EPIDEMIOLOGICAL AND CLINICAL CHARACTERISTIC OF SEPSIS CAUSED BY BURKHOLDERIA PSEUDOMALLEI INFECTION AT NATIONAL HOSPITAL FOR TROPICAL DISEASES FROM 2016 - 2021

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Summary

Objectives: Describing the epidemiological and clinical characteristics of sepsis caused by *Burkholderia pseudomallei* infection at the National Hospital for Tropical Diseases.

Patients and methods: We did a cross - sectional descriptive analysis of 68 patients, diagnosis of sepsis caused by *Burkholderia pseudomallei* between January 2016 and July 2021 at the National Hospital for Tropical Diseases.

Results and conclusions: The mean age was 52.69 years old, mainly male (82.4%). The patients live mostly in rural areas (89.7%), who are scattered in 19 provinces in North and Central Vietnam concentrated in Ha Tinh, Thanh Hoa, Nghe An, Bac Giang and Ha Noi. The majority of occupation is farming, accounting for 52.9%. The disease mainly occurs in the rainy season from June to November (79.4%). The disease occurs mostly in patients with underlying medical conditions of which the most common is diabetes (57.4%). The duration from symptom onset to hospital admission is mainly over 7 days (75%), max 90 days. Lungs were the most commonly affected organs (63.2%). Abscess manifestations occurred in multiple organs: lung (2.9%), spleen (20.6%), liver (7.4%), kidney (1.5%), skin (7.4%), muscle (7.4%), brain (5.9%), salivary gland (1.5%). The rate of septic shock was high 20.6%.

Key words: *Melioidosis, Burkholderia pseudomallei.*

INTRODUCTION

Sepsis is a systemic toxic infection caused by the penetration of microorganisms and their toxins in the circulatory system, causing an important public health problem in the United States particularly endemic areas in Southeast Asia and Northern Australia. *B. pseudomallei* infection may have a long incubation period; which progresses over acute, subacute, or chronic course with clinical manifestations causes a delay in diagnosis and treatment[1]. Mortality rate for melioidosis ranges from 14% to 40% and can be as high as 80% if effective antibiotics are not used[2]. Previously, *B. pseudomallei* was thought to had little role in human disease, but in recent years, it has received much more attention and is also one of the remarkable bacteria causing community many dangerous complications such as septic shock leading to multi - organ failure with a high death rate. Whitmore (also known as melioidosis) is a dangerous acute infectious disease caused by the bacteria *Burkholderia pseudomallei*, which exists in the natural environment (found in soil and dirty water) and is infections in the North Central provinces of Vietnam with many deaths. With the current high mortality rate and high antibiotic resistance rate, to improve the diagnostic and treatment efficiency in patients with *B. pseudomallei* infections, we conducted this study with the following objectives: Epidemiological and clinical characteristics description of sepsis caused by *Burkholderia pseudomallei* infection at the National Hospital for Tropical Diseases from 2016 to 2021.

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SUBJECTS AND METHODS

Research subjects: 68 patients diagnosis with sepsis caused by *B. pseudomallei* at the National Hospital for Tropical Diseases from 2016 to 2021.

Including criteria: Patients 18 years or older, are confirmed of diagnosis of sepsis caused by *Burkholderia pseudomallei* infection when meeting the criteria (a) and (b):

a. The occurrence of at least two of the following criteria[3].

- Fever > 38.0°C or hypothermia < 36.0°C.
- Tachycardia > 90 beats/minute.
- Tachypnea > 20 breaths/minute.
- Leucocytosis > $12*10^9$/l or leucopoenia < $4*10^9$/l.

b. Blood culture test of isolation specimens, with identifying results as *Burkholderia pseudomallei.*

Exclusion criteria: Culture results of specimens as being co - infected with other bacteria. HIV - infected patients are also excluded.

Research methods

Methods: a cross - sectional descriptive study.

Research variables:

Epidemiology: Age, sex, underlying conditions, habitats, occupation, period of onset.

