Clinical and epidemiological profile of melioidosis in a tertiary care teaching hospital from South India

Rosmi Jose[1*], Chithra Valsan[2], Sathiavathy K A[3]

[1]Assistant Professor, [2,3]Professor, [1-3]Dept. of Microbiology, [1-3]Jubilee Mission Medical College and Research Centre, Thrissur, Kerala, India

Correspondence Author: Rosmi Jose
Email: rosdinmi@gmail.com

Abstract
Melioidosis, which is mainly prevalent in Thailand and Australia, has shown an increasing trend in India in the last few years.
Aim: of this study was to evaluate clinical profile of melioidosis cases in South Indian state Kerala.
Materials and Methods: We retrospectively studied 37 culture proven cases of melioidosis admitted in a tertiary care teaching hospital in South India during January 2013 to December 2017. Demographic data, predisposing factors, clinical presentations, complications, management and outcome were noted and analysed.
Results: There was male preponderance (67.5%) in the study group and the mean age of study group was 43 years and majority of the patients were between the age group of 40-60 years. There was clustering of cases during the rainy season. Diabetes mellitus was present in 67.5% of the cases. Fever was present in 56.7% of cases. Skin and soft tissue (32.4%) involvement was the most common presentation followed by pulmonary melioidosis (29.7%). There were 40.5% of bacteremic melioidosis. Overall mortality was 24.3% and it was 40% among bacteremic cases and 13.6% among non bacteremic melioidosis.
Conclusion: Melioidosis is not uncommon in this part of the country. Clinical profile of Melioidosis cases here are not exactly same as that of other endemic areas of the world. Bacteremic melioidosis has a poorer prognosis than non-bacteremic melioidosis.

Keywords: Melioidosis, Clinical profile, South India.

Introduction
Melioidosis is an infectious disease caused by *Burkholderia pseudomallei* a Gram negative soil dwelling bacterium. It was first described by Alfred Whitmore and Krishnaswami in 1912.[1] Melioidosis emerged as an infectious disease of major public health importance in South East Asia and northern Australia in the latter half of 20th century.[2] Cases of melioidosis have been reported from India since 1991.[3] Now it is an emerging infectious disease in India, as is evident from many case reports and case series from various parts of the country, especially from the eastern and western coastal regions.[4-9]

In the endemic regions, *B. pseudomallei* is present in the surface water and soil. Humans are typically infected via percutaneous inoculation, inhalation and ingestion. Clinical presentations of melioidosis vary widely from acute fulminant septic illness to chronic infection. The protean manifestations of melioidosis often lead to clinical under-diagnosis of this fatal condition. In addition to this, poor awareness of melioidosis among the clinicians, lack of proper laboratory facilities as well as expert clinical microbiologists also contribute to the misdiagnosis of the disease. With this study, we have aimed to raise the awareness of melioidosis, especially the clinical profile and outcome of the cases as it is an emerging infection in our country.

Materials and Method
The study was carried out in a tertiary care teaching institute in central Kerala, a state in Southern India. The study group comprised of thirty seven cases with culture proven melioidosis diagnosed during a period of six years (1/1/2012 to 31/12/2017). In all the cases, the culture isolate was identified as *B.pseudomallei* by Vitek 2 (Biomerieux) system. Medical records of the patients were reviewed and analysed retrospectively for demographic data, clinical characteristics, management, complications and clinical outcomes.

The gender and age of the patients were recorded. Patients were classified into the following age groups- children (≤13 years), young adult (>13 to ≤18 years), adult (>18 to ≤ 40years), middle-aged (>40 to ≤ 60 years), old aged (>60 years). The age groups were assigned based on previous studies, which noted that usually an individual acquire the risk factors for melioidosis, in particular type 2 diabetes mellitus, after the age of 40.[7]

The month of admission of the patients was recorded and it was grouped into two seasons- dry season (October to May) and rainy season (June to September). This was done to study the influence of environmental factors on the occurrence of the disease. Based on clinical presentation of the disease and the type of specimen that gave positive culture for *B. pseudomallei*, cases were categorised as 1) Non-bacteremic 2) Bacteremic with focal lesions and 3) Bacteremic without focal lesions. Risk factors for melioidosis noted were diabetes mellitus, chronic disease of the lung, kidney or liver, chronic alcoholism, immunosuppression and malignancy.

