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Melioidosis in India: Epidemiological Insights and Predictions from 20-Year Review of Literature with Note on Inclusive Capacity Building

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Authors' contributions

This work was carried out in collaboration among all authors. Shared first Authors SK, HK. Author SK drafted the first manuscript that was improvised by author HK and from the expert contribution on melioidosis by authors CM, VKE. Authors MA, AS and MS contributed to the project management under project coordinator. Authors VAE and SC are project researchers at KMC. Authors CM, VKE are lead PIs at KMC and author HK the project coordinator. All authors read and approved the final manuscript.

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ABSTRACT

Background: Melioidosis caused by the infamous soil pathogen, *Burkholderia 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. Its higher prevalence in monsoon periods, floods, tsunamis make it an important disease in India.

Objective: To present an overall view of Melioidosis in India in last 20 years and future perspectives.

Methods: This article of ours focuses on literature retrieved from Pub Med (2004-2024) with two search criteria "Melioidosis prevalence India" and "Melioidosis risk factor India" and presented on the basis of – geographical location of Study site, environmental surveillance, clinical data, outbreak surveillance, risk factors, type of study, data pertaining to drugs, vaccine, diagnostics, novel therapy, medical practice and general lab diagnosis.

Results: In general, the number of publications from the Southern India on Melioidosis was highest followed by the East. Publications of review articles were mostly on clinical- epidemiological studies followed by other studies on environmental surveillance or outbreak surveillance. It was also observed from studies spanning from 2010-2022 in India that the symptoms observed in Melioidosis patients included fever that accounted for 86% (SD 12%), Cough that accounted for 26% (SD17%), Joint Pain 23% (SD 21%). The % of pre disposing factors averaged from 9 studies, included Diabetes 75% (SD 9%); Alcohol abuse 19% (SD 9%); Cancer 6% (SD 1%). Clinical presentation included bacteremia 50% (SD 38%); skin and soft tissue involvement 16% (SD 10%); Pneumonia 37% (SD 23%); Splenic abscess 18% (SD16%). 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: Using Diabetes and Poverty hotspots for presumed geographical mapping of melioidosis prone states, districts in India could possibly aid in better identification and control of the disease. Further, from this review study, it is noted that the awareness on melioidosis has increased over the last two decades. Publications on Melioidosis were mostly on clinical epidemiology studies and then followed by publications on anti-microbial susceptibility, vaccines, diagnostics, and environmental risks. Studies indicate that owing to out-of-pocket expense, Ceftazidime was seen to be preferred than Carbapenem in the following states from high to low preference: Tamil Nadu, Kerala, Goa, Jharkhand, Karnataka, Telangana and West Bengal. This could be further examined.

Keywords: Melioidosis; diabetes; poverty; hot spots; India.

1. INTRODUCTION

Melioidosis is predominately a disease of tropical climates, prevalent especially in Southeast Asia and northern Australia, caused by the bacterial soil saprophyte *Burkholderia 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 [1]. Moreover, limited awareness among clinicians and microbiologists about the disease leads to misdiagnosis and inappropriate treatment.

The first clinical reported case of melioidosis was from Myanamar 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 [2]. This pathogen could have been introduced to Madagascar 2000 years ago and in the America around 1650-1850 AD [2].

Environmental presence and studies from other South Asian Countries: *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 [3]. Further it is known that *B. pseudomallei* could be associated with regions of high rainfall, temperature, anthrasol and acrisol soil types [3]. The study done by Oxford University predicted that this bacterium 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 [3].

It has been shown in a study that higher temperature of 37-40c increases replication of this pathogen and accompanied by rainfall helps in its spread through soil [4]. Melioidosis that was known to have high endemecity in Thailand and Northern Australia as of 2005, was reported in other countries like China, South America, Africa, Asia later [5]. 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 [3] 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 [4].

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. [6]. 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 [7]. The other organs that have been reported in melioidosis infection include bone, prostrate, blood, liver, skin, soft tissue, spleen, aorta, brain, bone marrow, and kidney [7]. 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 [8]. One health approach has been suggested for melioidosis since its risk factors ranges from soil, animal and anthropogenic activities [9]. 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 [9].

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 [10]. Both India and Cambodia have neighbourhood 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 [11], 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 odd of 1.31/1.36 for medium and high-speed wind as compared to other professionals. Blood Glucose >150mg/dl had an odd 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 odd of 1.46/1.88 in medium and high-speed winds. People developing lung infection than other infection had an odd 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.

Importance of Melioidosis in India and need for awareness and studies on Melioidosis: 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.

Challenges posed by Melioidosis to Clinicians and Society adds to the need for conducting such literature review study: 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 [12]. Melioidosis is commonly present as community acquired pneumonia and pneumonic melioidosis is considered to be dangerous [13].

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 [14]. 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 [14]. 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 [14]. 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 [15]. Hence the disease could have varied clinical presentation and could confound the clinicians [16].

Clinical details of melioidosis includes bacteremia, sepsis, pneumonia, skin and soft tissue, intra-abdominal abscesses, lung abcesses, prostratic abcesses, renal abscess, parotid abscess, brain abscess, tubo-ovarian abscess, osteomylitis, 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, thalasemia, children less than 15 years are the main risk factors for melioidosis but its true prevalence is largely unknown.

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 [10]. 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 [10]. For febrile patients, ELISA using OPS and Hcp1 was used. For military personel, ELISA with exotoxin and whole-cell antigen was used [10]. 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 [10].

2. METHODS

This article of ours focuses on literature [17-86] 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.

