REVIEW ARTICLE

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AN UPDATE ON *BURKHOLDERIAPSEUDOMALLEI* INFECTION: EPIDEMIOLOGY, PATHOGENESIS, DIAGNOSTIC APPROACHES AND TREATMENT CHALLENGES

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ABSTRACT

The discovery of emerging organisms is the interesting part of medical science. Burkholderiapseudomalleiare the etiological agent of melioidosis, which can be a fatal disease due to high mortality rate and relapse rate. The two primary endemic zones are northern Australia and Southeast Asia, however, *B. pseudomallei*are found throughout the tropics. In addition, variable clinical presentation, pre-existing comorbidity, low awareness, and lack of diagnostic facilities are the contributing factors associated with disease severity. Despite notable progress in laboratory detection methods and treatment, *B. pseudomallei* continue to be a major global concern. Developing further successful disease diagnosis and preventive measures require an understanding of the organism's origin, transmission pathways, virulence factors and their roles in pathogenic mechanisms in human hosts. In this review, current knowledge of *B. pseudomallei* are discussed focusing on the epidemiology, transmission, risk factors, pathogenesis, clinical manifestations, available diagnostic methods, and antimicrobial drugs of *B. pseudomallei.*

Keywords: *Burkholderiapseudomallei,* Melioidosis, Pathogenesis, Laboratory diagnosis

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INTRODUCTION

Among the Burkholderia species, Burkholderiapseudomallei (*B. pseudomallei*), B. mallei, B. cepacia complex, and B. gladioli are recognized as causative agents of human disease[1]. *B. pseudomallei*, known as the causative agent of melioidosis, was first described by Alfred Whitmore and C. S. Krishnaswami in 1911[2]. *B. pseudomallei*are Gram-negative, non-spore-forming, motile, aerobic bacilli. They mostly reside in moist soil and water. In endemic regions, these saprophytic environmental organisms can be isolated from soil and water in rice paddy fields[1,2]. Melioidosis was once believed to be a disease that only occurred in tropical and subtropical countries. However, because of a rise in case reports and the difficulties in diagnosing and treating melioidosis, it has recently been considered as an emerging disease of global importance [3, 4]. Even with proper treatment, melioidosis have a high case-fatality rate of 10% to 50% due to pneumonia, multiple abscesses, and septicemia [5, 6].

Considering the facts, it is important to increase awareness among the clinicians and microbiologists. This review aims to highlight the epidemiology, pathogenesis, diagnostic tools and treatment of *B. pseudomalleiinfection.*

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MATERIALS AND METHOD

A comprehensive literature search was conducted using PubMed, Scopus and Google Scholar, focusing on specific keywords like "melioidosis," "Burkholderiapseudomallei," "pathogenesis," and "diagnosis of melioidosis". Original articles, review articles and other relevant published documents from any country were included.

EPIDEMIOLOGY

Melioidosis is endemic in the northern territory of Australia and Southeast Asia, where South Asia alone contributed to 44% of the global burden of melioidosis[1, 4]. There have been reports of high incidence in China, Taiwan, Malaysia, Singapore, and Thailand. Melioidosis is endemic in South Asia, specifically in Bangladesh, Sri Lanka, and India. In India, more than 80% of cases are reported from Tamil Nadu and Karnataka[1,4,7]. The sero-positivity rate among asymptomatic adults in South India was found to be 29% by sero-surveillance studies[7]. Bangladesh is known to be a "definite" endemic country for melioidosis[8]. The first isolation of *B. pseudomallei* was made from the soil of Gazipur district in 2011[3]. There have been more than 89 melioidosis cases reported in Bangladesh as of 2022 (both published and unpublished cases); the Gazipur, Tangail, Sylhet, Mymensingh, and Feni districts are thought to be melioidosis hotspots in Bangladesh[9, 10].

ROUTES OF TRANSMISSION

The *B. pseudomallei* enter through inoculation through skin lesions from contaminated soil. Ingestion of contaminated water and airborne transmission from contaminated soil have been documented in the endemic area[2,3,11,12]. The incubation period after entry lasts between one and twenty-one days, but it can extend from days to years[4].

