosis is endemic in India, it is no longer limited to humid climates of the coastal regions of South and East India. Cases reported from North India reveal only the tip of the iceberg. Increasing prevalence of diabetes, along with unpredictable climatic conditions are bound to expand the footprint of the disease in regions previously considered non-endemic. Lack of awareness, wide spectrum of clinical presentation, non-specific radiological findings and insufficient diagnostic laboratory facilities remain the major challenges in estimating the true burden of the disease. Consequently, efforts to spread awareness, wider availability of accurate diagnostic tests, improvements in referral systems for timely detection and management are key interventions required to reduce morbidity and mortality caused by under- and mis-diagnosed cases in North India.

CRedIT authorship contribution statement

Shweta Raina: Conceptualization, Data curation, Writing – original draft, Writing – review & editing, Visualization. **Disha Gautam**: Conceptualization, Data curation, Writing – original draft, Writing – review & editing, Visualization. **Kavita Sisodia**: Data curation Methodology and investigations. **Chiranjay Mukhopadhyay**: Resources, Visualization, Writing – review & editing. **Harpreet Kaur**: Resources, Writing – review & editing**. Rohit Kumar**: Resources, Visualization, Writing – review & editing. **Mohammed Ashiq**: conceptualization, data curation, resources and visualization. **Rushika Saksena**: Conceptualization, Data curation, Writing – original draft, Writing – review & editing, Visualization

Ethics committee

Approval was granted by the Institutional Ethics Committee- S.No. IEC/VMMC/SJH/Project/08-2022/CC-262, dated 24/08/2022.

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Declaration of competing interest

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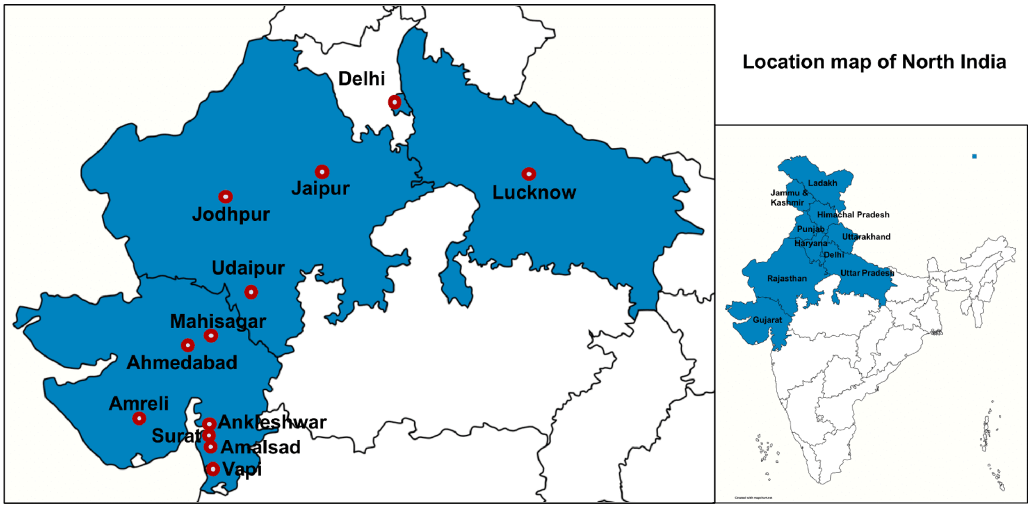

Fig. 1. Location map of melioidosis cases reported from North India, 2014–2024.

have appeared to influence the work reported in this paper.

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Data availability

No data was used for the research described in the article.

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