Statistical analysis was performed to check the frequencies of demographic data, clinical presentations and mortality. For association statistical analysis, single and multiple logistic regression estimations were used between the dependent (outcome of melioidosis) and independent variables (risk factors).

Results

There were 37 cases of melioidosis over a period of six years from January 2012 to December 2017. The study group included 25(67.5%) males and 12(32.5%) females. The mean age of patients was 43 years (SD +/-18.9). Majority of the patients belonged to the middle aged group (n=16, 43.2%). There were three paediatric patients (8.1%) in our study group. All the patients were from central part of Kerala – 15 cases from Thrissur, 15 cases from Palakkad and 7 cases from Malappuram districts. There were cases of melioidosis round the year but maximum cases presented during the rainy season, particularly in the months of July and August. (Fig. 1) Only three cases were diagnosed during the year 2012 which rose to 11 in the year 2014 with an average of six cases per year over 6 years. (Fig. 2)

The risk factors noted in our study population were diabetes mellitus (n=25, 67.5%), chronic liver disease (n=6, 16.2%), chronic lung disease (n=1, 2.7%) and chronic alcoholism (n=2, 5.4%). Other comorbid conditions noted include rheumatic heart disease, mixed connective tissue disorder, Steven Johnson syndrome, renal transplantation, carcinoma oesophagus and hypothyroidism. There were seven patients who had no risk factors or co morbidities. Three patients were on anti-tuberculous drugs at the time of diagnosis.

Patients had varying clinical presentations (Table 1). Bacteremic melioidosis was present in 40.5% patients (n=15), of whom two patients had multifocal involvement; eight had single focal involvement whereas in five cases no foci could be identified. Among the non-bacteremic cases (n=22), four patients had multifocal involvement whereas 18 patients had only one foci involved.

The most common clinical presentation was fever, present in 56.7% cases (n=21). Other clinical features included abscesses at various sites (n=11, 29.7%), respiratory infection (n=11, 29.7%), cervical lymphadenopathy (n=5, 13.5%) and cellulitis (n=5, 13.5%). Respiratory infections included pneumonia, lung abscess and pyothorax. (Fig. 3) Rare clinical features included osteomyelitis, otorrhoea, pelvic inflammatory disease and mediastinal lymphadenopathy.

Two patients had abscesses at multiple sites- one case had abscess at leg, liver and submandibular abscess; another case had psoas and prostatic abscess together. Splenomegaly was present in five cases (13.5%) and hepatomegaly in two cases (5.4%). Haemoglobin was below 10mg/FL in 13 cases (35.1%). Leukocytosis was present in 17cases (45.9%), leukopenia in 2 cases (5.4%) and neutrophilia in 18 cases (48.6%). *B. pseudomallei* was isolated from different samples. Blood culture was positive in 15 cases (40.5%). The organism was isolated from aspirated pus samples in 12 patients (32.4%). The samples from which *B. pseudomallei* have been isolated is listed in Fig. 4.

Standard treatment for melioidosis was initiated in 18 cases (48.6%) upon culture isolation of *B.pseudomallei*. Thirteen patients received complete multidrug therapy with Ceftazidime or Meropenem in the intensive phase followed by continuation therapy with Cotrimoxazole/ Doxycycline or Cotrimoxazole and Doxycycline. Nine patients who had received standard treatment recovered completely and no relapse was recorded. Five patients received mono therapy with either Ceftazidime or Meropenem. One patient with peri-tonsillar abscess cured with Ceftazidime monotherapy alone.

The mortality rate was 24.3% (n=9), six among them were not diagnosed of melioidosis at the time of death. Three patients died even after initiation of therapy, two of them were on Meropenem and one patient was on Ceftazidime and Doxycycline. Four cases were referred to other hospitals; three patients among them were not diagnosed at the time of discharge. One patient (2.7%) had relapse after 8 months of initial diagnosis and treatment with Ceftazidime and Doxycycline. It was a case of multiple abscesses (prostatic abscess and psoas abscess).

The important complications were sepsis (18.9%) and ARDS (13.5%). Among the bacteremic group, 40% developed sepsis and 26.6% had ARDS. Mortality rate was 40% among the bacteremic patients and 13.6% among the non-bacteremic group. (Table 4) Logistic regression analysis showed that there is definite association between septicaemia and mortality (p value <0.001). There were no other independent risk factors attributed to mortality.