RISK FACTORS

B. pseudomallei infection is associated with multiple risk factors. *B. pseudomallei* are widely found in soil, water and are known to be an environmental saprophyte. It grows in tropical climates with hot, humid weather and rainfall. The soil porosity increases during the rainy season and allows *B. pseudomallei* to move from deep to the superficial soil layer for its multiplication[1, 4].

One of the important occupational risk factors is farming, particularly rice cultivation. Construction site workers and barefoot workers are also at risk[4, 11].Pre-existing diabetes mellitus is considered as one of the commonest risk factors. In Bangladesh, India, and Sri Lanka, diabetes is said to be a risk factor for over 80% of melioidosis cases[4, 8, 11].According to a meta-analysis, individuals with diabetes mellitus had a threefold increased risk of developing melioidosis compared to those without the disease[10].Infection is more likely to occur in patients with chronic liver disease, thalassemia, alcoholism, steroid use, renal failure, and chemotherapy[11].

VIRULENCE FACTORS AND PATHOGENESIS

Following exposure, *B. pseudomallei* attach to and invade host cells, as well as multiply within them andspread to neighboring cells. Multiple virulence factors enhance the ability of *B. pseudomallei* to evade host defenses and replicate in host cells (Figure 1).

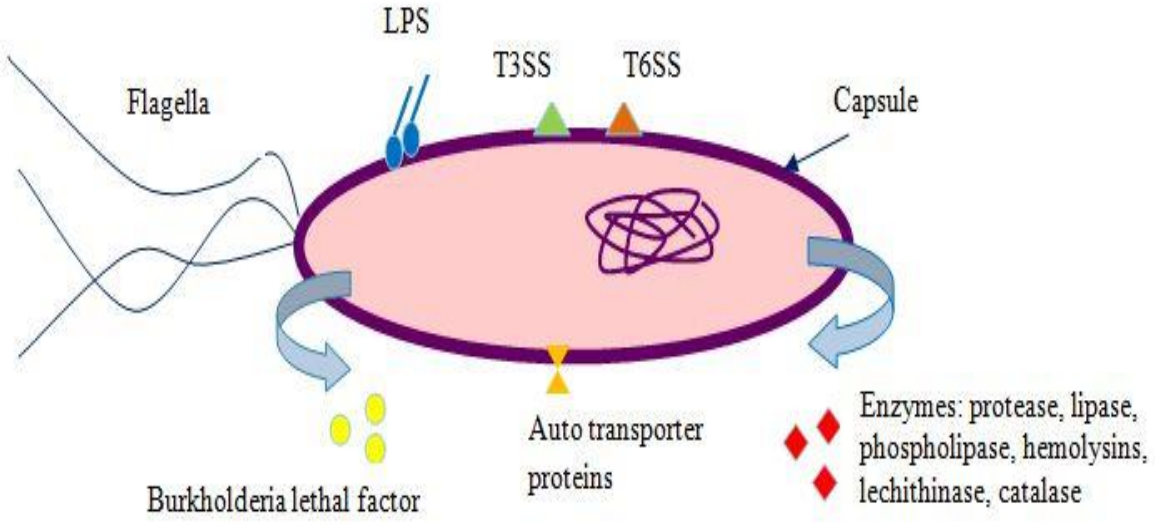

Figure 1: Virulence factors of *B. pseudomallei* include capsule, lipopolysaccharide, flagella, three type III secretion systems (T3SSs), six type VI secretion systems (T6SSs), Burkholderia lethal factor, autotransporter proteins like Burkholderia intracellular motility A (BimA) and enzymes[1, 13]

Flagella, pili, and polysaccharide capsule help in host cell attachment. Cellular invasion is facilitated by the T3SS, which injects bacterial effector molecules into the host cytoplasm. Escape from the endosome is mediated by the T3SS and protease inhibitor production. Survival within macrophages is mediated by suppressing nitric oxide synthase expression and blocking nitric oxide production. Autotransporter proteins like BimA promote cell-to-cell spread. Bim A polymerises host cell actin, propelling it to the host cell membrane, causing host cell fusion into multinucleated giant cell.The T6SS facilitates giant cell formation by bridging the gap between host cells and transferring effector proteins. In addition, biofilm formation, quorum sensing and morphotype switching enhance the ability of *B. pseudomallei* to evade host defense [1, 13- 15].

