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Clinical Profile and Outcome of Patients with Melioidosis- A Single Center Retrospective Study

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Abstract

Objective: The objective of the study was to study the clinical profile, epidemiological profile, laboratory features, and outcomes among melioidosis patients.

Methods: A retrospective observational study was conducted at a tertiary healthcare center and 30 patients diagnosed with melioidosis were included and their case records were retrieved. Data which included clinical profiles, laboratory details and health outcomes and follow up details were collected and analyzed.

Results: All patients had a mean age of 49.93±12.79 years and included more male participants (86.67%). Abnormal SGPT, SGOT, GGT, and APT levels were also observed. Blood was the most common specimen used for diagnoses (83.3%) and most patients were diabetic (83.33%). Common symptoms included fever (93.33%) followed by breathlessness (43.33%) with lung involvement in 53.33% of patients. Of all patients, 26.67% were deceased over the course of the study.

Conclusion: Abnormal liver function tests along with presence of symptoms of fever, lung involvement, and possible diabetic state may be indicated for diagnostic tests for melioidosis while meropenem, septran, and ceftazidime showed high sensitivity toward melioidosis disease.

Keywords: Melioidosis, Burkholderia pseudomallei, Epidemiology, Mortality, Diabetes, Liver function tests.

INTRODUCTION

Melioidosis is an infectious disease caused by a Gram-negative environmental bacterium named Burkholderia pseudomallei; it is a life-threatening infection that is estimated to account for approximately 89,000 deaths annually on a global scale. This disease is endemic to tropical and subtropical regions and the organism can be of soil and water origin [1]. Melioidosis has an approximate global burden of over 46 lakh disability-adjusted life-years (DALYs) and is much higher than other tropical diseases like leptospirosis schistosomiasis, intestinal

nematode infections and dengue [2].

Melioidosis usually presents as a sub-clinical disease in immunocompetent individuals who fight off the infection due to immunity. Patients who progress to clinical manifestations after acquiring the infection are suspected of having melioidosis and further microbiologic confirmation is done to establish the treatment. Diagnosed patients are targeted for management and proper drug therapy [2].

The transmission of B. pseudomallei is aided by infected humans and other animals since it can be found in the sputum, pus, urine, and feces of infected individuals. It has also been theorized that the virulence of the infecting strain and susceptibility of the host influences the development of the disease [3]. In the recent past, a plethora of case reports, case series, and clinical papers addressing the etiological, epidemiological, pathological, and microbiological aspects, and treatment have been published [4-8].

Data regarding epidemiology and risk factors for mortality in Indian patients are scarce since diagnosis and reporting are uncoordinated and sporadic. The demographic and environmental factors seen in tropical countries as well as the coastal areas of India can favor the transmission of melioidosis due to the increased rainfall and temperature, loose soil, paddy cultivation, percentage of the population with diabetes and construction boom [9]. Even though Melioidosis is an uncommon disease with varied presentation and outcome, it is important to understand the clinical, and laboratory profiles, risk factors, and its association with the outcome, so that the disease can be diagnosed early and treatment started promptly thus reducing mortality and morbidity. Melioidosis cases have previously been identified in Southeast Asia (Thailand, Malaysia, and Singapore) and northern Australia. However, cases have been reported in Central and South America, Africa, India, and the Caribbean in recent times [10].

The present study was conducted with the aim to study the clinical profile, epidemiological profile, laboratory features, and outcome in patients with melioidosis. The objectives of the present study were: (1) To study the clinical features of patients with melioidosis, (2) To study the risk factors associated with melioidosis and its outcome and (3) To study the laboratory parameters, microbiological features, and its relation with treatment outcomes of patients.

METHODOLOGY

A retrospective observational study was conducted at a tertiary healthcare center located in South India between January 2010 and December 2022. All patients diagnosed with Melioidosis during the study period were included in the study.

Patients were included in the study if they were diagnosed with melioidosis with culture positivity (blood, sputum, tracheal aspirate, pus or tissue culture) and patients were excluded if they were diagnosed with melioidosis and the case records were missing.

The present study was conducted after obtaining clearance from the Institutional Human Ethics Committee (Ref no: PSG/IHEC/2023/Appr/Exp/070). Case records of the Patients whose cultures grew Burkholderia pseudomallei were retrieved and data which included clinical profile, outcome and follow up details was collected and analyzed. A total of 30 patients diagnosed with melioidosis were included in the final analysis.

