

## Comparing four sets of 5-year literature in the last 2 decades to further strengthen epidemiological studies on melioidosis in India with a note on family inclusive capacity building strategy

### Abstract

**Background:** Melioidosis caused by the infamous soil pathogen, *B. pseudomallei* could have lethal outcome in patients with diabetes or any other chronic illness like kidney or liver disease. Unfortunately, it being spread through contaminated soil and water makes farmers and children prone to the diseases.

**Method:** This article of ours focuses on literature retrieved from Pub Med with two search criteria “Melioidosis prevalence India” and “Melioidosis risk factor India” from 2019-2024, 2014-2019, 2009-2014, 2004-2009. This data was analysed for Study site (South, North, West, East, Central India), type of data (environmental surveillance, clinical data, outbreak surveillance, risk factors); type of study (longitudinal, cross sectional, retrospective, review, case study); data pertaining to (drugs, vaccine, development of diagnostics, novel therapy, medical practice and general lab diagnosis); site of authors location (south, west, north, east, central or international). **Results:** In general, the number of publications from the Southern India on Melioidosis was highest followed by the East. The publications showed increasing trend from other parts of India apart from South in 2019-2024 as compared to 2014-2019 or 2009-2014 periods. Publications of review articles were highest mostly on clinical- epidemiological studies followed by other studies on environmental surveillance or outbreak surveillance. It was observed from 9 studies spanning from 2010-2022 in India, that out of the symptoms, fever accounted for 86% (St Dev 12%); Cough accounted for 26% (St Dev 17%); Joint Pain 23% (St Dev 21%). The pre disposing conditions included Diabetes 75% (St.Dev 9%); Alcohol abuse 19% (St.Dev 9%); Cancer 6% (St.Dev 1%). Clinical presentation included bacteraemia 50% (St Dev 38%); skin and soft tissue 16% (St. Dev 10%); Pneumonia 37% (St.Dev 23%); Splenic abscess 18% (St.Dev 16%). In studies from 2012 and 2021, it has been noticed that risk due to environmental exposure has not been significantly high in India and people working outdoor and indoor in varied professions are prone thus delineating the risk to diabetes, lifestyle factors. **Conclusion:** The awareness on melioidosis is increasing all over India as observed by publications in different parts of India in the last 5 years as compared to last decade. Overall importance was on clinical epidemiology studies with data less reported on anti microbial, vaccines, diagnostics, and environmental studies. Owing to out of pocket expense, ceftazidime is preferred than carbapenem in low resource settings which could result in an increase of ceftazidime resistant pathogen causing melioidosis.

**Comment [w1]:** The abstract should provide a clear and concise summary of the study, including background, methods, results, and conclusions. Currently, it lacks clarity and structure.

## Introduction

Melioidosis is predominately a disease of tropical climates, prevalent especially in Southeast Asia and northern Australia, caused by the bacterial soil saprophyte *B. pseudomallei*, which is a tier 1 select agent because of its biothreat potential. *Soil and water are the common habitats of B. pseudomallei*. Humans and animals generally get the disease by inhalation of contaminated dust or water droplets, ingestion of contaminated water, and/or contact with contaminated soil, primarily through skin abrasions (Chakravorty & Heath, 2019). Moreover, limited awareness among clinicians and microbiologists about the disease leads to misdiagnosis and inappropriate treatment. Currently, there is no formal surveillance for melioidosis in South Asia, particularly in India. Melioidosis may even be mistaken for other diseases such as tuberculosis or more common forms of pneumonia (CDC, Melioidosis symptoms). India may be considered the diabetic capital of the world, with a 77 million diabetic populations and an 8.9% prevalence (International Diabetes Federation, 2019). Understanding the prevalence of the diabetic status, state-wise average annual rainfall and distribution of paddy cultivation (which are the contributory factors of the prevalence of the disease), it is very evident that India has the high potential to be the endemic country for the disease.

The first clinical reported case of melioidosis was from Myanmar in 1911, although the origin of this pathogen could be from Australia that got transferred to Asia, South East Asia ago 16000-225000 years ago through migrating population, trade routes and animals (Webb, 2020). This pathogen could have been introduced to Madagascar 2000 years ago and in the America around 1650-1850 AD (Webb, 2020).

Melioidosis is an emerging infectious disease with 4.64 million DALY globally. Although fatal cases of melioidosis have obvious risk factors like diabetes, alcohol, chronic pulmonary disease, it has been noted that 20-36% cases do not have any evident predisposing factor and this could be a cause to worry for such a deadly pathogen (Kottarathil, 2024). Timely detection and treatment with antibacterial agents could reduce mortality. Although culture based detection is reliable, antibiotic therapy could result in culture negativity in which PCR is better to be adapted as it is also not time consuming (Kottarathil, 2024). Since melioidosis is a mimicker for tuberculosis, patients who are suspected for TB but their AFB and GeneXpert are negative need to be screened for melioidosis and patients suspected of extra pulmonary tuberculosis need to be screened for melioidosis (Kottarathil, 2024). In a study involving 2 brothers from Kerala, India, who tested positive for melioidosis, one of the brothers had developed Pneumonia, ARDS, Septic shock and the other had developed fever, sore throat and lymphadenopathy in which the latter survived and the former died of melioidosis (Bhaskaran, 2022). Hence the disease could have varied clinical presentation and could confound the clinicians.

**Comment [w2]:** The introduction should be revised to provide a more coherent overview of the importance of studying melioidosis in India, with a clear statement of the research objectives.