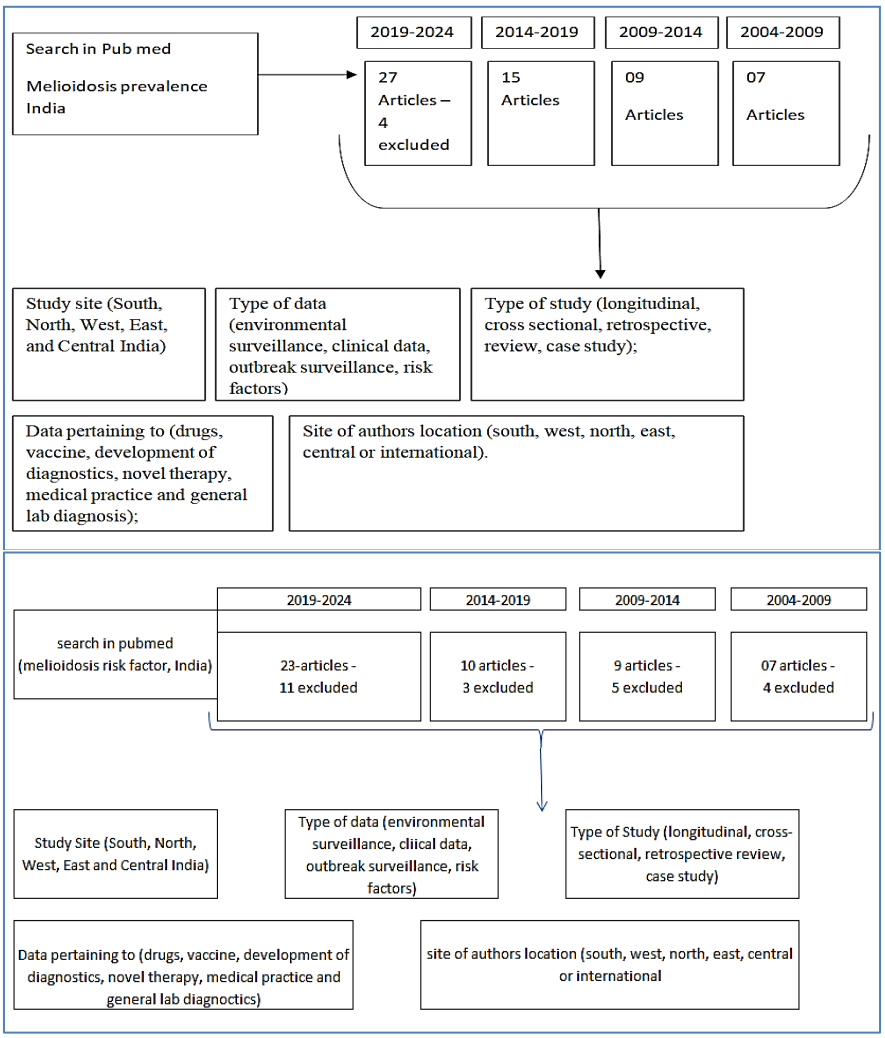

Chart 1. Schematics of article selection with search words "Melioidosis prevalence India" (top chart); and "Melioidosis risk factor India" (bottom chart)

3. RESULTS AND DISCUSSION

a. Comparison of publications over years on melioidosis: The number of publications on melioidosis from India certainly increased from 2004 (7Nos) to 2024 (23Nos) as retrieved from Pub Med. But it can also be noticed in Table 1 and Fig. 2. 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.

It can be seen in Figs. 3-5, that the publications manly focused on clinical epidemiological data ranging from 19 in 2024-2019; 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 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 [87].

b. Outcome of pooling up study data on symptoms of melioidosis: As seen in Table 3, 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% (SD 12%); Cough accounted for 26% (SD 17%); Joint Pain 23% (SD 21%). The pre disposing conditions included Diabetes 75% (SD 9%); Alcohol abuse 19% (SD 9%); Cancer 6% (SD 1%). Clinical presentation included bacteremia 50% (SD 38%); skin and soft tissue 16% (St. Dev 10%); Pneumonia 37% (SD 23%); Splenic abscess 18% (SD 16%).

c. Environmental and health risk factors of melioidosis in India as compared to other countries: In a study from south India [88] 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 [89]. Water and rain has been strongly associated with Melioidosis and even 1000ppm chlorine is found to be not useful in elimination of the bacterium [90].

d. Socio economic and health factors reported in different countries as for melioidosis: In a study that involved isolates from pyogenic lesions in eastern India [91], *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, Meropenenem in 12% patients and imipenem in 3% patients. The eradication therapy involved Co-Trimoxaozole 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 [92].

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 [93] 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%) [94]. 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.

e. Mapping of Indian states with diabetes as melioidosis risk factor: Taking into consideration diabetes as the risk factor as shown in Figs. 1a-b, the following states could be hypothesized to have higher incidence of melioidosis namely Gujarat, Kerala, West Bengal, Tamil Nadu, 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, Tamil Nadu, 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.

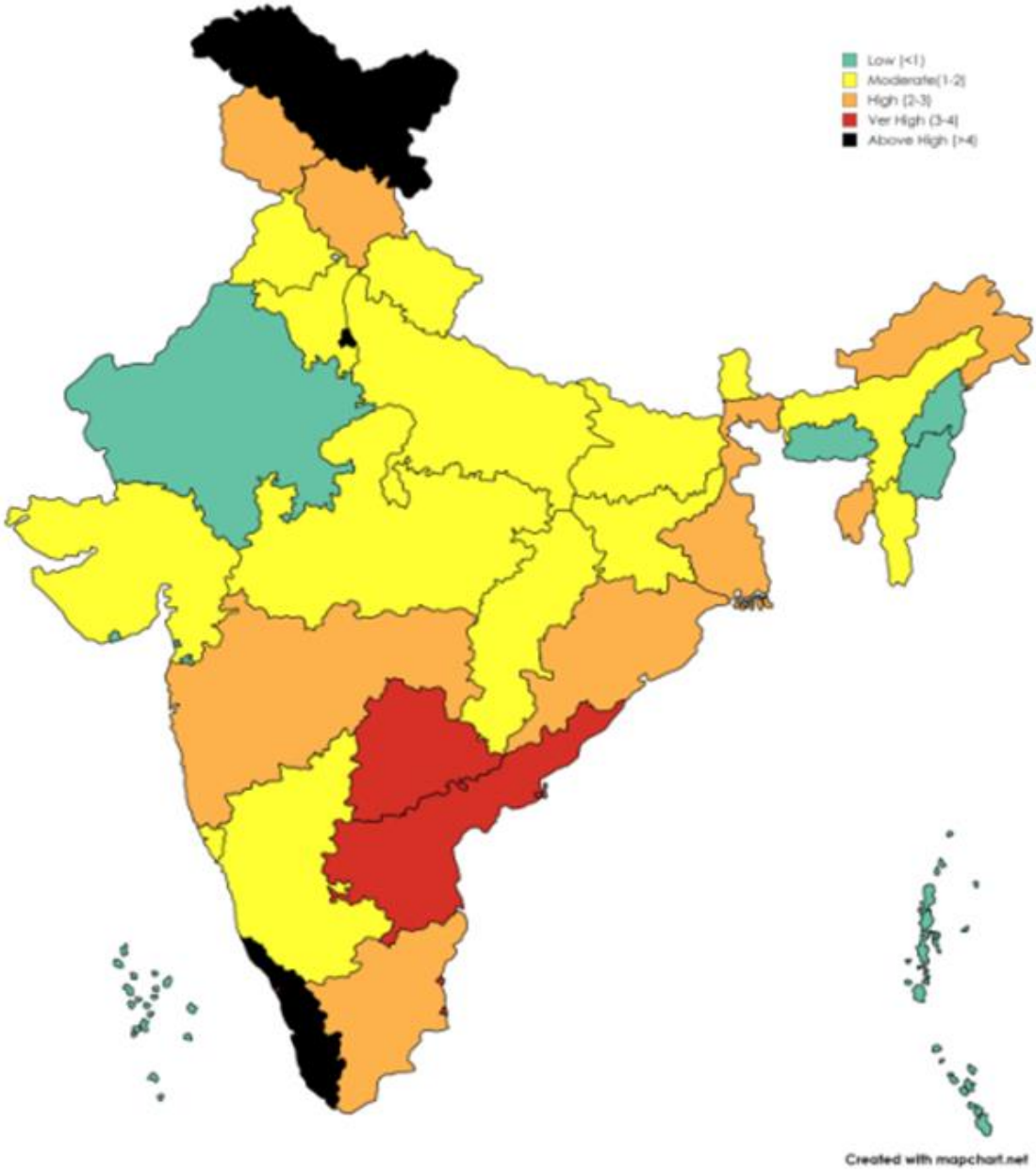

Fig. 1a. Prevalence of Diabetes in male population of Indian States (NFHS-5 data) – 2019-2020 (Black > Red > Orange > Yellow > Green)