Table 1: Clinical profile

Clinical feautures	% (n==37)
Skin & soft tissue	32.4
Cervical lymphadenitis	13.5
Genitourinary	10.8
Bone infection	5.4
Internal abscess	5.4
Neurological	2.7
Peritonsillar abscess	2.7
submandibular abscess	2.7
Otorrhea	2.7
Mediastinal lymphadenopathy	2.7

Table 2: Clinical types

Clinical type	% (n=37)
Non bacteremic	59.45%
Bacteremic without foci	13.5%
Bacteremic with foci	27%

Table 3: Abscess profile

Abscess site	Number
Peritonsillar	1
Submandibular	1
Arm	1
Elbow	1
Wrist	1
Thigh	2
Leg	1
Psoas	1
Lung	1
Liver	1
Spleen	1
Prostatic	2

Table 4: Complications and outcome

	Number	Sepsis	ARDS	Death
Bacteremia	15	6(40%)	4(26.6)	6(40%)
Non bacteremic	22	1(4.5%)	1(4.5%)	3(13.6%)
Total	37	7(18.9%)	5(13.5%)	9(24.3%)

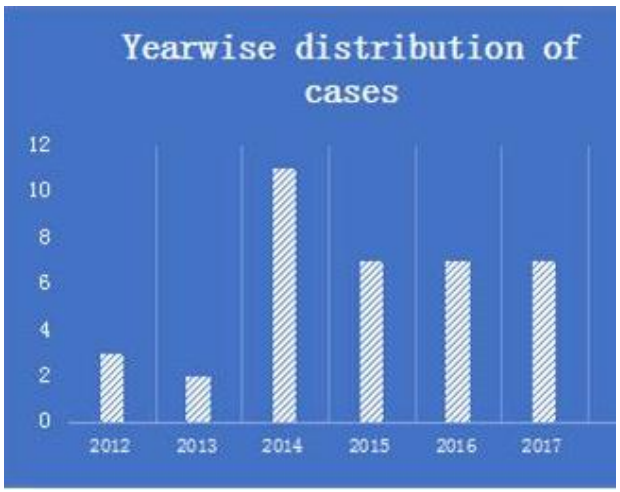

Fig. 1: Yearwise distribution of cases

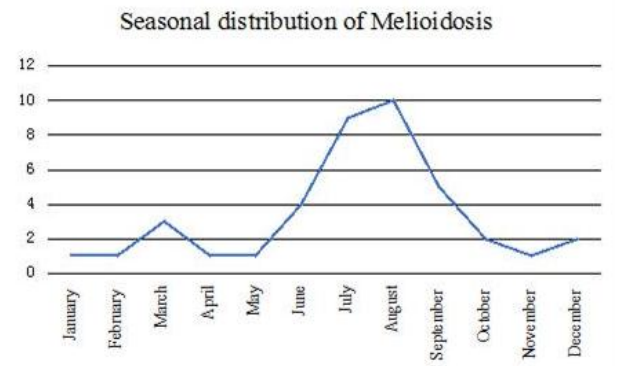

Fig. 2: Seasonal distribution of melioidosis

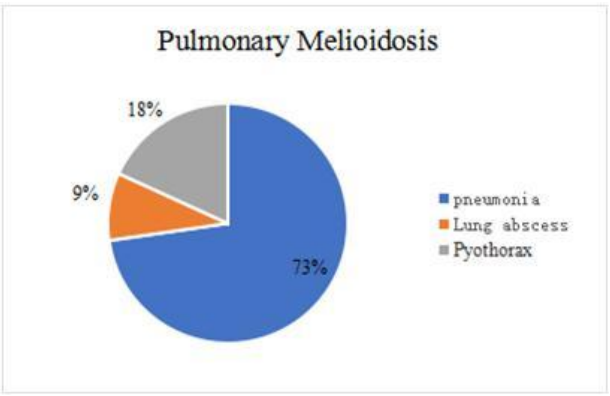

Fig. 3: Pulmonary melioidoisis

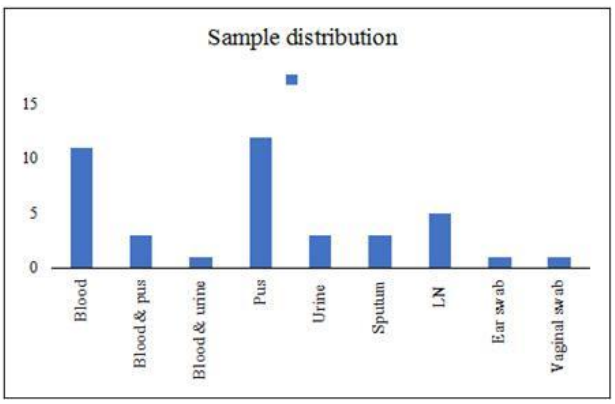

Fig. 4: Sample distribution

Discussion

The study was conducted in a tertiary care teaching hospital located in central Kerala, which is a 1500 bedded hospital which caters to patients mainly from three districts of central Kerala. Melioidosis cases have been diagnosed in this hospital since 2003, but more cases have been

diagnosed since 2012, this may be due to the installation of automated systems for bacterial identification. The increased awareness among the microbiologists about melioidosis in the recent times, might have also contributed to the increased number of case detection.

There was male preponderance as was found in other studies from India and other endemic areas probably due to their outdoor works.[10,11] Age distribution of cases was similar to that of other studies, maximum number of cases were noted between 40 to 60 years of age. This study showed 8.1% (n=3) paediatric melioidosis cases. Another study from South India also had 8% paediatric cases out of a total of 140 cases.[4] Studies from endemic areas have also shown 5-15% paediatric cases. [10, 11]

In our study, cases were clustered (75.6%) between June to September, corresponding to the monsoon season in Kerala. The association between melioidosis and rainfall has long been recognised with 75% and 85% of melioidosis cases occurring in the wet season in northeast Thailand and northern Australia respectively.[12, 13] In the above regions, the number of seasonal cases correlated with the total amount of rainfall. The increase in the transmission rate during the rainy season is due to the fact that bacteria move to the surface with the rising water table.[14]