Clinical details of melioidosis includes bacteremia, sepsis, pneumonia, skin and soft tissue, intra-abdominal abscesses, lung abscesses, prostatic abscesses, renal abscess, parotid abscess, brain abscess, tubo-ovarian abscess, osteomyelitis, septic arthritis, neurological disease (Raj, 2023). According to a 10 years study data, the predictors for in-hospital mortality in melioidosis with significant odds ratio included age (OR 1.01), male gender (OR 0.47), diabetes mellitus (OR 0.89), hypertension (OR 1.48), CKD (OR 0.71), CLD (OR 3.81), AKI (OR 7.63), Hyponatremia (OR 3.05) (Rao et al.,2022). Another study has shown high risk population to be patients with septic arthritis, children with suppurative parotitis and serosurveillance to be high in tsunami survivors and military personnel. In general people with soil and water exposure, renal failure, thalassemia, children less than 15 years are the main risk factors for melioidosis but its true prevalence is largely unknown.

*Burkholderia pseudomallei* is known to be present in soil of depth preferentially more than a foot and could rise to surface during monsoon season or due to man-made activities including agriculture, construction, sports (Limmathurotsakul et al.,2016). Further it is known that *B. pseudomallei* could be associated with regions of high rainfall, temperature, anthracite and Acrisol soil types (Limmathurotsakul et al.,2016). The study done by Oxford University predicted that this bacteria is ubiquitous throughout the tropics and risk zones included South Asia, parts of Australia, South America and west sub Saharan Africa. This study from Oxford University involved a 5km x 5km gridded covariate that included soil characteristics from harmonized world soil database, climatic condition and moisture (Limmathurotsakul et al.,2016).

It has been shown in a study that higher temperature of 37-40°C increases replication of this pathogen and accompanied by rainfall helps in its spread through soil (Zheng, 2023). Melioidosis that was known to have high endemicity in Thailand and Northern Australia as of 2005, was reported in other countries like China, South America, Africa, Asia later (Shaw, 2022). A Modeling study predicted global incidence of 165000 cases and 89000 deaths per year with India having a burden of 52000 cases and 31425 (13405-75601) deaths annually (Limmathurotsakul et al.,2016) but in contrast in India 583 cases were reported between 1991 – 2016 with 231 cases from Manipal between 2006-2016 and this could be due to poor diagnostic facilities, lack of awareness and possible zones of hotspots which needs to be determined (Shaw, 2022).

Environmental factors that have been attributed for melioidosis includes monsoon, inhalation of aerosolized bacteria, skin abrasion, ingestion of contaminated water, occupational hazard, thorn pricks etc. (Vinayan & Bhat,2022). Studies have indicated that male agricultural workers are prone for this

disease with fever as the most common symptom followed by involvement of musculoskeletal system and lungs as the most common target organ (Subbalaxmi, 2023). The other organs that have been reported in melioidosis infection include bone, prostate, blood, liver, skin, soft tissue, spleen, aorta, brain, bone marrow, and kidney (Subbalaxmi, 2023). Apart from these symptoms, melioidosis could be of cutaneous form due to skin infection or dissemination from other infected organ. This skin manifestation could range from papules, nodules, pustules, ulcers and could be similar to other infectious diseases like tuberculosis, plague, anthrax, cat scratch disease, sporotrichosis (Anjaneyan, 2023). One health approach has been suggested for melioidosis since its risk factors ranges from soil, animal and anthropogenic activities (Mariappan, 2022). Malaysia for example has action plans for one health approach by collaboration with ministry of agriculture, food industry, department of veterinary services, pharmaceutical services, medical development division, medical research, department of fisheries, ministry of education (Mariappan, 2022).

In recent studies from South East Asian countries it has been shown that patients with diabetes and exposure to environmental contaminant have the highest odds for acquiring the disease and people with access to poor drinking water are also at risk which in turn highlights the importance of using chlorinated and boiled drinking water (Selvam, 2022). Both India and Cambodia have neighbouring countries that are endemic to melioidosis and Cambodia has low number of cases of melioidosis reported, presumably due to lack of diagnostic facilities and awareness, which might be the case in India too. In a study in Cambodia it has been shown that environmental factors like rainfall, wind speed, humidity and low visibility are significantly associated with melioidosis.

In a study in Cambodia, that considered wind speed (<10km/h-(low), 10-13km/h-(medium) &>13km/h-(high)) as a risk factor for melioidosis, the odds ratio for Female Gender vs. Male Gender was 0.74/0.73 in medium and high speed wind indicating males are more prone for melioidosis incidences acquired through wind. As in between adult and child, odds were 1.44/1.13 for child for medium and high speed winds indicating children could get melioidosis more than adults through wind with medium speed having higher risk than high speed. Rice farmers had an odds of 1.31/1.36 for medium and high speed wind as compared to other professionals. Blood Glucose >150mg/dl had an odds of 1.07/1.09 as for medium and high speed winds. People with medical history of melioidosis had odds of 0.87/1.06 for medium and high speed winds. This could be interesting that people with history of diabetes are prone to melioidosis in high speed winds (>13km/h) and people without any history of diabetes are prone to melioidosis in medium speed winds (10-13km/h). People developing disseminated infection than localised infection had an odds of 1.46/1.88 in medium and high speed winds. People developing lung infection

