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Utility of Laboratory Biomarkers as Mortality Predictors for Melioidosis: A Systematic Review and Meta-Analysis

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ADMINISTRATIVE INFORMATION**Support** - None.**Review Stage at time of this submission** - Completed but not published.**Conflicts of interest** - None declared.**INPLASY registration number:** INPLASY202570001**Amendments** - This protocol was registered with the International Platform of Registered Systematic Review and Meta-Analysis Protocols (INPLASY) on 1 July 2025 and was last updated on 1 July 2025.**INTRODUCTION**

Review question / Objective Population: Melioidosis Patients ; Interventions: N/A; Control: N/A; Outcome: Relative risk/ Odds ratio/hazard ratio of mortality predictors.

Rationale Melioidosis, caused by *Burkholderia pseudomallei*, is a frequently overlooked yet often fatal infectious disease endemic to Southeast Asia and Northern Australia, with an estimated global burden of 165,000 cases and 89,000 deaths annually. Despite its high mortality and significant impact on health systems in low- and middle-income countries, it remains underrecognized and is not yet classified as a neglected tropical disease (NTD) by the WHO. Recent evidence suggests the potential for spread to non-endemic regions, including parts of Africa, the Americas, and the southern United States, driven by global travel, environmental shifts, and rising rates of diabetes.

Clinically, melioidosis is known as the “great mimicker” due to its wide range of non-specific

and often severe presentations, which contribute to diagnostic challenges and high mortality rates (30–50%). Identifying reliable predictors of mortality is critical to improve clinical outcomes. While several studies have explored risk factors, especially laboratory-based biochemical markers, no systematic synthesis of these predictors currently exists.

This study aims to systematically review and, where feasible, meta-analyze existing evidence on biochemical markers associated with mortality in Melioidosis, to aid in risk stratification and clinical decision-making.

Condition being studied The condition being studied is Melioidosis, a severe and often fatal infectious disease caused by the Gram-negative bacterium *Burkholderia pseudomallei*. It is endemic in Southeast Asia and Northern Australia but is increasingly being reported or detected in non-endemic regions, raising global health concerns. The study specifically focuses on

identifying biochemical predictors of mortality in patients with melioidosis.

METHODS

Search strategy ‘ (“Melioidosis”) OR (“Burkholderia”) OR (“Whitmore’s disease”) AND (“mortality”) OR (“lethality”) OR (“fatality”))OR (“treatment outcomes”) OR (“prognosis”) OR (“survival”) AND (“risk factors”) OR (“determinants”) OR (“predictors”))’.

Participant or population All Patients of Melioidosis(culture-confirmed).

Intervention N/A.

Comparator N/A.

Study designs to be included All types of original research studies such as observational, analytical, case-control, cohort, and cross-sectional studies, etc.

Eligibility criteria Studies assessing culture-confirmed melioidosis patients. Studies reporting effect estimates in the form of unadjusted or adjusted odds ratio(OR)/hazard ratio(HR)/ relative risk(RR) for mortality in melioidosis patients with respect to any routine laboratory indicator OR reporting sufficient data to enable the authors to calculate the relevant crude effect estimates. The umbrella of tests under routine laboratory indicators was kept broad, and included complete blood counts, liver function tests, kidney function tests, inflammation markers, etc. Reviews including systematic reviews, case reports, case series, letters to the editor, commentaries, abstracts, conference proceedings, studies on animals, and studies in languages other than English were excluded.

Information sources PubMed/MEDLINE, Scopus, and Embase.

Main outcome(s) Pooled odds ratio/relative risk/hazard ratio of mortality predictors in melioidosis patients.

Quality assessment / Risk of bias analysis The Joanna Briggs Institute Critical Appraisal Checklist was used to assess the methodological quality of each included study.

Strategy of data synthesis For laboratory parameters with the unadjusted/adjusted effects estimates available in at least 3 studies, a meta-analysis was done to evaluate the overall effect.

Heterogeneity between studies was assessed using I^2 statistics. In cases of $I^2 > 50\%$, a random effects model was employed. For the parameters for which a formal meta-analysis was not possible, the findings were qualitatively summarized. Statistical analysis was performed using R (Version 2024.09.0 – 375).

Subgroup analysis No sub-group analysis with respect to gender/ region/ clinical presentation could be performed due to lack of available data from individual studies.

Sensitivity analysis Sensitivity analysis was performed using leave-one-out method wherever pooled analysis revealed a high heterogeneity.

Country(ies) involved India.

Keywords Melioidosis, Burkholderia pseudomallei, Albumin, Bicarbonate, Mortality.

Contributions of each author

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