CLINICAL MANIFESTATIONS

Melioidosis presents with a variety of clinical features. According to studies, one of the most frequent clinical manifestations is pneumonia (35.7%-45.8%). Other reported clinical features include sepsis, skin and soft tissue abscess, splenic abscess, septic arthritis, osteomyelitis, prostatic abscess, liver abscess, brain abscess, meningoencephalitis, pyelonephritis, and perinephric abscess [6, 16]. A study in Bangladesh found that skin and soft tissue infection is the common feature, followed by septic arthritis, pneumonia, deep-seated abscess, urinary tract infection, bacteremia, and neurologic involvement[9]. According to another study conducted in Bangladesh, septicemia was the most common presentation, followed by skin and soft tissue abscess[8]. The clinical spectrum is categorized into four types, acute septicaemic, subacute, chronic and latent type[17]. Ten percent cases of acute melioidosis can progress to chronic melioidosis. Moreover, the relapse rate is 15%-30% even after prolonged antimicrobial therapy [18].

LABORATORY DIAGNOSIS AND ANTIMICROBIAL SENSITIVITY

Blood, respiratory secretions, pus, wound swab, urine and cerebrospinal fluid are common specimens. Gram staining reveals Gram-negative bacilli with bipolar staining resembling safety pin[1]. Culture can be done on MacConkey's agar, blood agar, selective Ashdown's agar, *B. pseudomallei*selective agar, and Francis medium. On MacConkey's agar, pink or colourless, non-lactose fermenting colonies grow after 2 days of incubation and by day 4, the colonies become dry and wrinkled. Smooth, creamy colonies with a metallic sheen appear on blood agar media. On Ashdown's agar, pinpoint, flat, dry, wrinkled and purple colonies appear. The organisms exhibit motility, catalase, oxidase, and citrate positivity and grow at 42°C. There is either no change or a slight oxidation in triple sugar iron media. The API 20NE, Vitek-2 are the improved and reliable methods of identification[18- 20].

Rapid antigen detection by latex agglutination assay (94% sensitivity, 83% specificity), immunofluorescence assay (97.4% sensitivity, 100% specificity) and lateral flow assay (98.7% sensitivity, 97.2% specificity) have been developed for the identification of *B. pseudomallei*. Both *B. pseudomallei* IgM and IgG can be detected by enzyme-linked immunosorbent assay and immunochromatographic test. Identification by mass spectrometry and direct molecular detection are other options for confirmatory identification[1,19- 21].

*B. pseudomallei*are intrinsically resistant to penicillin, ampicillin, first - and second-generation cephalosporins, aminoglycosides such as gentamicin, tobramycin, streptomycin, and polymyxin. Previous study showed that the isolated organisms are usually susceptible to ceftazidime, carbapenem, amoxicillin-clavulanic acid, trimethoprim-sulfamethoxazole, piperacillin-tazobactum, tetracycline and ciprofloxacin[8, 14, 22].

DISCUSSION

The recent high burden of *B. pseudomallei* infection in South Asia, including Bangladesh, is a new challenge for clinicians. Climatic factors, along with the high prevalence of diabetes, made Bangladeshi people more susceptible to melioidosis. In addition, most people living in rural areas and working in the agricultural fields have a greater chance of acquiring the infection from contaminated water and soil[23-25].

Intracellular invasion with subsequent survival is a crucial component of the pathogenesis of *B. pseudomallei.* Clinical presentations and severity may differ depending on the host immune system. Latent infections with subsequent reactivation have been reported[13, 16]. The diagnostic techniques for *B. pseudomallei* detection include gram staining, culture, rapid antigen detection, and molecular methods. By antibody detection, it is difficult to differentiate if a seropositive patient has an acute, chronic, or past infection or exposure without infection. Despite its low sensitivity, *B. pseudomallei* culture is still considered the "gold standard"[1, 19]. Inherent resistance to certain drugs and clinical latency are the main challenges for effective treatment. Early identification and appropriate treatment are essential to reduce morbidity and mortality associated with this potentially fatal infection[22].

Melioidosis is known as the "great mimicker" because of its variety of clinical characteristics that can be confused with other illnesses, such as tuberculosis in our country. Low awareness, mimicking clinical features, and lack of laboratory support in rural areas are multiple factors that lead to diagnostic failure and subsequent inappropriate drug management. Moreover, there is a lack of data on the true burden.