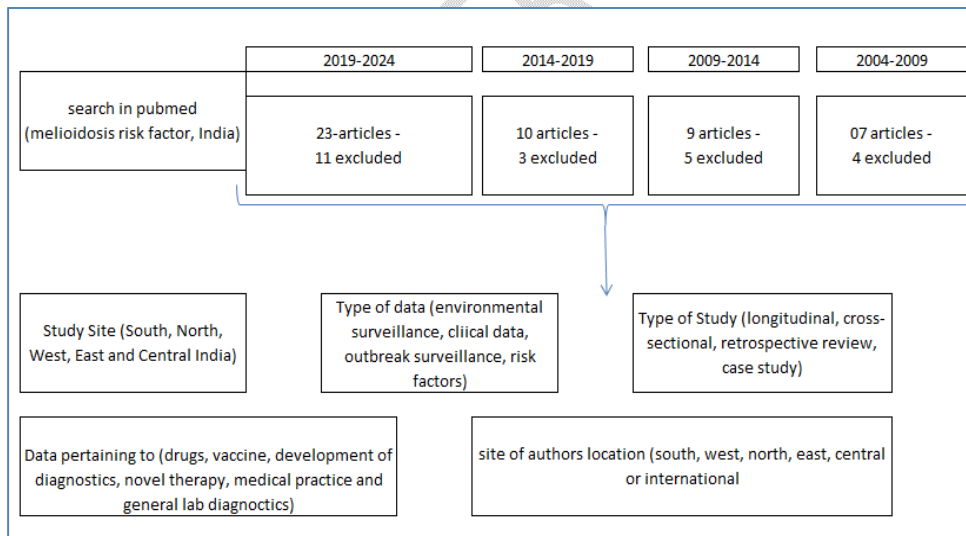
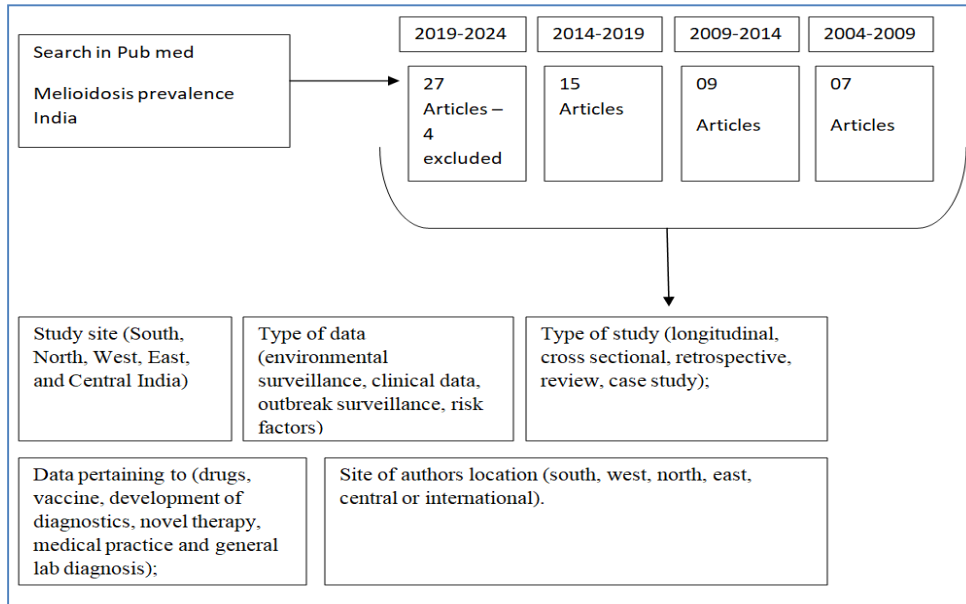
than other infection had an odds of 1.34/1.93 in medium and high speed winds respectively. People developing skin/soft tissue infection than other organs had as odds of 1 / 0.68 in medium and high speed winds respectively.

## Method

In a review conducted from south East Asian countries which included Thailand, Malaysia, it was observed that the diagnostic assays that were used include blood culture, sputum culture, synovial culture, pus culture, parotid culture, multiplex PCR, VITEK2, AST, AMD-LFA (Selvam,2022). Within the target population of culture-positive tuberculosis patients, antibody detection with IHA, IFA-IgM, IFA-IgG was used. For tsunami survivors, antibody detection with IHA was used (Selvam,2022). Patients with suspected melioidosis, antibody detection with IFA-IgM were used. Patients with fever, sepsis of unknown origin, ELISA-IgG with OPS was used (Selvam,2022). For febrile patients, ELISA using OPS and Hcp1 was used. For military personnel, ELISA with exotoxin and whole-cell antigen was used (Selvam,2022). Risk factors for melioidosis as documented in Thailand, Malaysia include high soil & water exposure, diabetes mellitus, hematologic or solid tumour, renal disease, thalassaemic disease, open wound, eating food contaminated with soil, dust, exposure to rain, dust, drinking untreated water, water inhalation, smoking, steroid intake (Selvam,2022).

Melioidosis in children manifests as parotitis and cutaneous infection which occurs 4 times more likely in children than adults. In adults, melioidosis most commonly occurs as pneumonia which has 3 times more likelihood in adults than in children (Jarrett,2023).Melioidosis is commonly present as community acquired pneumonia and pneumonic melioidosis is considered to be dangerous (Paul, 2020).

**Comment [w3]:** "Method: This article of ours focuses on literature retrieved from Pub Med with two search criteria "Melioidosis prevalence India" and "Melioidosis risk factor India" from 2019-2024 2014-2019 2009-2014 2004-2009." should be "Methods: This article focuses on literature retrieved from PubMed using two search criteria, 'Melioidosis prevalence India' and 'Melioidosis risk factor India', covering the periods 2019-2024, 2014-2019, 2009-2014, and 2004-2009."