Different parameters were considered for the present study. The normal levels of WBC

are 4,500 to 11,000 WBCs/uL, normal levels of neutrophils are 40% to 60%, the normal platelet count is 150,000 to 450,000 platelets/uL, normal creatine level is 0.7 to 1.3 mg/dL for adult males and 0.5 to 1.1 mg/dL for adult females, the normal range for blood sodium levels is 135-145 mEq/L, the normal range of bicarbonate is 22-29 mEq/L, normal SGPT level is between 7 to 56 U/L, normal SGOT level is 8-45 U/L, the normal range of ALP is 44 to 147 U/L and the normal level of GGT is 5 to 40 U/L, normal albumin range is 3.4 to 5.4 g/dL, mean direct bilirubin is 0 to 0.3 mg/dL in adults and mean indirect bilirubin is 0.2 to 0.8 mg/dL.

Data analysis:

All the analyses were performed using spreadsheets on Microsoft Excel 2021 (Office 365, Microsoft Corporation). The continuous variables were expressed by mean, standard deviation, minimum and maximum value. The categorical variables were expressed by frequency and percentage and results were provided by tables and figures.

RESULTS

Demographic data

Table 1 depicted the demographic characteristics of patients and shows that the present study included mostly of male participants (86.67%) when compared to females and all participants had a mean age of 49.93±12.79 years. The mean duration of clinical presentations among participants was 31±46.39 days and the mean duration of hospital stay was 9.43±6.69 days.

Table 1: Demographic Characteristics of patients ----------

Variable		N=30		%	
Gender	Male	26		86.67%	
	Female	4		13.33%	
		Mean	Standard deviation	Minimum value	Maximum value
Age (in years)		49.93	12.79	16	77
Duration of clinical presentation (in days)		31	46.39	1	180
Duration of hospital stay (in days)		9.43	6.69	1	25

Laboratory findings:

Table 2 depicted the laboratory findings of patients and the mean total WBC was 11.33±4.94x103/uL which was abnormally high, the patients reported mean neutrophil percentage of 82.78±11.05% which was also higher than the normal values and mean platelet count was 247666.67±131515.13 x103/uL which was higher than the normal range. The mean creatine level of all participants was 1.50±1.46 mg/dL which was abnormal, the mean bicarbonate level was 18.97±4.36 mEq/L which was lower than the normal range, mean sodium level was 131.70±6.90 mEq/L which was within the normal range. The liver function tests showed significant results with mean SGPT levels of 61.78±67.37 U/L which were abnormally high while mean SGOT level was 99.89±126.32 U/L which was also abnormally high, mean ALP was found to be 227.70±159.51 U/L which was higher than the normal range and mean GGT was 176.22±174.05 U/L which was considerably higher than the normal range. The mean albumin level was 2.60±0.56 g/dL which was lower than the normal range, mean bilirubin-direct was 1.30±1.35 mg/dL which was higher than the normal range and mean bilirubin-indirect level was 0.45±0.60 mg/dL which was within the normal range.

Table 2: Laboratory findings of patients with melioidosis

Variable	Mean	Standard deviation	Minimum value	Maximum value
Total count (x10^3/uL)	11.33	4.94	0.70	21.00
Neutrophil (in %)	82.78	11.05	54.70	97.10
Platelet (x10^3/uL)	247666.67	131515.13	37000.00	492000.00
Creatinine (mg/dL)	1.50	1.46	0.44	7.31
Bicarbonate (mEq/L)	18.97	4.36	6.70	26.50
Sodium (mEq/L)	131.70	6.90	119.00	150.00
SGPT (U/L)	61.78	67.37	6.00	351.00
SGOT (U/L)	99.89	126.32	16.00	495.00
ALP (U/L)	227.70	159.51	64.00	720.00
GGT (U/L)	176.22	174.05	14.00	834.00
Albumin (g/dL)	2.60	0.56	1.60	4.10
Bilirubin-direct (mg/dL)	1.30	1.35	0.10	5.50
Bilirubin-indirect (mg/dL)	0.45	0.60	0.10	2.80

Note: %-percentage, SGOT-Serum Glutamic Oxaloacetic Transaminase, SGPT-Serum Glutamic Pyruvic Transaminase, ALP-Alkaline phosphatases, GGT-Gamma-glutamyl transferas

Clinical profile

Table 3 depicted the clinical profile of the patients and showed that the most common symptom observed was fever (93.33%) followed by breathlessness in 43.33% patients. Diabetes mellitus was also a major finding with it being the comorbidity reported by a majority of the patients (83.33%) with lungs being the most involved (53.33%).