Rising cases in recent years might reflect a possible "tip of the iceberg" of

Burkholderia infection, indicating that many individuals may remain undiagnosed and untreated[4,26,27]. Therefore, it is time to raise awareness among clinicians and microbiologists about diagnosis and management. Improvement of diagnostic techniques along with conducting training for laboratory personnel from national and international institutions is worthwhile.

CONCLUSION

The increasing prevalence of diabetes and climatic factors in South Asia is leading to a rise in melioidosis. Under diagnosis of the disease and insufficient diagnostic facilities are key challenges. Improved awareness by conducting workshops and proper reporting of the *B. pseudomallei* detection can facilitate disease surveillance and preventive interventions. Furthermore, increasing public awareness is important for avoiding contact with the source, for safe drinking water, and for control of other risk factors.

CONFLICT OF INTEREST

There is no conflict of interest.

REFERENCES

1. Gassiep I, Armstrong M, Norton R. Human Melioidosis. Clinical Microbiology Reviews. 2020; 33(2):e00006-19. doi: 10.1128/CMR.00006-19.

2. Lee SH, Nathan S. Burkholderiapseudomallei: an update on disease, virulence and host interaction. Malaysian Applied Biology. 2013; *42*(1).

3. Jilani MSA,Farook S. Mysteries of Melioidosis: Unearthing the Enigma. Bangladesh Journal of Medical Microbiology. 2018; 12(1) 1–3. doi:10.3329/bjmm.v12i1.51683.

4. Mohapatra PR, Mishra B. Burden of melioidosis in India and South Asia: Challenges and ways forward. The Lancet Regional Health Southeast Asia. 2022; 2:100004. doi:10.1016/j.lansea.2022.03.004.

5. Chowdhury FR, Roy CK, Barai L, Paul S, Chowdhury FU H, Mazumder S et al. Melioidosis: A Neglected Infection in Bangladesh. J Medicine. 2021 *22*(2), 139–45. doi:10.3329/jom.v22i2.56705

6. Birnie E, Virk HS, Savelkoel J, Spijker R, Bertherat E, Dance DAB et al. Global burden of melioidosis in 2015: a systematic review and data synthesis. The Lancet. Infectious diseases. 2019; *19*(8), 892–902. doi:10.1016/S1473-3099(19)30157-4.

7. Raina S, Gautam D, Kumar R. Unearthing the burden of melioidosis in North India - an emerging threat in a non-endemic region. Current research in microbial sciences. 2025; 8:100344. doi:10.1016/j.crmicr.2025.100344

8. Barai L, Saha MR, Rahman T, Sukanya M, Jafrin J, Ferdous J et al. Trends in laboratory detection of Burkholderiapseudomallei and their antibiotic susceptibility pattern from clinical samples over twenty one years from 2001 to 2021 in a tertiary care hospital of Bangladesh. Bangladesh J Med Microbiol. 2021; *15*(1), 8–14. doi:10.3329/bjmm.v15i1.57806

9. Chowdhury FR, Jilani MSA, Barai L. Melioidosis in Bangladesh: A Clinical and Epidemiological Analysis of Culture-Confirmed Cases. Tropical medicine and infectious disease. 2018; 3(2):40. doi:10.3390/tropicalmed3020040

10. Chowdhury S, Barai L, Afroze SR, Ghosh PK, Afroz F, Rahman H et al. The Epidemiology of Melioidosis and Its Association with Diabetes Mellitus: A Systematic Review and Meta-Analysis. Pathogens. 2022; 11(2):149. doi: 10.3390/pathogens11020149.

11. Haque HF, Debnath S, Afroze SR, Afroz F, Rahim MA, Musa A. Septicaemic Melioidosis Complicated by Septic Arthritis in A Bangladeshi male: A Case Report. Bangladesh J Med. 2018; 29 (2):94-96. doi:10.3329/bjmed.v29i2.37946.

12. Chen PS, Chen YS, Lin HH, Liu PJ, Ni WF, Hsueh PT et al. Airborne Transmission of Melioidosis to Humans from Environmental Aerosols Contaminated with B. pseudomallei. PLoS neglected tropical diseases. 2015; 9(6):e0003834. doi: 10.1371/journal.pntd.0003834.