**Chart 1: Schematics of article selection with search words “Melioidosis prevalence India” in the top; and “Melioidosis risk factor India” in the bottom.**

**Results and Discussion**

**Table1. Five years grouping of publication on melioidosis in India based on various factors obtained by search word “melioidosis prevalence India”**

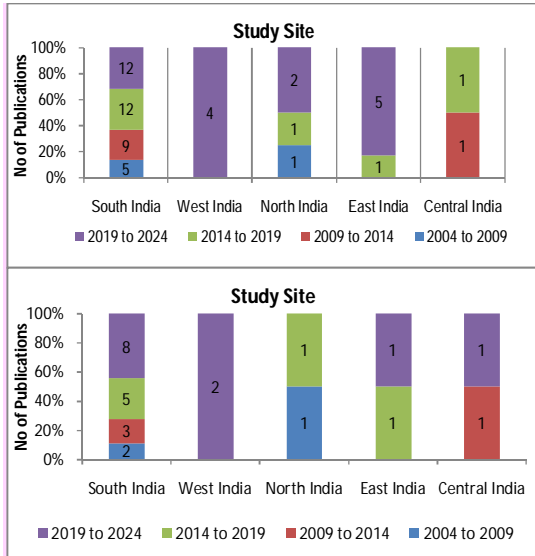
**Comment [w4]:** The results section presents data in a somewhat disorganized manner. Tables and figures are included but not always referenced clearly in the text. Additionally, the statistical data are sometimes presented without adequate context or explanation.

Study Site	South India	West India	North India	East India	Central India	Total articles / Excluded
2004 to 2009	5		1			
2009 to 2014	9				1	Total 9; Excluded 0
2014 to 2019	12		1	1	1	Total 15; Excluded 0
2019 to 2024	12	4	2	5		Total 27; Excluded 4
<b>Data reported</b>	<b>Environmental surveillance</b>	<b>Clinical</b>	<b>Outbreak Surveillance</b>	<b>Risk factors</b>		
2004 to 2009	1	6				
2009 to 2014	1	8				
2014 to 2019	5	12		1		
2019 to 2024	2	19	1	1		
<b>Study type</b>	<b>Longitudinal</b>	<b>Cross sectional</b>	<b>Review</b>	<b>Case series</b>	<b>Prevalence reporting</b>	<b>Retrospective cohort</b>
2004 to 2009			3	1	3	
2009 to 2014				6	3	
2014 to 2019			5	3	6	1
2019 to 2024	1		13	4	6	1
<b>Data on</b>	<b>Drugs</b>	<b>Vaccine</b>	<b>Development of diagnostics</b>	<b>Novel therapy</b>	<b>Medical practice</b>	<b>General (lab diagnosis)</b>
2004 to 2009						6
2009 to 2014					1	8
2014 to 2019	2		4		5	8
2019 to 2024	2	1	4	1	6	10
<b>Authors institute</b>	<b>South India</b>	<b>West India</b>	<b>North India</b>	<b>East India</b>	<b>Central India</b>	<b>International</b>
2004 to 2009	5		1			1
2009 to 2014	9				1	
2014 to 2019	12		1	1	1	1
2019 to 2024	15	4	2	6		4

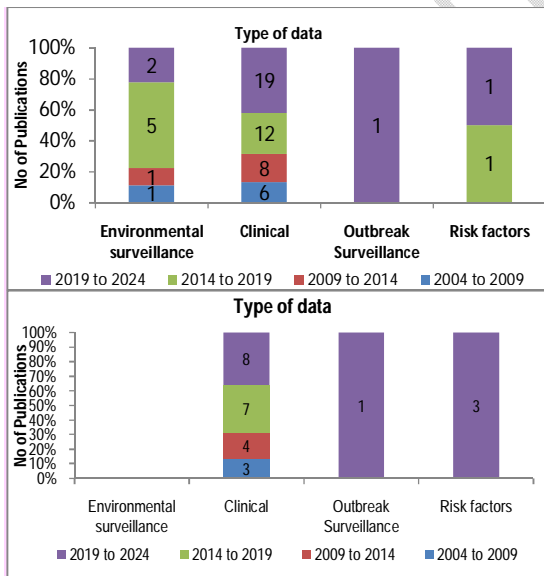
**Table 2 Five years grouping of publication on melioidosis in India based on various factors**

Obtained by search word “melioidosis risk factor India”

Study Site	South India	West India	North India	East India	Central India	Total articles / Excluded
2004 to 2009	2		1			7 – 4 excluded
2009 to 2014	3				1	9- 5 excluded
2014 to 2019	5		1	1		10 – 3 excluded
2019 to 2024	8	2		1	1	23 – 11 excluded
<b>Data reported</b>	Environmental surveillance	Clinical	Outbreak Surveillance	Risk factors		
2004 to 2009		3				
2009 to 2014		4				
2014 to 2019		7				
2019 to 2024		8	1	3		
<b>Study type</b>	Longitudinal	Cross sectional	Review	Case series	Prevalence reporting	Retrospective cohort
2004 to 2009			1	2		
2009 to 2014				4		
2014 to 2019			2	4		1
2019 to 2024			4	6	2	
<b>Data on</b>	Drugs	Vaccine	Development of diagnostics	Novel therapy	Medical practice	General (lab diagnosis)
2004 to 2009						3
2009 to 2014					3	1
2014 to 2019	1		4		2	1
2019 to 2024			3		3	7
<b>Authors institute</b>	South India	West India	North India	East India	Central India	International
2004 to 2009	2		1			
2009 to 2014	3		1			
2014 to 2019	5		1	1		
2019 to 2024	8	1		1	1	2