Table 3: Clinical profile of patients with melioidosis

Symptoms	n=30	%
Fever	28	93.33
Cough	12	40.00
Breathlessness	13	43.33
Headache	3	10.00
Vomiting	5	16.67
Abdomen pain	5	16.67
Loose stools	3	10.00
Dysuria	6	20.00
Joint pain	8	26.67
Skin involvement	7	23.33
Altered mental status	2	6.67
altered sensorium	1	3.33
seizures	1	3.33
weight loss	4	13.33
Comorbidities	**n=30**	**%**
Diabetes mellitus	25	83.33
Hypertension	3	10.00
CKD	2	6.67
CLD	3	10.00
COPD	1	3.33
Others *	9	30.00
Immunosuppressive state	2	6.67
Organ system	**n=30**	**%**
Brain	2	6.67

Symptoms	n=30	%
Lung	16	53.33
Kidney	2	6.67
Liver	8	26.67
Spleen	7	23.33
Skin, soft tissue and muscle	9	30.00
Bone and joints	8	26.67

Note: n-number of patients, %-percentage of patients, * other comorbidities-Pancreatitis, hyperthyroidism, Hansen's disease, multiple sclerosis, rheumatoid arthritis, tuberculoma, post renal transplant, pulmonary tuberculosis, # Certain patients showed more than one symptom.

Treatment outcomes

The specimen collected, drug sensitivity and treatment outcomes were depicted in table 4 and the results showed that blood was the most common specimen provided by patients (83.3%). Drug sensitivity was found to be present regarding Piptaz among 83.33% patients, Meropenem in 100% of patients, Septran in 93.33% of patients, ceftazidime in 100% of patients and doxycycline in 76.67% of patients. With regard to outcome, 26.67% patients were deceased which was an important finding, and 66.67% patients were discharged and 6.67% patients had discharged themselves against medical advice.

Table 4: Specimen collected, drug sensitivity and treatment outcome from patients with melioidosis

Specimen collected			
Type of specimen		**n**	**%**
Blood		25	83.3
Urine		0	0.0
Sputum		1	3.3
Tracheal aspirate		2	6.7
Pus		6	20.0
Tissue/muscle		1	3.3
Drug sensitivity			
Drug	**Sensitivity to isolate**	**n**	**%**
Piptaz	Yes	25	83.33
	No	3	10.00
	NA	2	6.67
Meropenem	Yes	30	100
Septran	Yes	28	93.33
	No	1	3.33
	NA	1	3.33
Ceftazidime	Yes	30	100
Doxy	Yes	23	76.67
	NA	7	23.33
Treatment outcome			
Outcome	**n**	**%**	**2 weeks follow up**
Discharged	20	66.67	19 cured, 1 symptomatic
Deceased	8	26.67	Not applicable
AMA	2	6.67	Not applicable

Note: n-number of patients, %-percentage of patients, AMA-Against medical advice. The total percentage may not be equal to 100 as there was more than one specimen collected from certain patients.

DISCUSSION

According to the National Centre for Disease Control, India was predicted to have the highest burden for the disease with 20,000-52,000 new cases/year and an approximate mortality rate of 32,000 deaths per year [11]. Between 1991 to 2018, 583 melioidosis cases were reported, with the southern coastal region of Karnataka and Tamil Nadu representing almost 80% of these cases [12]. The increased incidence of melioidosis in India subcontinent could be due to increased amount of diabetic patients with diabetes being a risk factor for melioidosis incidence [1]. Melioidosis has been found to affect multiple organ systems in previous studies which results in the high mortality rate of the disease [13].

The present study consisted mostly of male participants when compared to females and this was similar to the results of a study conducted by Hui et al, 2022 which aimed explore the clinical features, manifestations and drug resistance of melioidosis and also included 84.44% males [14]. Another study conducted by Tang et al, 2018 also reported all male melioidosis patients [15]. This has been reinforced in other studies [16-18]. The male predominance of melioidosis infection can be explained by bacterial transmission by soil and most farmers being male.