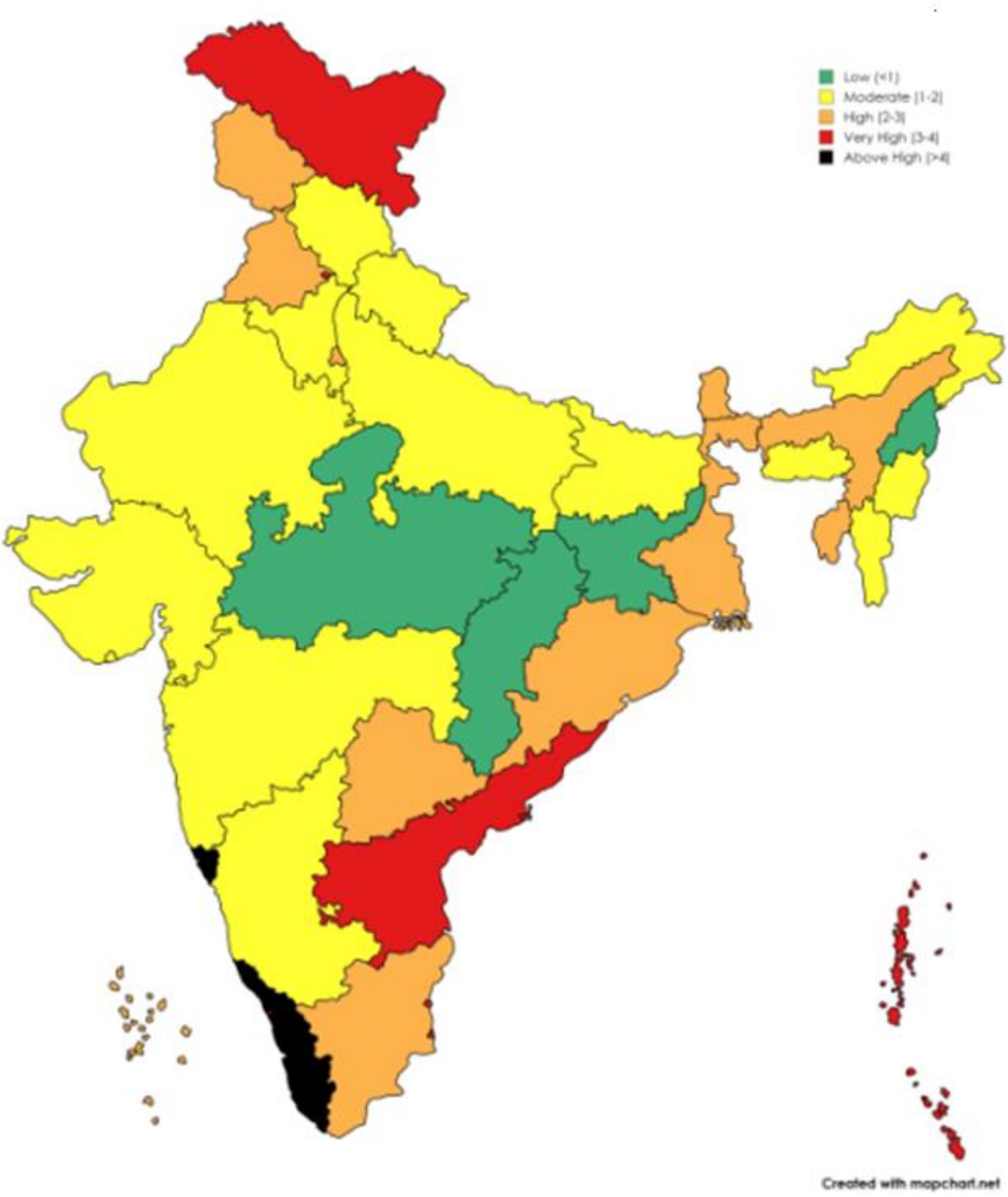

Fig. 1b. Prevalence of Diabetes in male population of Indian States (NFHS-5 data) – 2019-2020 (Black > Red > Orange > Yellow > Green)

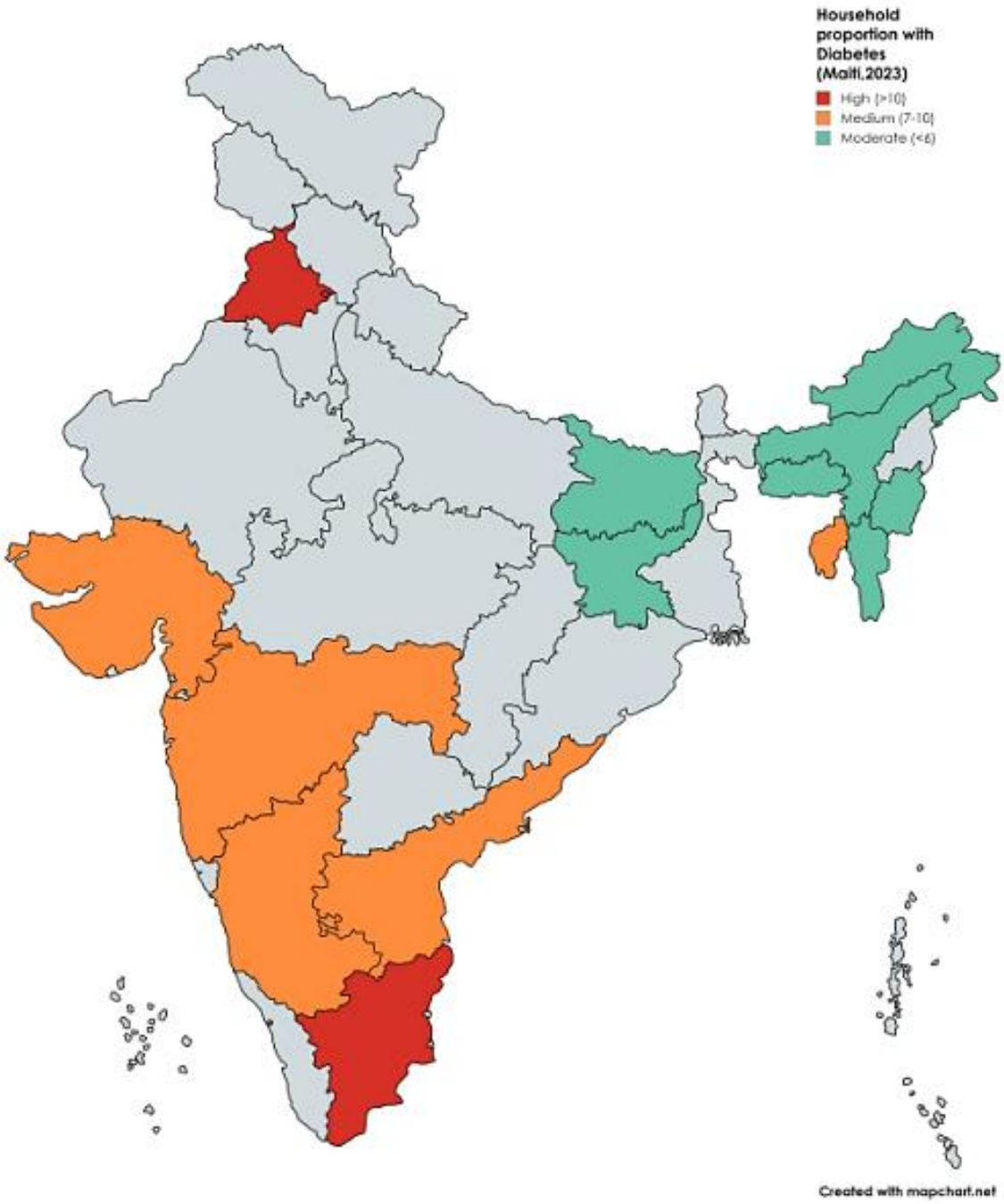

Fig. 1c. Prevalence of Diabetes in selected states as extracted from [93] – Grey color not included in study; Red – High incidence; Green –low incidence; orange- moderate incidence