Clinical:

- Systemic symptoms: fever, sepsis shock.
- Lung.
- Skin and soft tissue.
- Nervous system infections.
- Bone/marrow.
- Liver, spleen, kidney.
- Parotid gland.
- Rate of the organ.

Paraclinical: Changes in blood count, inflammatory bilan (CRP, PCT), blood culture, and imaging were performed at the Central Hospital of Tropical Diseases. Blood culture in sheep blood agar, Ashdown agar,... Method of identification by automatic identifier Vitek 2 Compact (Biomerieux) to *B. pseudomallei*.

Data processing: According to statistical algorithms in SPSS 20.0 software.

RESULTS

There were 68 patients eligible for the study from 2016 to 2021.

Table 1. Epidemic characteristics (n = 68)

Characteristics		Case (%)
Sex	Male	56 (82.4)
	Female	12 (17.6)
Mean age		52.69 ± 12.98
Habitats	Rural	61 (89.7)
	Urban	7 (10.3)
Underlying conditions	Mellitus diabetes	39 (57.4)
	Chronic cardiovascular diseases	8(11.8)
	Cirrhosis/Chronic liver diseases	8 (11.8)
	Chronic kidney diseases	1 (1.5)
	Hematological diseases	2 (2.9)
	Alcoholism	10 (14.7)
	Immune suppressor/steroid	5 (7.4)
Occupation	Farmer	36 (52.9)
	Business owner	11 (16.2)
	Worker	8 (11.8)
	Pensioner/Housewife	13(19.1)
Period of onset	June to November	54 (79.4)
	December to May	14 (20.6)
Duration	≤ 7	17 (25)
	7-14	24 (35.3)
	>14	27 (39.7)

Comments: During the 5 - year study period (2016 - 2021), a total of 68 patients with a confirmed microbiological diagnosis were included in the study. The mean age was 52.69. A total of 82% of the patients were male. Most of the patients lived in rural areas, accounting for 86.1%. The patients were distributed in 19

provinces and cities, mainly in the Central Viet Nam region, most of whom were from Thanh Hoa, Ha Tinh, Nghe An, Bac Giang, and Ha Noi. The majority of the patients were farmers, accounting for more than half of the cases (53.2%). Symptom onsets were mostly from June to November which accounted for 59/79 (74.7%). Diabetes was the most common risk factor accounting for nearly 60% of cases. In addition, the rates of cardiovascular diseases, cirrhosis/chronic liver disease, and alcoholism were 15.2%, 11.4%, 12.7% respectively. The duration from symptom onset to hospital admission is mainly over 7 days (75%).

Table 2. Clinical signs and test/imaging results(n = 68)

Characteristics			Cases (%)
Systemic symptoms	- Fever - Sepsis shock		65 (95.6) 14 (20.6)
Lung (n = 43)	- Consolidation - Interstitial pneumonia - Pleural effusion - Pneumothorax - Abcess - Mediastinal lymphodema		23 (33.8) 13 (19.1) 15 (22.1) 1 (1.5) 2 (2.9) 6 (8.8)
Skin, soft tissue (n = 15)	- Pustules - Skin ulcer - Cellulatitis - Skin abscess - Muscle abscess		6 (8.8) 5 (7.4) 5 (7.4) 5 (7.4) 5 (7.4)
Bone/marrow (n = 6)	- Purulent arthritis - Osteomyelitis		5 (7.4) 3 (4.4)
Liver Spleen Kidney	- Liver abcess - Splenic abcess - Kidney		5(7.4) 14 (20.6) 1 (1.5)
CNS (n = 7)	- Meningitis - Brain abscess - Encephalitis		3 (4.4) 4 (5.9) 2 (2.9)
Parotid gland	Parotid abscesses		1 (1.5)
Main test results	WBC (G/l) (n = 68)		9.35 ± 4.86
	Mean CRP (mg/l) (n = 66)		170.124 ± 107.453
	Procalcitonin (ng/ml) (n = 50)	≤ 0.05	0
		0.05 - 2	22 (44)
		2 - 10	10 (20)
		>10	18 (36)