**Figure 1 Publications on melioidosis in India (top with prevalence as key search word & bottom with risk factor as key word)**



**Figure 2 Type of data presented in publication (top with prevalence as key search word & bottom with risk factor as key word)**

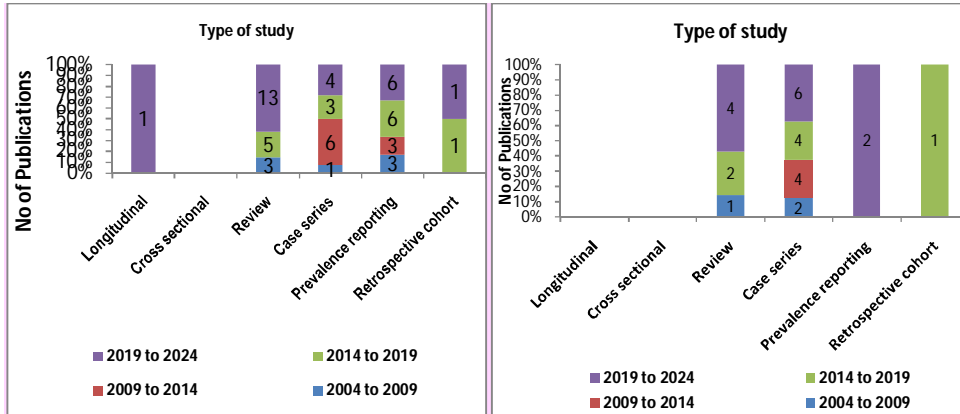


Figure 3 Type of study presented in the publication (top with prevalence as key search word & bottom with risk factor as key word)

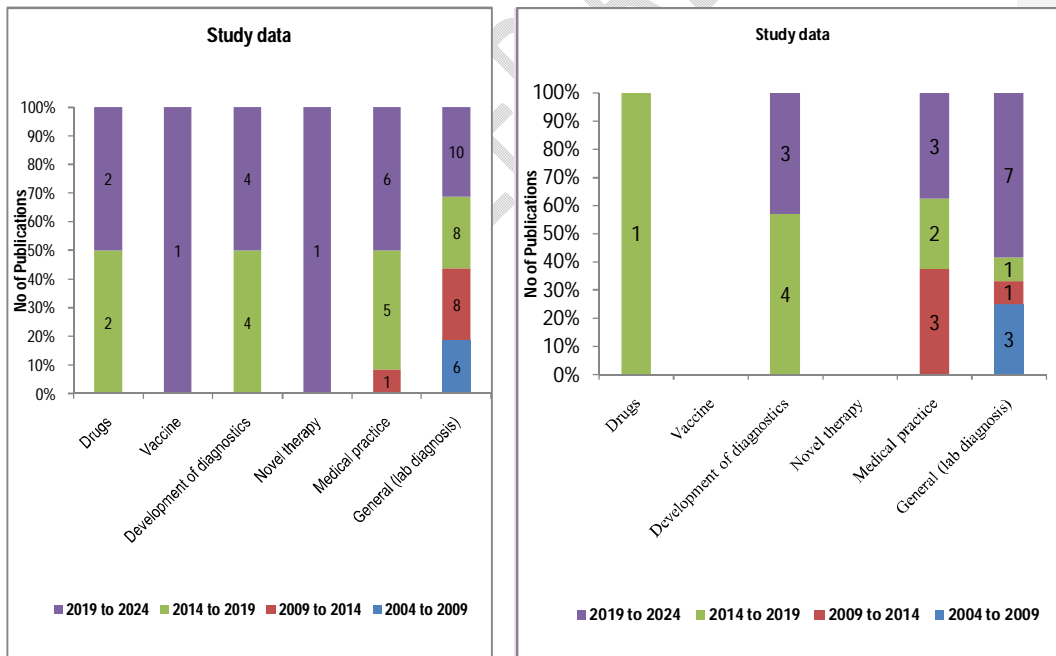


Figure 4 Study describing data on (top with prevalence as key search word & bottom with risk factor as key word)