The participants of the present study had a mean age of 49.93±12.79 years. This was similar to results of a previously conducted study which reported melioidosis patients aged between 36 to 63 years [15]. A meta-analysis conducted by Chowdhury, 2022 also reported that the mean age of melioidosis infection was 46 years in India which is similar to the present study [16]. This result has been strengthened by that of another study stating that mean age of infection was 47.4±13.9 years [17].

The mean duration of clinical presentations among participants was 31±46.39 days, this was in disagreement with results obtained in an older study were clinical presentations were observed from 28 to 34 days which is much lower when compared to that of the present study [15]. A study conducted by Basheer et al, 2020 reported that the mean duration of melioidosis symptoms was 14 days which is considerably lower to that reported in the present study [17]. This difference could be explained by the difference in medical facilities available for management of the clinical symptoms.

The laboratory findings the study reported an abnormally high mean total WBC among the melioidosis patients. A high WBC count was also reported among melioidosis patients in a previously conducted study [14]. The liver function tests shows that mean SGPT, SGOT, ALP and GGT levels were high, this result was in accordance with that of a study conducted by Basheer, 2020 which reported that melioidosis infection had resulted in a mild rise in liver transaminases levels [17].

The mean albumin level was found to be lower than the normal range, this was in agreement with the results of a previously conducted study which reported similar mean albumin levels (2.8±0.7 g/dL) and reported that 83.8% patients had abnormally lower albumin levels. Similar findings were observed with regard to mean sodium levels with 66.7% showing abnormally lower serum sodium levels while the present study shows normal sodium levels [17].

Table 3 depicted the clinical profile of the patients and showed that the most common symptom observed was fever (93.33%) followed by breathlessness in 43.33% patients. This was in line with the results of a previous study that reported low fever to be

the most common symptom followed by respiratory infection [14]. Similar results were also reported in a study by Tang, 2018 where high grade fever was an initially reported symptom [15].

Diabetes mellitus was the comorbidity reported by a majority of the patients and this was reinforced by the results of a systematic review and meta-analysis conducted by Chowdhury et al, 2022 which identified diabetes as predominant comorbidity as well as predisposing factor for melioidosis. They also reported that a diabetic patient is three times more likely to develop melioidosis when compared to a non-diabetic [16]. This finding was reinforced by a previously conducted review on studies of melioidosis disease which reported that diabetes is an important risk factor for melioidosis being reported among 37 to 56% cases in Australia, 17 to 47% cases in Thailand, and up to 75% cases in in Malaysia [12].

During the course of the present study, lungs were found to be the most involved organ with melioidosis infection and the results of a study by Basheer, 2020 observed that pulmonary manifestations were common among melioidosis patients and was also independently associated with mortality of patients [17]. According to a review conducted in 2020 by Gassiep et al, pneumonia is the most commonly reported presentation of melioidosis, ranging from 51 to 61% patients [12]. This result was also in accordance to that of a case series conducted in Kerala by George, 2019 which stated that lungs were the most common organ involved in melioidosis patients [18].

The most common specimen provided by patients was blood and this was in agreement with a previously conducted studies that also reported that blood was the most provided specimen by patients [14,17]. All of the melioidosis isolates were found to be sensitive to Meropenem and this was similar to the results of a previously conducted study which reported that meropenem was found to be sensitive in 16 of 18 melioidosis isolated [18]. The results of a previously conducted study had also reported that all diagnosed melioidosis patients were sensitive to Septran (Sulfamethoxazole + Trimethoprim) [15]. The results showed that all melioidosis isolates showed sensitivity toward ceftazidime and this was similarly reported in a previously conducted study with 93% patient isolates showing sensitivity [14]. Another previously conducted study had reported similar results with ceftazidime showing susceptibility for all melioidosis isolates [18].

When considering health outcomes, 26.67% patients were deceased in hospital, 66.67% patients were discharged with no recurrence seen at 2 week follow up and 6.67% patients were discharged against medical advice. The reported mortality this is much higher when compared to the findings of a previously conducted study which showed only 2 deaths out of 45 patients over a five-year period [13]. A case series of 18 melioidosis patients over a period of 7 years showed only 1 death and much lower when compared to that of the present study [18].