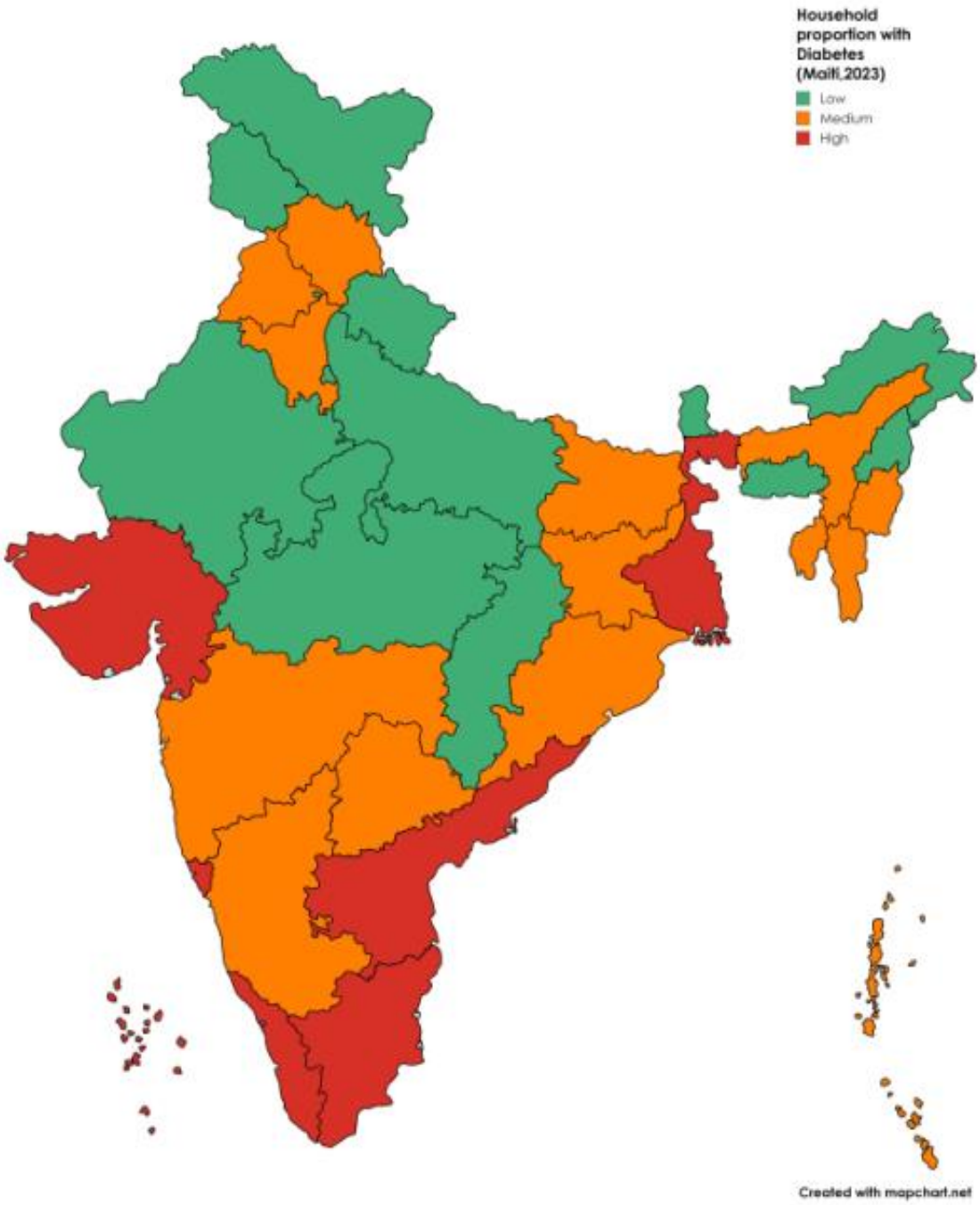

Fig. 1d. Household proportion with diabetes as extracted from [94]