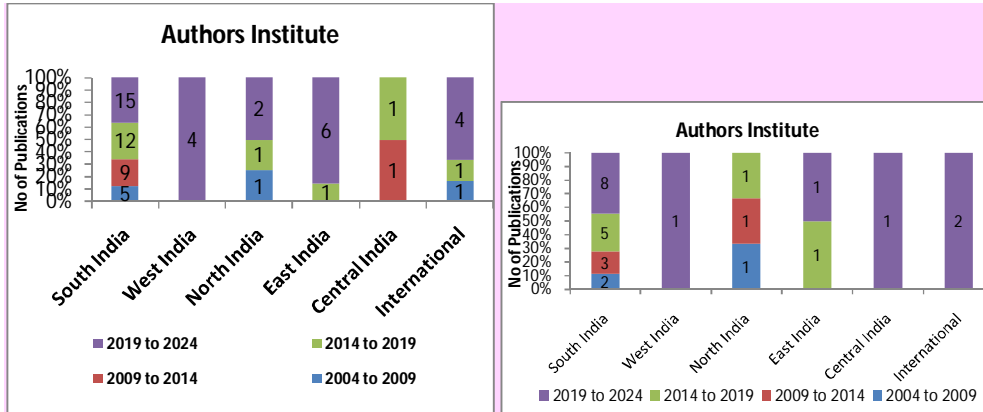
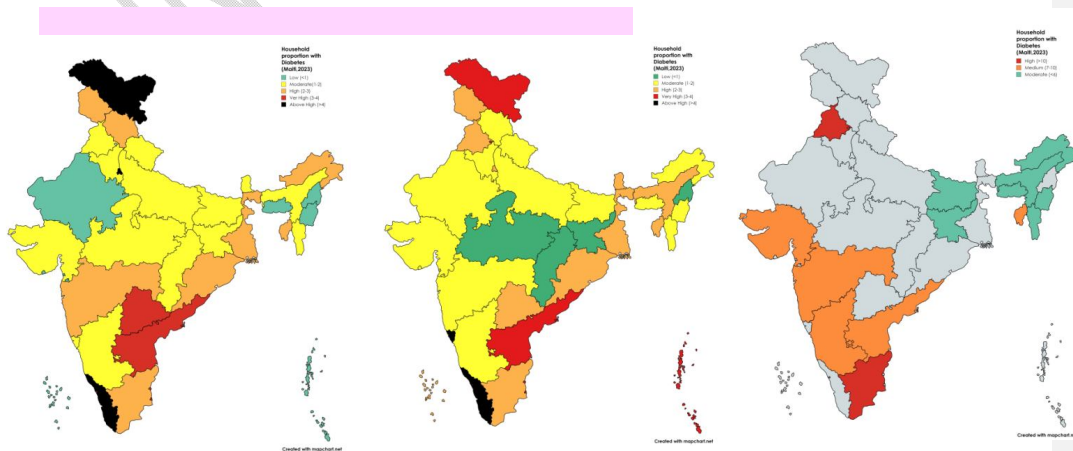
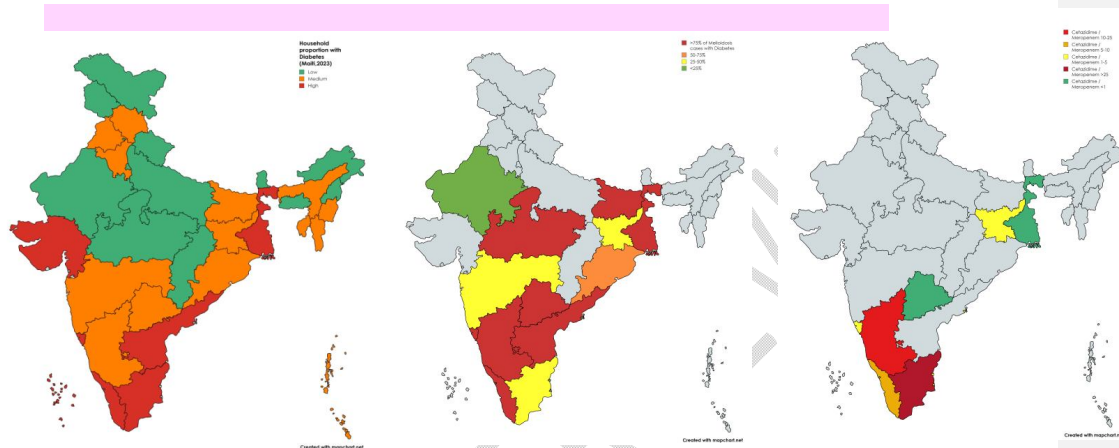


Figure 5 Publication authors location (top with prevalence as key search word & bottom with risk factor as key word)





**Figure 6** Prevalence of Diabetes in India (created with Map chart). (Top left)

Prevalence of Diabetes in male population of Indian States (NFHS-5 data – 2019-2020&(Top middle) Prevalence of Diabetes in female population; Red – High incidence; Green –low incidence; orange- moderate incidence. Proportions of household with at least one member having diabetes as reported in Maiti, 2023 (Low <20; Medium 20-30; High>30). Black – very high incidence; Red – High incidence; Orange- moderate incidence; Yellow- moderate incidence; Green- low incidence. (Top Right)Prevalence of Diabetes in selected states (data from Anjana, 2017) – Grey color not included in study; Red – High incidence; Green –low incidence; orange- moderate incidence.(Bottom Left) Household proportion with diabetes – data from Maiti,2023 (Bottom middle) Diabetes cases with melioidosis – data from Mukhopadhyay, 2018 (Bottom Right) Ratio of Ceftazidime / Meropenem consumed by melioidosis patients – data from Mukhopadhyay, 2018 (higher the ratio shows preference to ceftazidime than meropenem as seen in Tamilnadu> Karnataka> Kerala> Odisha, Goa>Telangana>West Bengal.

**Table 3** Clinical profile reported in literature

			Behera, 2022 Bacteraemic melioidosis	Behera 2022 Non-Bacteraemic melioidosis	Menon 2021	Koshy, 2019	Vidyalakshmi, 2012 Bacteraemic cases melioidosis	Vidyalakshmi, 2012 Non Bacteraemic cases melioidosis	Chrispal, 2010	Saravu, 2010
	Yadav, 2023	Singh, 2022								