13. Bzdyl NM, Moran CL, Bendo J, Sarkar-Tyson M. Pathogenicity and virulence of *Burkholderiapseudomallei*. Virulence. 2022;13(1):1945-1965. doi: 10.1080/21505594.2022.2139063.

14. Meumann EM, Limmathurotsakul D, Dunachie SJ, Wiersinga WJ, Currie BJ. Burkholderiapseudomallei and melioidosis. Nature reviews. Microbiol. 2024; *22*(3), 155–169. doi:10.1038/s41579-023-00972-5

15. Wiersinga W, van der Poll T, White N.. Melioidosis: insights into the pathogenicity of *Burkholderiapseudomallei*. Nat Rev Microbiol, 2006; 4, 272–82 doi:10.1038/nrmicro1385

16. Hin HS, Zainulabid UA, Ibrahim MSM, Mahmud F, Chiu LB, Singh KKB et al. Five Years Melioidosis Registry Data from 2011-2015 in Pahang, Malaysia: A Retrospective Study. Bangladesh J Infectous Dis. 2023; 9(1):7-14. doi:10.3329/ bjid.v9i1.67259.

17. Karunanayake P. Melioidosis: clinical aspects. *Clinical medicine (London, England)*. 2022; *22*(1), 6–8. doi:10.7861/clinmed.2022-0014

18. Mariappan V, Vellasamy KM, Barathan M, Girija ASS, Shankar EM VadiveluJ. Hijacking of the Host's Immune Surveillance Radars by *Burkholderiapseudomallei*. Front in immunology. 2021; *12*, 718719. doi:10.3389/fimmu.2021.718719

19. Lau SK, Sridhar S, Ho CC, Chow WN, Lee KC, Lam CW et al. Laboratory diagnosis of melioidosis: past, present and future. Experi Biol Medi (Maywood, N.J.). 2015; 240(6), 742–51. doi:10.1177/1535370215583801

20. Dance DA, LimmathurotsakulD, Currie BJ. Burkholderiapseudomallei: Challenges for the Clinical Microbiology Laboratory-a Response from the Front Line. J Clin Microbiol, 2017; *55*(3), 980–982.doi:10.1128/ JCM.02378-16

21. Songsri J, Chatatikun M, Wisessombat S, Mala W, Phothaworn P, Senghoi W et al. Diagnostic accuracy of automation and non-automation techniques for identifying Burkholderiapseudomallei: A systematic review and meta-analysis. J Infec Public Health. 2024; *17*(7), 102438.doi:10.1016/j.jiph.2024.04.022

22. Rout SS, Roy S, Mishra SN, Sahoo LK, Sahu KK, Panigrahy R. Melioidosis and Burkholderiapseudomallei: Disease mechanisms, drug resistance, and treatment challenges. J Integrative Med 2025;3(1):14-23.

23. Phillips ED & Garcia EC. Burkholderiapseudomallei. Trends in microbiology. 2024; *32*(1), 105-6.doi: 10.1016/j.tim.2023.07.008

24. Dance DA, Limmathurotsakul D. Global Burden and Challenges of Melioidosis. Tropical Med Infectious Dis. 2018; 3(1):13. doi:10.3390/ tropicalmed3010013

25. Kain MJW, Reece NL, Parry CM, Rajahram GS, Paterson DL, Woolley SD. The Rapid Emergence of Hypervirulent *Klebsiella* Species and *Burkholderiapseudomallei* as Major Health Threats in Southeast Asia: The Urgent Need for Recognition as Neglected Tropical Diseases. Tropical Med Infec Dis. 2024; 9(4):80. doi:10.3390/ tropicalmed9040080

26. Currie BJ, Meumann EM, Kaestli M. The Expanding Global Footprint of Burkholderiapseudomallei and Melioidosis. American J Tropical Med hygiene. 2023; 108(6):1081-3. doi: 10.4269/ajtmh.23-0223.

27. Savelkoel J, Dance DAB, Currie BJ, Limmathurotsakul D, Wiersinga WJ. A call to action: time to recognise melioidosis as a neglected tropical Disease. The Lancet. Infectious diseases. 2022; 22(6):e176-e182. doi: 10.1016/S1473-3099(21)00394-7.