In this study, 30 cases (81%) had risk factors either single or multiple. Diabetes mellitus was the most common predisposing factor (67.5%) in our study group which was similar to other South Indian studies.[4,5] In Thailand and Australia the estimated relative risk of melioidosis in diabetic patients has been reported to be 13.1 and 5.9 respectively.[13, 15] In our study, chronic liver disease (16.2%) was the next common predisposing factor, though it was not described in other studies. Chronic alcoholism (5.4%) was a less frequent risk factor in our study group compared to other similar studies.[4, 10] There were seven cases (18.9%) in this study without any risk factors or co morbidities, out of which three were paediatric patients. Various studies have shown that in contrast to adult patients, paediatric patients have no or less risk factors.[16, 17]

Melioidosis is well known to manifest as a febrile illness, ranging from an acute fulminant septicaemia to chronic debilitating localised infection. It can affect any system in the body and often mimic pyogenic bacterial infection, Gram negative septicaemia or tuberculosis. In our study majority of the cases (48.6%) had non-bacteremic localised infections. Superficial abscesses at various sites and cellulitis were the common clinical presentation next to fever. From the clinical profile, it is evident that melioidosis abscesses can develop anywhere in the body including both superficial and internal organs. It has been suggested that melioidosis should be considered in the differential diagnosis, when abscesses are encountered at unusual sites, such as spleen, prostate, and parotid with chronic presentation.[18] The next common clinical presentation was respiratory infections (29.7%), it was less when compared to studies from other endemic areas. Vidyalaksmi et al in their study from South India, has reported 32% cases of pulmonary melioidosis.[4]

In our study, cervical lymphadenopathy was present in 13.5% (n=5) cases. Although rare, lymph node involvement by *B. pseudomallei* has been reported earlier. There are studies which have reported suppurative involvement of inguinal nodes, mediastinal nodes as well as lymph nodes of the head and neck region by *B. pseudomallei*.[5, 15] Out of the five patients with cervical lymphadenopathy; three had received anti-tuberculous treatment, as their FNAC reports were suggestive of tuberculosis. Chronic melioidosis can be confused with tuberculosis clinically as well as histopathologically. Histopathology of these lesions can show granulomas[19] Isolation of *B. psuedomallei* from lymph nodes by culture can help to differentiate between tuberculosis and melioidosis. So in the endemic areas of melioidosis, in all cases of cervical lymphadenitis, it is important to send lymph node aspirate for bacteriological culture.