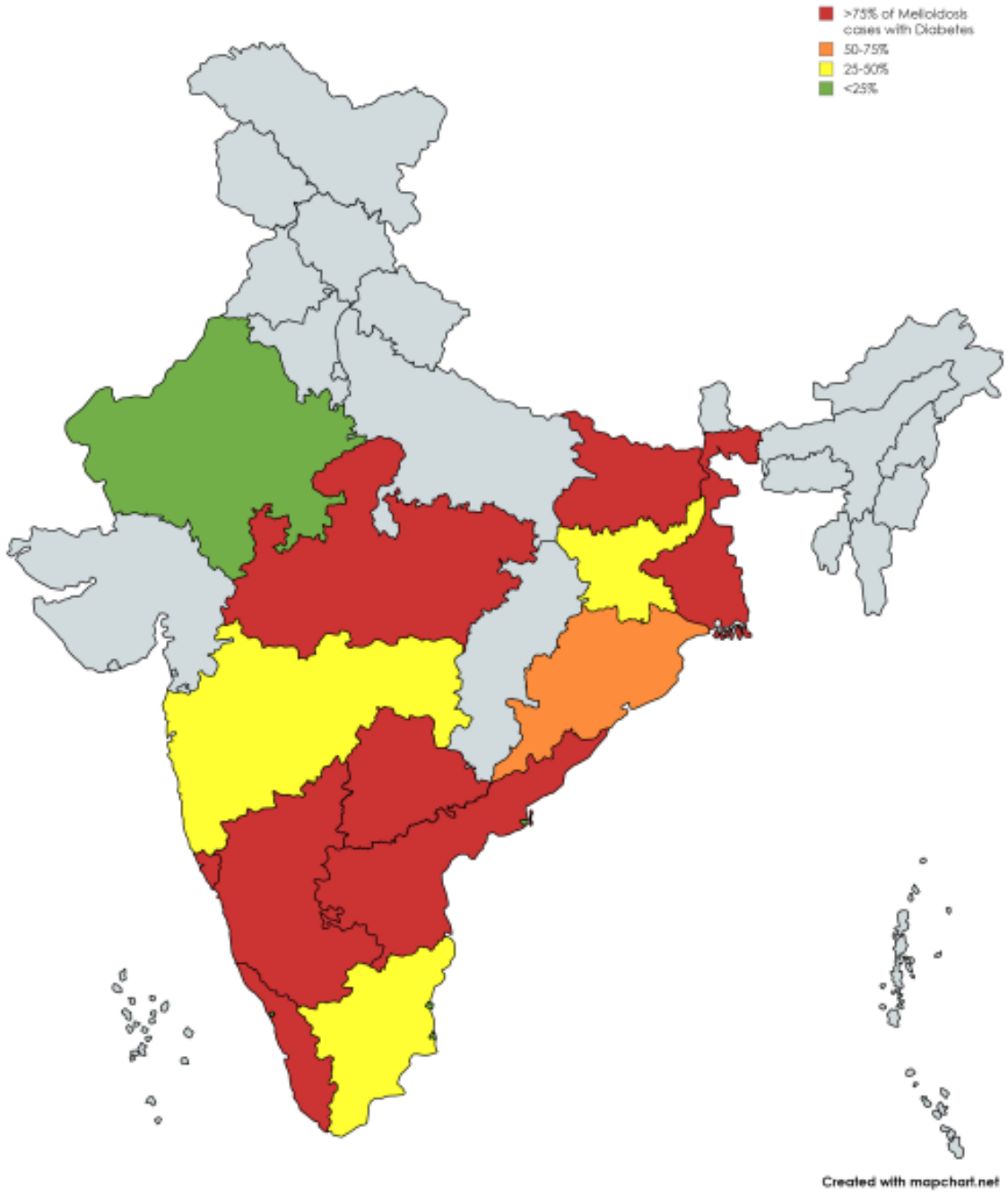

Fig. 1e. Diabetes cases with melioidosis – data extracted from (53) (Grey – not included and high to low is indicated in red>orange>yellow>green

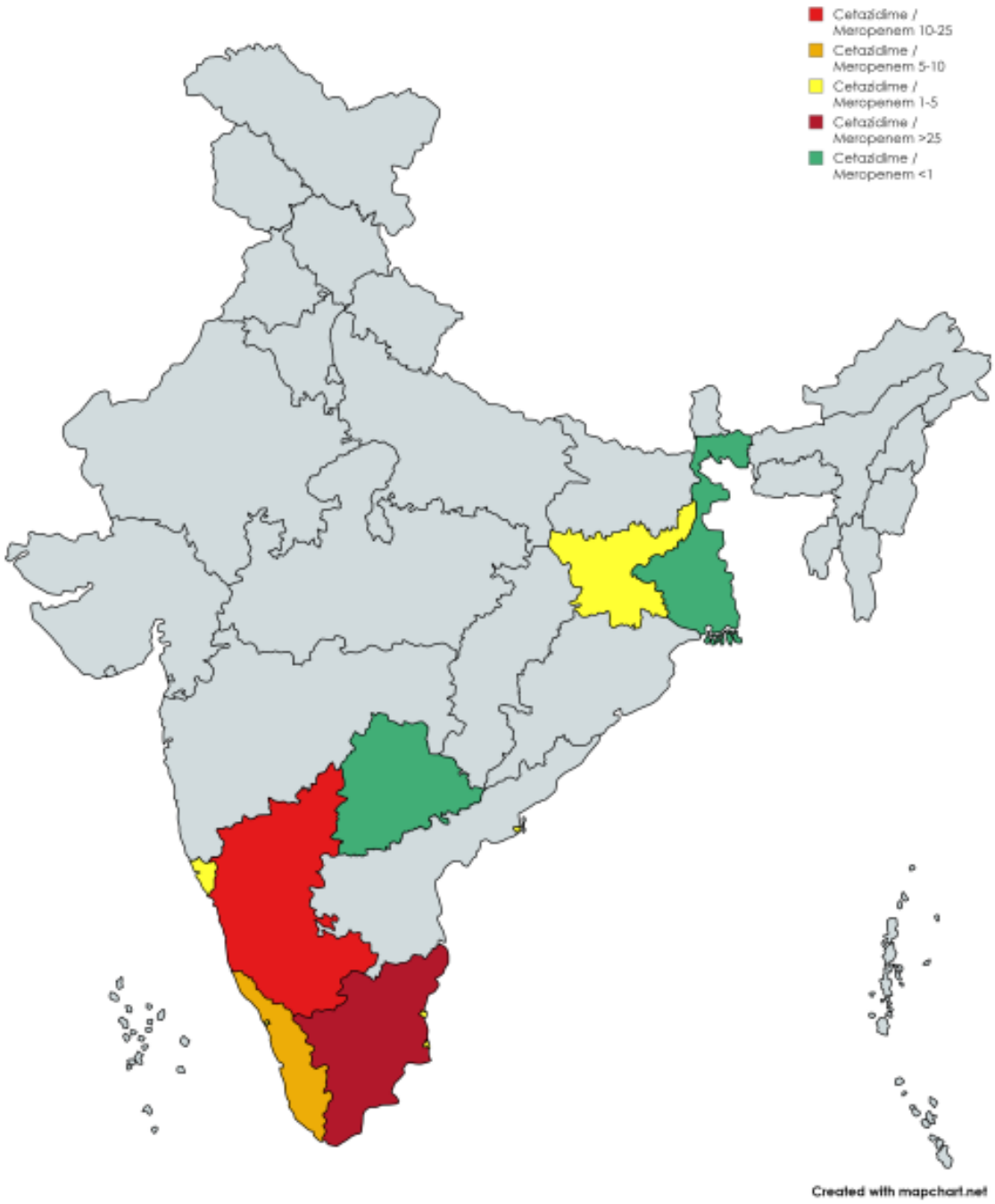

Fig. 1f. Ratio of Ceftazidime / Meropenem consumed by melioidosis patients – data extracted from (53) (higher the ratio shows preference to Ceftazidime than meropenem as seen in Tamilnadu > Karnataka> Kerala> Odisha, Goa>Telangana>West Bengal

Table 1. Five years grouping of publication on melioidosis in India based on various factors obtained by search word "melioidosis prevalence India"

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

Table 3. Clinical profile reported in literature

Studies (95-101,88)	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%					
Bacteremia		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%								

Table 4. Districts in northeastern states that have conducive factors for melioidosis – Diabetes, Pneumonia hotspots, overty as extracted from studies [102-104]

State	Diabetic hotspot District
Assam	Jorhat, Sivasnagar, Majuli, Dhemaji, LAkhimpur
Mizoram	Aizawl, Champhai, Lunghai, Serchip
Meghalaya	East Khasi Hill
Manipur	Chandel, Tangnoutal, Churachandpur, Bishnupur, Pherzawl
Nagaland	Mon, Wokha,Tuensang, Zunheboto, Longieng, Mokochung, Kohima
Sikkim	mostly with highest from west sikkim
Tripura	South Tripura, Gomati, Khowai, West Tripura, Sepahuala
Arunachal	Tawang
	** In Meghalaya- mostly it is Diabetic coldspot except east khasi hill and in Arunachal, Tawang is a Diabrtic cold spot
State	**Below Poverty line Districts**
Assam	Nagoan, Hajai, Kkrajhar, Chirang, Dhuburi, Goalpara
Mizoram	
Meghalaya	
Manipur	mostly
Nagaland	
Sikkim	
Tripura	Unokoti, North Tripura, , South Tripura, Gomati
Arunachal	Anjaw, Changlang, Khonsa, Khasa
State	**Pneumonia Hotspot districts**
Assam	Morigoan, Golaghat, Lakhimpur
Mizoram	
Meghalaya	widely prevalent
Manipur	
Nagaland	
Sikkim	
Tripura	South Tripura, Gomati, Khowai
Arunachal	Tawang, Kurung Kurmey, Anjaw
State	**Pneumonia Death Hotspots**
Assam	Districts near Bangladesh - Dima Hasan, Cacha, Sonitpur, Nagaon, Dispur, Kamrup, Barpeta
Mizoram	Saiha, Manmit
Meghalaya	East Khasi Hill