The advantage of this study is that it is one of the first studies conducted to assess the clinical and laboratory profile among melioidosis patients in India. With the increased risk of melioidosis among diabetic patients and the prevalence of Diabetes Mellitus and impaired fasting blood glucose (IFG) in India reported to be 9.3% and 24.5% respectively in a study conducted by Mathur, 2022, it is essential to study the clinical and laboratory signs of melioidosis to ensure early diagnosis for a population prone to

infection [19].

The limitations of the present study include the lack of follow up data on discharged patients beyond 2 weeks as melioidosis shows a high chance of recurrence among recovered patients [14]. Future research should include extended follow-up durations to more accurately evaluate recurrence rates and long-term outcomes in patients with melioidosis. Establishing a systematic follow-up plan will yield significant insights into patient healing and recurrence. The present study's concentration on a singular healthcare facility in an area with a high prevalence of melioidosis may not accurately reflect the wider population. Extending the research to encompass many centers across diverse geographies will facilitate a more thorough understanding of illness prevalence and clinical manifestations.

Future directions include implementing a national surveillance system for melioidosis which would have the potential to greatly improve the accuracy of data collection and reporting. This would aid in comprehending the actual impact of the disease throughout India, particularly in areas that are often overlooked in reports. Investigations ought to delve into the pathways connecting diabetes with heightened vulnerability to melioidosis and pinpoint possible preventive measures. Promoting teamwork among microbiologists, epidemiologists, and public health officials can enhance the distribution of resources, the formulation of policies, and the implementation of public health initiatives focused on managing this overlooked disease. Future studies ought to focus on implementing clinical trials aimed at assessing innovative treatment protocols or preventive strategies specifically designed for high-risk groups, including individuals with diabetes.

CONCLUSION

The results of the present study state that diabetes is a predominant risk factor in the development of melioidosis infection. Fever is a common initial symptom of infection alongside increase in liver enzymes and lung involvement can be seen in the form of pneumonia. Meropenem, Septran and ceftazidime showed high sensitivity toward melioidosis isolates and can be used in its treatment after diagnoses after early recognition of symptoms.

Footnotes:

Ethical considerations: The study was approved by the Institutional Human Ethics Committee (IHEC, PSG/IHEC/2023/Appr/Exp/070).

Patient consent: Since this was a retrospective study and no patient details have been disclosed, patient consent was not obtained.

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Conflicts of interest: The authors declare no conflicts of interest.

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الملف السريري ونتائج المرضى المصابين بداء المليوئيدات: دراسة استرجاعية في مركز واحد

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الملخص

الخلفية والاهداف : كان الهدف من الدراسة دراسة الملف السريري والملف الوبائي والخصائص المعملية والنتائج بين مرضى داء المليويدات.

منهجية الدراسة أجريت دراسة مراقبة بأثر رجعي في مركز رعاية صحية ثالثي وتم تضمين 30مريضًا تم تشخيص إصابتهم بداء المليويدات وتم استرجاع سجلات حالاتهم .تم جمع البيانات التي تضمنت الملفات السريرية وتفاصيل المختبر والنتائج الصحية وتفاصيل المتابعة وتحليلها.

النتائج :كان متوسط عمر جميع المرضى 12.79 ± 49.93 عامًا وشملوا عددًا أكبر من المشاركين الذكور86.67) ٪ .(كما لوحظت مستويات غير طبيعية من SGPT و SGOT و GGTو .APT كان الدم هو العينة الأكثر شيوعًا المستخدمة للتشخيص83.3) ٪ (وكان معظم المرضى مصابين بمرض السكري83.33) ٪ .(وشملت الأعراض الشائعة الحمى 93.33)٪ (تليها ضيق التنفس43.33) ٪ (مع إصابة الرئة في53.33 ٪ من المرضى .من بين جميع المرضى، توفي26.67 ٪ منهم خلال فترة الدراسة.

الاستنتاجات يمكن أن تكون اختبارات وظائف الكبد غير الطبيعية إلى جانب وجود أعراض الحمى وإصابة الرئة والحالة السكرية المحتملة بمثابة مؤشرات للاختبارات التشخيصية لمرض المليويدوز، في حين أظهرت الميروبينيم والسيبتران والسيفنازيديم حساسية عالية تجاه عزلات داء المليويدوز.

الكلمات الدالة: داء المليوئيدات، البكتيريا الزائفة البوركهولديرية، علم الأوبئة، الوفيات، مرض السكري، اختبارات وظائف الكبد.