We had one case of osteomyelitis of hip joint. Even though bone and joint melioidosis is rare, there are reports of skeletal melioidosis from India as well as other parts of the world.[20, 21] Pelvic involvement is extremely rare in melioidosis, even in the endemic areas. Gynaecological manifestations of melioidosis are genital ulcer, cervicitis, pelvic inflammatory disease and tubo-ovarian abscess.[22] Otorrhoea is also a very rare clinical presentation of melioidosis.

The recommended treatment of melioidosis is divided into two phases: Intensive phase, consisting of in-patient treatment for at least 10-14 days with Ceftazidime or Carbapenems (Imipenem or Meropenem). Any one of these may be combined with Sulfamethoxazole-trimethoprim for neurologic, cutaneous, bone and prostatic melioidosis. In the eradication phase, treatment is given with oral Trimethoprim- Sulfamethoxazole for 3-6 months with or without Doxycycline.[23] *B. pseudomallei* is intrinsically resistant to many antibiotics including aminoglycosides and early generation cephalosporins. One of the commonly prescribed antibiotic, betalactam–betalactamase inhibitors are also not recommended for treating melioidosis. Betalactam – betalactamase inhibitors may decrease the bacterial load to some extent, but the patient may come back with relapse. Even after the microbiological confirmation and recommendation of the proper treatment, it is found in some occasions that the treating clinician refused to follow the recommendation, as the patient showed clinical improvement with other antibiotics.

In this study one case (2.7%) had relapse after completing treatment with Ceftazidime and Doxycycline. Recurrent melioidosis, after an apparent cure following the first episode, is well documented and has been studied extensively in the endemic areas. The reported rates of recurrent melioidosis are 16% in Thailand and 6% in Northern Australia.[24, 25] The reported determinants of relapse are the choice and duration of oral antimicrobial therapy, bacteremia on initial admission, multifocal distribution and diabetes mellitus. The present study shows that most of the patients, who died, were not diagnosed of melioidosis at the time of death. Therefore, early diagnosis

as well as initiation of standard treatment has a key role to play in decreasing the mortality and improving the patient outcome.

The development of septic shock appeared to be a strong predictor of mortality from melioidosis ($p < 0.001$) and correlates well with other studies. Non-bacteremic melioidosis appears to have a favourable outcome as compared to bacteremic melioidosis. Such trends have also been observed in Darwin study, in which mortality was 20% in bacteremic patients where as it was only 7% in non-bacteremic patients.[16] Vidyalakshmi et al reported that mortality was seen only in patients with bacteremia.

Conclusion

This study shows that melioidosis is not a rare disease in this part of the country. The epidemiological profile of Melioidosis cases in different parts of the Indian subcontinent and other endemic regions of the world are similar with respect to the age group, gender, risk factors and association with monsoon. We cannot generalise the clinical profile of Melioidosis due to the diverse clinical manifestations in different studies. But still, diabetic patients presenting with abscesses in unusual anatomical sites Melioidosis should be considered in differentail diagnosis. The presence of septic shock is a strong predictor of mortality. Bacteremic melioidosis has a poorer prognosis than non-bacteremic melioidosis. Good communication between the treating clinician and clinical microbiologist can reduce the delay in initiation of prompt treatment. More studies on melioidosis including environmental and seroprevalence studies are required to assess the actual burden of this disease in India.

Conflict of Interest: None.