State	Diabetic hotspot District
Manipur	Imphal
Nagaland	Peren, Mon
Sikkim	south west sikkim, souh sikkim bordering West Bengal
Tripura	districts bordering Bangladesh
Arunachal	Tirap, Langding

Table 5. Districts in selected states where ICMR – KMC TF study has been implemented on Melioidosis (Green – Higher cases of Diabetes, Yellow – lower cases of anemia, Orange – higher cases of anemia as in Poshan tracker website https://www.poshantracker.in/)

State / UT	Districts with high incidence of Diabetes		Low Anaemia		High Anaemia
Delhi	South Delhi		North East		North West
Arunachal	Changlang	Papumpare	East Siang		
Assam	Kamrup	Cachar, Tinsukia	Kamrup		Nagoan
Manipur	Tamenglong	Imphal	Churachandpur	Thoubal	Imphal
Meghalaya	Ribhoi		East Garo	Ribhoi	East Khasi
Mizoram	Saiha		Kolasib		Aizawl
Nagaland	Mon	Zunheboto	Mokoching		Dimapur
Odisha	Gajam, Sambalpur, Khordha	Kalahandi, Kandhamal	Sundargarh		Ganjam
Rajasthan	Pratapgarh		Nagaon		Jaipur
Sikkim	South District	North District	North District		East District
Tripura	Dhalai		Dhalai		West Tripura
Madhya Pradesh	Raigarh	Sehore	Jabalpur		Indore
Kerala	Idukki, Kottayam	P theta, Thrissur	Kannur		Malappuram
Karnataka	Bangalore, Kodagu	Mandya	Raichur		Bangalore

Table 6. Hospitals in specified Indian states that have publications on Melioidosis [105-124]

Kerala
Kerala Institute of Medical Sciences (KIMS), Trivandrum, Kerala.
Department of Neurology, Sree Chitra Tirunal Institute for Medical Sciences and Technology, Kerala,
BMH Gimcare Hospital, Kannur, Kerala, India
St. James Hospital, Chalakudy, Kerala, India
Department of Orthopaedics, Government Medical College, Kozhikode
Government Medical College, Thiruvananthapuram, Kerala, India
Department of Neurosurgery, Lisie Hospital, Ernakulam, Kerala, India
Karnataka
Department of Microbiology, Father Muller Medical College, Mangalore, India
Department of Medicine, MVJMC and RH, Hoskote, Bengaluru - 562 114,
Department of Pulmonary Medicine, K.S. Hegde Medical Academy, NITTE
Odisha
Department of General Medicine, KIMS, Bhubaneswar
Department of Microbiology, All India Institute of Medical Sciences, Bhubaneswar
Internal Medicine, Srirama Chandra Bhanja (SCB) Medical College and Hospital
Department of Microbiology, Kalinga Institute of Medical Sciences, Bhubaneswar
Rajasthan
Fortis Escorts Hospital, Jaipur, Rajasthan, India.
Department of Medicine, All India Institute of Medical Sciences, Jodhpur
Assam
ICU and Critical Care, Ayursundra Super Speciality Hospital
Department of Microbiology, Excelcare Hospitals, Guwahati
Department of Medicine, GMCH, Guwahati, Kamrup (Metro)
Delhi
Department of Microbiology, Fortis Flt. Rajan Dhall Hospital, Vasant Kunj
Neurology, AIIMS, New Delhi
Department of Medicine and Microbiology, Army Hospital (Research and Referral)
Department of General Medicine, Sir Ganga Ram Hospital

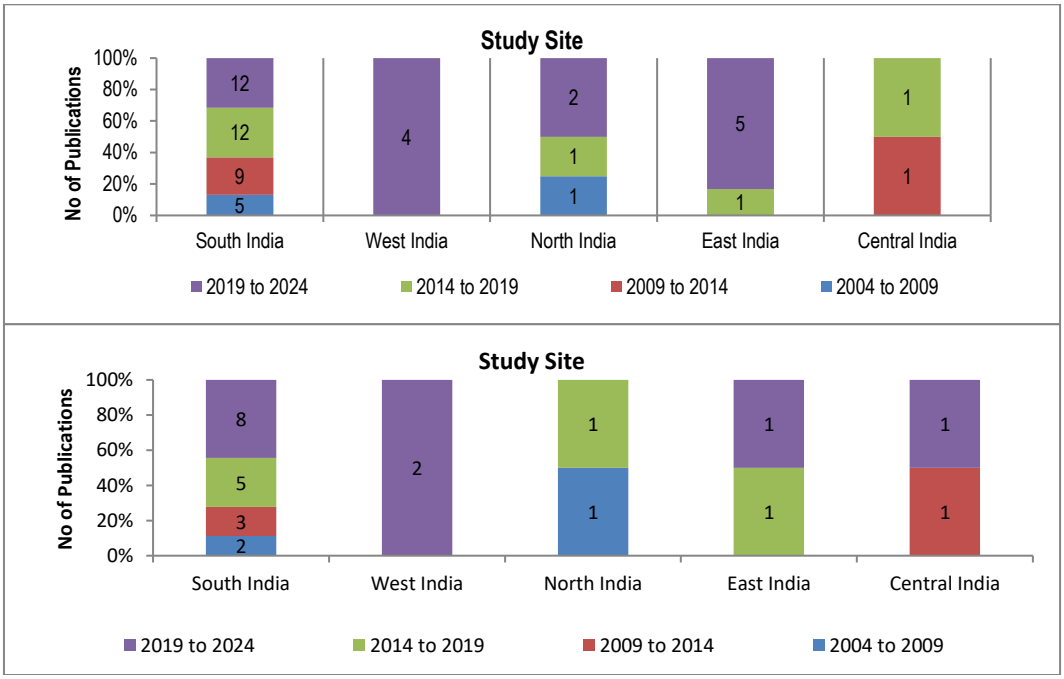

Fig. 2a. Publications on melioidosis in India (top with prevalence as key search word & bottom with risk factor as key word)