	N=7	N=19	N=26	N=21	N=73	N=114	N=37	N=58	N=41	N=25
Location	Central India	South India	East India	East India	South India	South India	South India	South India	South India	South India
Fever	100%	89%	100%	67%		97%			83%	80%
Cough		42%	23%	5%		16%			46%	
Joint Pain	100%	37%	4%	0%		25%				48%
Abscess		16%								
Diabetes	100%	84%			72%	82%	62.2%		79%	68%
Hypertension					32%					
CKD		10%			10%	4%	24.3%			
COPD		10%								
Liver disease		10%								
Alcohol						14%	8.1%		24%	28%
Tuberculosis		5%								
Cancer		5%			7%					
Bacteraemic		58%	100%	0%	34%	55%	100%	0%	54%	
Skin and Soft tissue / Cutaneous		11%			25%	13%		3.2%	27%	
Septic arthritis / Arthritis		11%	4%		12%	19%	5.3%	10.5%		
Pneumonia /Respiratory Involvement	71%	5%			41%		54%	12.6%	61%	48%
Splenic abscess / involvement of spleen		5%	8%		40%	43%	2.1%	2.1%	22%	24%
Neuromelioidosis / Brain abscess		5%	4%	5%				1.1%	5%	
No focus		5%								

**Comment [w5]:** Figures and tables should be better integrated into the text, with each one clearly referenced and its significance explained. The quality and readability of some figures, such as Figure 6, should be improved.

The number of publications on melioidosis from India certainly increased from 2004 (7) to 2024 (23) as retrieved from Pub Med. But it can also be noticed in Table 1 and Figure 1. that in 2004, predominantly South India was involved in publishing articles on melioidosis and after 20 years, it has not only increased in south India but also from eastern parts of India and the rest. This trend indicates that awareness on melioidosis is increasing in different part of India but although more work needs to be done in Central India, North and North eastern India that had fewer publications.

The publications mainly focused on clinical epidemiological data ranging from 19 in 2014-2019; 12 in 2014-2019; 8 in 2009-2014 and 6 in 2004-2009. Articles that focused on environmental surveillance included 2 to 5 in last decade and 2 more in the previous decade. There were 1-2 articles on outbreak surveillance and risk factors in the last decade. Hence it can be noted that work needs to be done in the fields of environmental surveillance, outbreak surveillance both of which will increase if melioidosis becomes a notifiable disease in India. In the last 5 years, publications on general clinical and lab data accounted for 10; 6 on medical practices; 1 on novel therapy; 4 on developmental diagnostics; one on vaccine; 2 on drugs.

In a study from Kasturba medical college, Manipal it has been documented 20 year data on prevalence of melioidosis in many states in India. The state of Karnataka had reported 499 melioidosis cases (8% mortality) (age range of 0-84, 78% diabetic and Male-female ratio of 3:1). Tamilnadu had reported 210 melioidosis cases (22% mortality) (age range of 4-65, 57% diabetic and Male-female ratio of 3:1). Kerala had reported 58 melioidosis cases (10% mortality) (age range of 9-66, 56% diabetic), Pondicherry had reported 79 cases (18% mortality) (age range of 0-58, 26% diabetic with male: female ratio of 3:1). Telangana had reported 36 cases (11% mortality) (age range of 30-66, 77% diabetic with male: female ratio of 2:1). Maharashtra had reported 10 cases (40% mortality) with age range 10-65, 60% diabetic and 9:1 male-female ratio. Goa had reported 7 cases (34-53 age range, 85% diabetic and male: female of 5:0). Bihar had reported 5 cases (age range of 50-65, all diabetic and male-female ratio of 4:1). Jharkhand had reported 2 male cases of age range 32-33. Madhya Pradesh, Andhra Pradesh, Gujarat had reported each 1 case.

Deriving average of nine studies (3 in 2022; 1 in 2021; 1 in 2019; 2 in 2012; 2 in 2010), it was observed that out of the symptoms, fever accounted for 86% (St Dev 12%); Cough accounted for 26% (St Dev 17%); Joint Pain 23% (St Dev 21%). The pre disposing conditions included Diabetes 75% (St.Dev 9%); Alcohol abuse 19% (St.Dev 9%); Cancer 6% (St.Dev 1%). Clinical presentation included bacteraemia 50% (St Dev 38%); skin and soft tissue 16% (St. Dev 10%); Pneumonia 37% (St.Dev 23%); Splenic abscess 18% (St.Dev 16%).

In a study by Vidyalakshmi, 2012, it can be noted that, Diabetic patients were higher in India than in northern Australia, Thailand and Malaysia. Environmental exposure and mortality was comparatively less in India as compared to northern Australia, Thailand and Malaysia. In a recent study it has been pointed out that people of varied occupation are prone for melioidosis and the concept of environmental exposure doesn't hold good and acknowledging post rainfall risk as 79%. Further, It has been noted that not only

rural areas associated with agriculture but urban slums and urban villages could harbor this environmental pathogen as shown of its presence in an urban market area at New Delhi (Kannan et al., 2023). Water and rain has been strongly associated with Melioidosis and even 1000ppm chlorine is found to be not useful in elimination of the bacterium (Howard and Inglis, 2003).

In a study that involved isolates from pyogenic lesions in eastern India (Purushotham, 2021), *B. pseudomallei* accounted for 25% of isolates (34/137). Out of the 34, 35% were laborers, 6% military personnel, 6% driver and 6% farmers, homemakers (24%), student (15%), office worker (6%), teacher (3%). The risk factor included diabetes (29%), diabetes and alcoholism (15%), alcoholism (12%). The initial treatment therapy involved ceftazidime in 82% patients, meropenem in 12% patients and imipenem in 3% patients. The eradication therapy involved co-trimoxazole in 88% of patients, doxycycline in 6% of patients and amoxicillin- clavulanate in 3% of patients. But due to economic constraints in India, carbapenems are less preferred than ceftazidime (Shaw, 2016).