Comments: Most of the patients (95.6%) had fevers. Among the clinical signs, respiratory infections and soft tissue skin infections were the main causes leading to admission and hospitalization. Lungs were the most common site of infection (n = 43, 63.2%), followed by skin, soft tissue (n = 15, 22.1%); spleen (n = 14, 20.6%); bone and joint (n = 6, 8.82%); central nervous system (n = 8, 10.3%); liver (n = 5, 7.4%). Kidney abscess, salivary gland inflammation presented in 1 case each, accounting for 1.5%. Significant test results: The average white blood cell count on admission day was: 9.35 ± 4.86G/l. The average CRP index on admission day was 170.124 ± 107.453mg/l. Patients with procalcitonin from 0.05 - 2ng/ml accounted for 44%, followed by 36% of patients with procalcitonin > 10ng/ml.

DISCUSSION

The average age of patients in the study was 52.69 years old, mainly male (82.4%), male: female ratio was about 5 to 1. The average life expectancy of the population was higher than before and chronic diseases often appear at this age, the ages beyond 50 are still working age and patients still had contact with soil or mud. The intracellular phase of *Burkholderia pseudomallei* bacteria is very long so when suffering from chronic diseases, the patient will show signs of acute infection. The ratio of male: female was about 5 times, similar to Kingsley's study[4], 3 times higher than that of Nguyen Quang Huy's[5]. The cause of male predominance can be explained by more frequent exposure to soil and water in occupations such as agriculture or higher rates of alcoholism or chronic diseases (diabetes, cancer, etc) among men.

In our study, melioidosis patients mainly lived in rural areas, accounting for 89.7%. According to research by Nguyen Quang Huy at Bachmai Hospital, 85% of patients lived in rural areas[5]. *B. pseudomallei* is a bacterium mostly found in soil and water, so people in rural areas have higher exposure rates. In our study, the patients are mainly farmers, accounting for more than of the cases (53.2%), followed by pensioners, housewives, businessmen, and workers similar to our study. Nguyen Quang Huy accounted for

57.4%[5]. It could be explained that the patients are mainly exposed through occupational activities through the compromised mucosa or skin. In addition, an infection can happen if contact with soil and water around the house or through inhalation. Patients were distributed in 19 provinces and cities in Vietnam, mostly in the North and Central regions. There was 1 patient in the Central Highlands. Most of the patients were concentrated in Thanh Hoa, Ha Tinh, Nghe An, Bac Giang, and Ha Noi, which have also been reported in their previous epidemiology studies of melioidosis[5]. The main symptoms of the disease occurred from June to November, coinciding with the wet and rainy season of the North and Central regions 59/79 (74.7%). It could be explained that bacteria *B. pseudomallei* live mainly in the soil, when the water is wet, a large number of them accumulate in the soil, this surface water can grow in the air (aerosol) which could infect humans.

Diabetes is the most common risk factor of 57.4%, most of these cases had uncontrolled blood sugar, followed by, alcoholism, hypertension and cirrhosis/chronic liver disease accounting for 14.7%, 12.8%, and 11.8%; similar to the studies of Kingsley in Malaysia[4] and Nguyen Quang Huy[5]. The mechanism of the above factors affecting the likelihood of disease is the decline in neutrophil functions including chemotaxis, phagocytosis, and intracellular killing of bacteria.

In our research, the duration from symptom onset to hospital admission is mainly over 7 days(75%). Among them, 7 - 14 days accounted for 35.3%, over 14 days accounted for 39.7%. This was similar to that in Nguyen Quang Huy[5]. Most of the patients (95.6% or 65/68) had fevers. Most of the fever characteristics are high fever and chills, accounting for 83.5% in the setting of sepsis. In our study, septic shock occurred in 14/68 cases (20.6%) all had sepsis. This result is similar to the study of Currie and Nguyen Quang Huy, where the rate of septic shock was 21% and 19.1%, respectively[1,5].