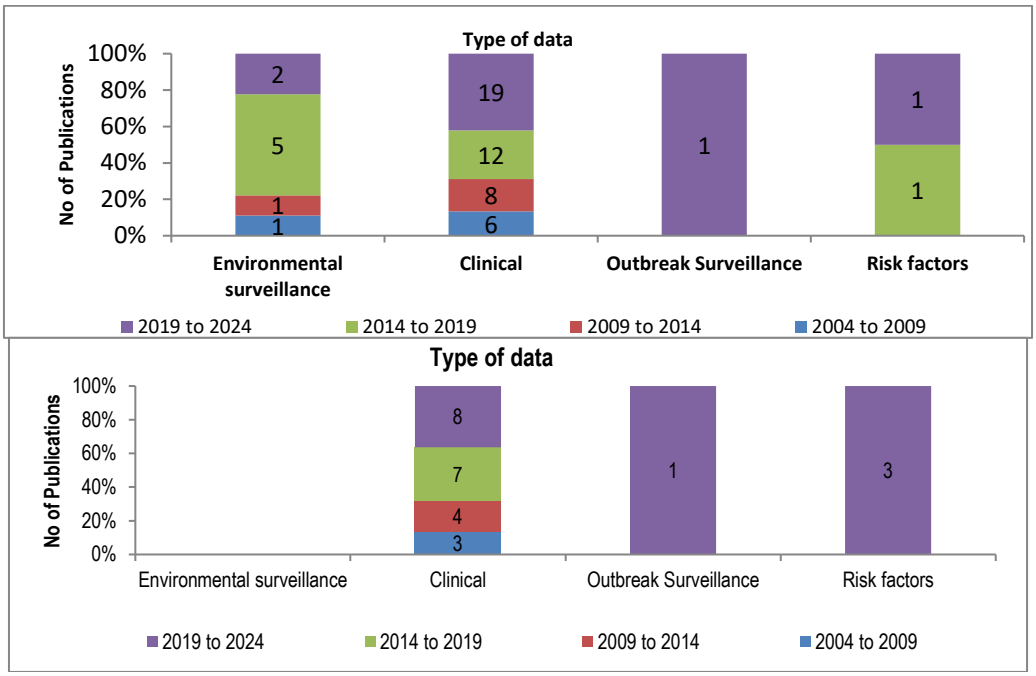

Fig. 2b. Type of data presented in publication (top with prevalence as key search word & bottom with risk factor as key word)

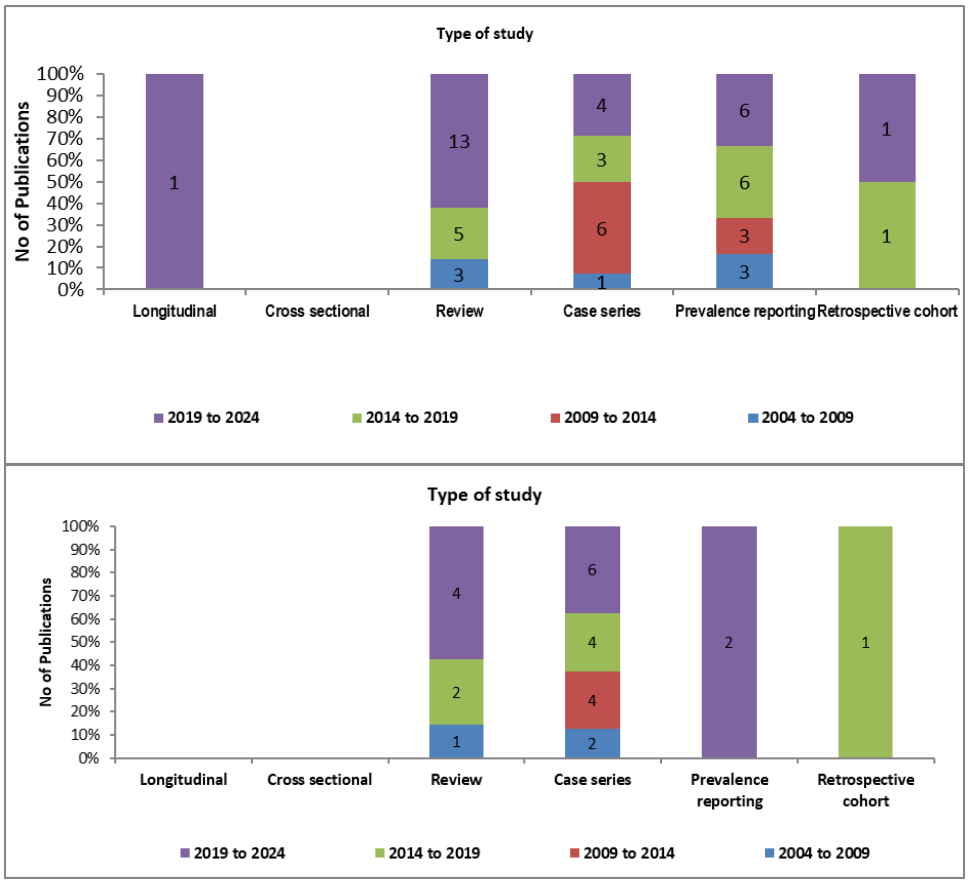

Fig. 3 Type of study presented in the publication (top with prevalence as key search word & bottom with risk factor as key word)