Comparing the risk factors of melioidosis in India to that of any south east Asian country, it could be noticed that diabetes, CKD, alcoholism are common risk factors but in a study from Thailand (Chantratita et al., 2023) it can be noticed that other risk factors that have been correlated with melioidosis cases which are not present in Indian studies include dyslipidemia, chronic corticosteroid therapy, Gout.

In a review work from Australia that involved 31 melioidosis cases with cardiac involvement that included 4 from Thailand, 5 from Malaysia, 3 from Vietnam, 3 from Singapore, 9 from India, 2 from Srilanka, 2 from China, 1 from Australia, 1 from Panama, 1 from Puerto Rico, it was noted that 95% of the cases were male with mean age 58 years. The risk factors included soil exposure (49%), water exposure (11%), travelling (5%), Diabetes (38%), Coronary artery disease (8%), Airways disease (3%), smoker (21%), hypertension (8%), alcohol (8%), malignancy (5%), chronic liver disease (3%), chronic kidney disease (5%).

The known risk factors of melioidosis in adults from a study in Indonesia included Diabetes mellitus (56%); CKD (19%); CLD (7%); Malignancy (7%); alcohol abuse (4%); chronic lung disease (4%); malnutrition (0%), none (26%) (Tauran, 2018). Risk factors as characterized in 1121 patients with melioidosis in Thailand included Diabetes (71%), Hypertension (31%), Dyslipidemia (8%), CKD (16%), Smoking (35%), Heart disease (5%), Stroke (3%), Lung disease (12%), Tuberculosis (8%), alcohol use disorder (5%), HIV (1%) (Coston, 2024). The soil exposure referred to occupations like farmer,

lumberjack, landscaper, agriculturist, construction/renovator, military personnel and water exposure referred to occupations like sailor, shipyard worker.

Taking into consideration diabetes as the risk factor as shown in Figure 6, the following states could be hypothesized to have higher incidence of melioidosis namely Gujarat, Kerala, West Bengal, Tamilnadu, Andhra Pradesh, Goa. According to NFHS-5 data (2019-2020), As per NFHS5 data of 2019-2020, states with very high incidence of diabetes included Kerala, Delhi, Ladakh followed by Andhra Pradesh, Telangana. States with high incidence included Maharashtra, Tamilnadu, Odisha, West Bengal, Arunachal, Tripura, Jammu, Himachal. States with moderate level included Goa, Karnataka, Chhattisgarh, Madhya Pradesh, Jharkhand, Punjab, Haryana, Uttarakhand, Bihar, Sikkim, Assam, and Mizoram. States with low level included Rajasthan, Meghalaya, Nagaland, and Manipur. The states that had highest female diabetic population in NFHS 5 data (2019-2020) were Kerala, Goa followed by Andhra Pradesh, Ladakh. This is followed by Tamilnadu, Punjab, Jammu, Telangana, Odisha, West Bengal, Assam, Sikkim, Tripura. Moderate incidence included Karnataka, Maharashtra, Gujarat, Rajasthan, Haryana, Uttarpradesh, Bihar, Arunachal, Meghalaya, Mizoram, and Manipur. The least was in Madhya Pradesh, Chhattisgarh and Jharkhand.

#### **The FIRE Approach: Inclusion of Friends, Relatives, Even Enemies!!! in Capacity Building for Melioidosis – learning from COVID scenario**

Fire, Water, Earth and Air are four essential elements in this Universe. Out of which, water, earth and air could transmit Melioidosis. The COVID pandemic made even an illiterate to know about mask and the basics of viral infection. This happened due to the involvement of the entire society and not only the medical professionals for handling the COVID pandemic. What if, this is used as a lesson for capacity building for other diseases like Melioidosis. Hereby we coin the FIRE approach in capacity building – Inclusion of Friends, Relative, Even Enemies!!! in capacity building.

Kasturba Medical College steered and ICMR funded MISSION project on Melioidosis in India helps to cover 15 centres spread all over India. Apart from usual mode of capacity building amidst Clinicians, family inclusive capacity building of few staffs working in Melioidosis project were inducted about the disease through participation in social dinner with Scientists working on Melioidosis. This included school teachers and village officer in profession (names mentioned in acknowledgement). Such practices would help to encompass vulnerable groups like children, farmers. Discussion with school teachers helped to understand how teaching methods during COVID prevented fomite transmitted infection and

**Comment [w6]:** The discussion section could be expanded to provide a more in-depth analysis of the findings. The manuscript should discuss the implications of the results in the context of existing literature, highlight the significance of new findings, and suggest directions for future research.

discussion with Village Officer helped to understand how they govern soil transport within districts and based on these policies could be planned. Suggested policies that could be worked on include

- Reduction of fomite in schools like correction of test papers that could be done by computer based
- School teachers being inducted about the skin lesion in Melioidosis would help them to casually look for it in their class children
- Village officers could be informed about sites where Melioidosis has been positive so that they can include it as a criterion to prevent soil transport from a district that tested positive to a district that has tested negative.

### Conclusion

- The prevalence of Melioidosis in India is not yet known for all states although it could be extrapolated from the incidence of risk factors like diabetes
- Out of pocket expense for melioidosis treatment could be a crucial factor for drug resistance since ceftazidime is cheaper than carbapenem
- Studies on Vaccines and diagnostics is poor and this area needs to be worked upon
- Based on publications it can be observed that South and Eastern India have more awareness on Melioidosis and cases detected than other parts

**Comment [w7]:** The conclusion should succinctly summarize the main findings and their implications, avoiding unnecessary detail.

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**Comment [w8]:** Some references are incomplete or incorrectly formatted. Ensuring all citations are properly formatted according to journal guidelines is crucial.

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