References

1. Whitmore A, Krishnaswami CS. An account of the discovery of a hitherto underscribed infective disease occurring among the population of Rangoon. *Indian Med Gazette* 1912;47:262-7.
2. White NJ. Melioidosis. *Lancet* 2003;361:1715-22
3. Vidyalakshmi K, Lipika S, Vishal S, Damodar S, Chakrapani M. Emerging clinico-epidemiological trends in melioidosis: Analysis of 95 cases from western coastal India. *Int J Infec Dis* 2012;16:491-7.
4. saravu K, Mukhopadhyay C. melioidosis in southern india: Epidemiological and clinical profile. *Southeast Asian J Trop Med Public Health* 2010;41:401-9.
5. Gopalakrishnan R. Melioidosis: An emerging infection in India. *J Assoc Physicians India* 2013;61:612-4.
6. R Raghavan, K. Melioidosis in India. *Indian Pediatr* 1991;28:184-8.
7. Jesudasan MV, AmbarasuA, JohnTJ. Septicaemic melioidosis in a tertiary care hospital in South India. *Indian J Med Res* 2003;117:119-21.
8. John TJ, Jesudason MV, Lalitha MK. Melioidosis in India: the tip of the iceberg? *Indian J Med Res* 1996;103:62-5.
9. Kanungo R, Pradhan P, Battacharya S, Sriman- narayana J, Jayanthi S, Swaminathan RP. Melioidosis: a report from Pondicherry, South India. *J Assoc Physicians India* 2002;50:1438-9.
10. Currie BJ, Ward L, Cheng AC. The epidemiology and clinical spectrum of melioidosis: 540 cases from the 20 year Darwin prospective study. PLoS Negl Trop Dis 2010;4:900.
11. Zenter AR. The epidemiology and clinical spectrum of Melioidosis in a teaching hospital in North-Eastern state of Malaysia, a fifteen – year review. *BMC Infect Dis* 2016;16:333
12. Currie BJ, Fisher DA, Howard DM, et al. Endemic melioidosis in tropical northern Australia: a 10-year prospective study. *Clin Infect Dis* 2000;31:981-6.
13. Suputtamongkol Y, Hall AJ, Dance DA, Chaowagul W, Rajchanuvong A, Smith MD et al. The epidemiology of melioidosis in Ubon Ratchatani, northeast Thailand. *Int J Epidemiol* 1994;23:1082–90.
14. Thomas A, Forbes-Faulkner J, Parker M. Isolation of Pseudomonas pseudomallei from clay layers at defined depths. *Am J Epidemiol* 1979;110:515-21.
15. Cheng AC, Currie BJ. Melioidosis: epidemiology, pathophysiology and manage- ment. *Clin Microbiol Rev* 2005;18:383–416
16. Mohan A, Podin Y, Tai N, Chieng C-H, Rigas V, Machunter B, et al. Pediatric melioidosis in Sarawak, Malaysia: Epidemiological, clinical and microbiological characteristics. *PLoS Negl Trop Dis* 2017;11(6): 5650.
17. Sanderson C, Currie BJ. Melioidosis: a pediatric disease. *Pediatr Infect Dis J* 2014;33(7):770–71
18. Mathew S, Perakath B, Mathew G. Surgical presentation of melioidosis in India. Natl Med J India 1999;12:59-61.
19. Allen C. Cheng, Bart J Currie. Melioidosis: Epidemiology, Pathophysiology, and Management. *Clin Microbiol Rev* 2007;20(3):533
20. Pandey V, Rao SP, Rao S, Acharya KK, Chhabra SS. Burkholderia pseudomallei musculoskeletal infections (melioidosis) in India. *Indian J Orthop* 2010;44(2):216–20.
21. Raja NS, Scarsbrook C. Burkholderia pseudomallei causing bone and joint infections: a clinical update. *Infect Dis Ther* 2016;5:17–29.
22. Nernsai. A case report of Tubo-ovarian abscess caused by Burkholderia pseudomallei. *BMC Infect Dis* 2018:18:73
23. Currie BJ.Mandell,Douglas,and Benett's Principles and Practice of Infectious diseases. 7th edition2010:2869-80
24. Limmathurotsakul D, Chaowagul W, Chierakul W, Stepniewska K, Maharjan B, Wuthiekanun V, White NJ, Day NP, Peacock SJ. Risk factors for recurrent melioidosis in northeast Thailand. *Clin nfect Dis* 2006;43:979–86.
25. Maharjan.B, Chantratita.N, Vesaratchavest. Recurrent melioidosis in patients in northeast Thailand is frequently due to reinfection rather than relapse. J Clin Microbiol 2006;4:6032-4.

How to cite this article: Jose R, Valsan C, Sathiavathy KA. Clinical and epidemiological profile of melioidosis in a tertiary care teaching hospital from South India. *Int J Med Microbiol Trop Dis* 2019;5(2):107-111.