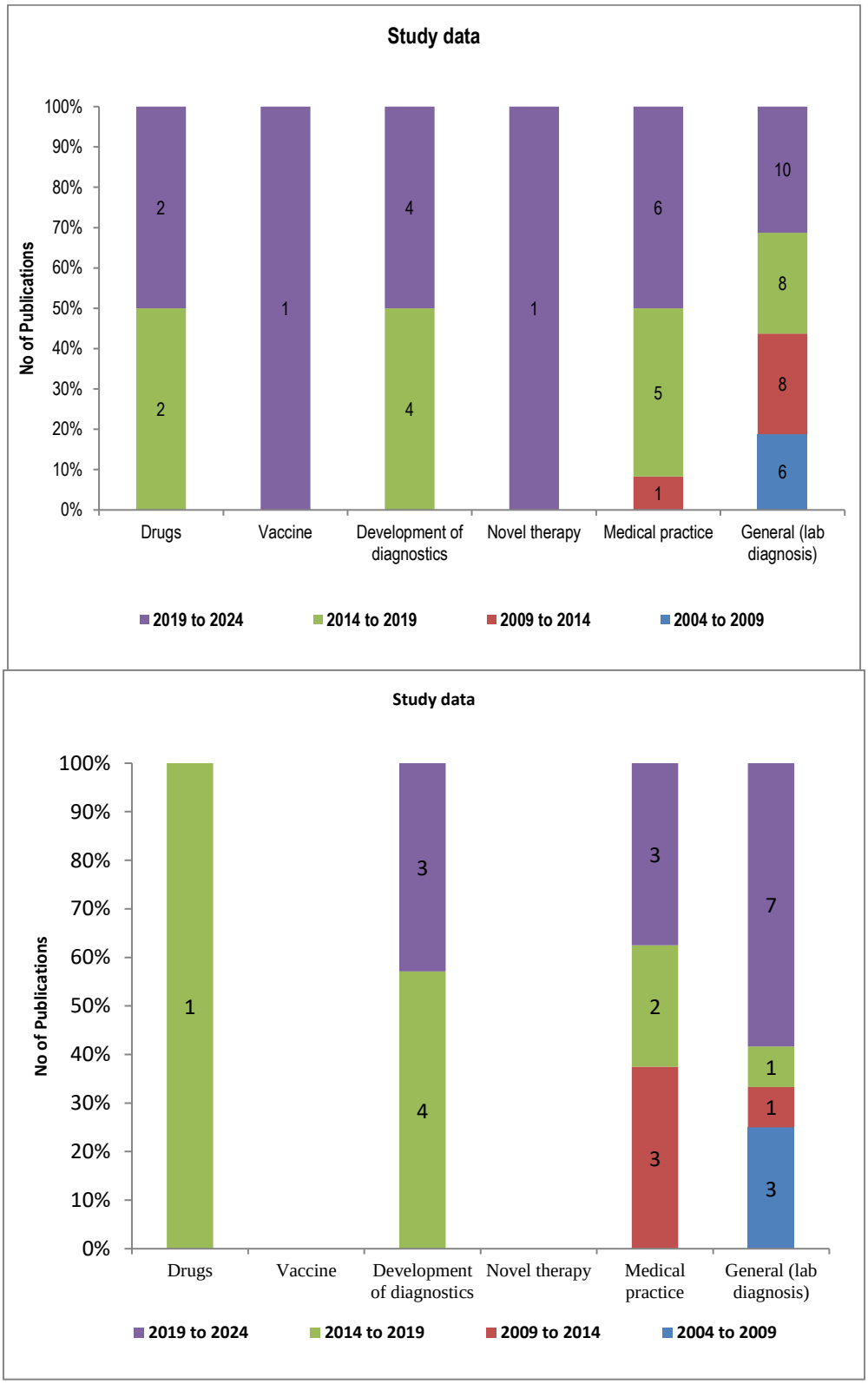

Fig. 4. Study describing data on (top with prevalence as key search word & bottom with risk factor as key word)

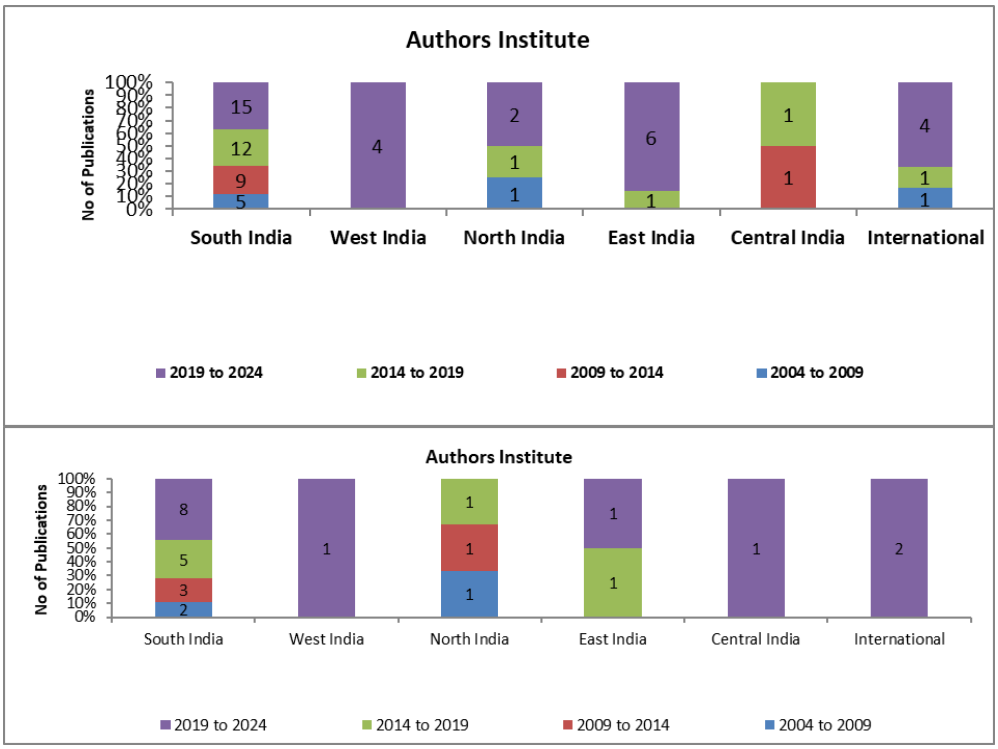

Fig. 5. Publication authors location (top with prevalence as key search word & bottom with risk factor as key word)

The states that had highest female diabetic population in NFHS 5 data (2019-2020) were Kerala, Goa followed by Andhra Pradesh, Ladakh as shown in Fig. 1b. This is followed by Tamil Nadu, Punjab, Jammu, Telangana, Odisha, West Bengal, Assam, Sikkim, Tripura. Moderate incidence included Karnataka, Maharashtra, Gujarat, Rajasthan, Haryana, Uttar Pradesh, Bihar, Arunachal, Meghalaya, Mizoram, and Manipur. The least was in Madhya Pradesh, Chhattisgarh and Jharkhand.

Two other studies (93,94) indicating diabetes incidence in India is shown in Figs. 1c and 1d. In another study from Kasturba medical college, Manipal it has been documented 20-year data on prevalence of melioidosis in many states in India (Fig. 1e). 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). Tamil Nadu 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. Further as seen in Fig. 1f, the Ratio of Ceftazidime / Meropenem consumed by melioidosis patients from Mukhopadhyay, 2018 indicated preference to Ceftazidime than Meropenem in the following states with high to low preference - Tamil Nadu, Karnataka, Kerala, Odisha, Goa, Telangana, West Bengal.

f. Family inclusive capacity building and other unconventional ways like use of agricultural portal of soil health card (SAMC Conference 2023):

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 [95-98].

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. Such practices would help to encompass vulnerable groups like children, farmers [99-101]. Discussion with school teachers helped to understand how teaching methods during COVID prevented fomite transmitted infection and 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.

The use of agricultural softwares like soil health card could aid in identification of soil that has favourable parameters to harbour *B. pseudomallei.*

Possible recommendations and future directions: The manuscript highlights areas that need to be worked upon for better control of melioidosis in India. In 2022, ICMR funded project has been implemented by KMC Manipal in 14 states including all the 8 northeastern states, but the overall prevalence in every other state of India is not yet known. Hence one other way is to focus on known risk factors of melioidosis like diabetes, poverty to reach out to states that has highest of these or to predict districts within a state.

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, Tamil Nadu, Odisha, West Bengal, Arunachal, Tripura, Jammu, Himachal. Hence these states could have higher cases of melioidosis.

Further in the northeast India, districts predicted with higher possibilities of melioidosis due to risk factors of diabetes, poverty and pneumonia are shown in Table 4 and in the states where ICMR study has been implemented on melioidosis, the possible districts with higher incidence of diabetes and anemia is represented in Table 5. Table 6 represents hospitals that have publications on melioidosis but not under a centralized ICMR sponsored project.

4. CONCLUSION

In Countries wherein melioidosis hotspots are not known, risk factor hot spots could be used as surrogate presumptive hot spots like that of diabetes, poverty in case of melioidosis.

Out of pocket expense for melioidosis treatment could be a crucial factor for drug resistance since Ceftazidime is cheaper than carbapenem. Different states had different levels of preference for Ceftazidime over other antibiotics. Hence the socio-economic status of patients could play a role in the choice of antibiotics in different states of India. It was observed that the studies on Vaccines and diagnostics were poor and this area needs to be worked upon largely. Based on publications it can be observed that South and Eastern India have more awareness on Melioidosis and cases detected than other parts.

Unconventional modes of capacity building like use of soil health card and family inclusive capacity building could be beneficial for rapid capacity building in a vast and populated country like India.

DISCLAIMER (ARTIFICIAL INTELLIGENCE)

Author(s) hereby declare that NO generative AI technologies such as Large Language Models

(ChatGPT, COPILOT, etc) and text-to-image generators have been used during writing or editing of manuscripts.

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COMPETING INTERESTS

Authors have declared that no competing interests exist.

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