Our study has the same pneumonia rate (63.2%) as Stewart's study at 61%[6] and Nguyen Quang Huy's study[5]. Most of the 43 patients (63.2%) with respiratory manifestations in our study had chest radiographs. Consolidation lesions accounted for 33.8%, followed by pleural effusions 22.1%. Patchy, interstitial and mediastinal lymphodema lesions accounted for a small proportion.This result was also similar to the Carrillo-Bayona study in which it reported 15 cases of pneumonia caused by Melioidosis, the most common was consolidation lesions followed by patchy lesions, cavity lesions, pleural effusion, and mediastinal lymphadenopathy[7]. Our study showed that lung damages caused by *B. pseudomallei* were diverse.

15 cases (22.1%) had soft tissue skin manifestations. Among them skin pustules accounted for 8.8%. Skin multiple pustules are common lesions caused by bacteremia migrated to the skin, as reported in the Gibney study[8]. Pneumonia and soft tissue skin infections accounted for the highest proportion of affected organs. It can be recognized that airborne and percutaneous infections were the most common routes of major infections of the disease.

Our study on clinical and diagnostic imaging has 6 cases of musculoskeletal system manifestation (8.82%). These data are similar to Kingsley's study was 9.3%[4] and Nguyen Quang Huy's study was 10.3%[5]. Among them, Purulent arthritis accounted for 7.4%, osteomyelitis 4.4%. In a study by Pui and Tan[9], the knee joint was the most common site of manifestation; which was consistent with our study as 4/5 cases of arthritis were shown at the knee joint.

From clinical, cerebrospinal fluid tests and imaging results, 8 patients presented neurological infection accounted for 10.3%. Brain abscess and menigitis are the two most common types. Our nerve infection rate was 7.4% higher than that of Nguyen Quang Huy[5] and Kingsley's study was[4].

Our study on the manifestation of visceral abscesses and other infectious foci in clinical and imaging studies found that the most common were splenic abscesses (20.6%); followed by liver abscesses (7.4%); renal abscess and salivary gland inflammation all accounted for total of 1.5%. Our results are similar to the study of Churuangsuk, where the rate of splenic abscesses was also the most common in the visceral abscess (20.9%)[10]. Inflammation of the parotid and submandibular salivary glands was detected in 1 patient (1.5%) in our study with red, painful swelling of the parotid and submandibular glands. This result is similar to Kingsley's study[4]. Salivary gland inflammation is more common in children than in adults, and has been reported in previous studies[1].

Septic shock is a dangerous complication of sepsis, especially in cases of Gram-negative bacteremia. In our study, septic shock occurred in 14/68 cases (20.6%). This result is similar to the study of Nguyen Quang Huy and Currie, where the rate of septic shock was 19.1% and 21%, respectively[1,5].

The average white blood cell count was 9.35 ± 4.86G/l, most of the patients had increased neutrophil counts 44.1%, followed by a normal white blood cell count is quite high (41.2%). The CRP and procalcitonin values increased very high, indicating severe infection. Serum C-reactive protein (CRP) is a rapid marker of acute-phase hyperactivity in inflammatory reactions and tissue damage, though it is not a marker of inflammation in bacterial sepsis, with lower specificity than PCT. However, in sepsis, CRP is often elevated. CRP > 100mg/L is a risk factor for mortality in patients with sepsis.

CONCLUSIONS

Surveying 68 cases of sepsis caused by *B. pseudomallei* infection at the National Hospital for Tropical Diseases from 2016 to 2021, we drew some mainly conclusions as follows:

- The patients lived mainly in rural areas (89.7%) and were distributed in 19 provinces in North and Central Vietnam, concentrated in Hatinh, Thanh Hoa, Nghe An, Bac Giang and Ha Noi.

- The main occupation was farmers, accounting for 52.9%. The disease mainly occurred in the rainy season from June to November (79.4%).

- The disease occurs mainly in patients with underlying diseases in which the most common are diabetes (57.4%), alcoholism (14.7%), hypertension and cirrhosis/chronic liver disease (11.4%).

- The duration from symptom onset to hospital admission is mainly over 7 days (75%).

- The most common were lung injuries (63.2%), soft tissue skin infections (22.1%), splenic abscesses (20.6%), neurological infections (10.3%), arthritis/osteomyelitis (8.8%). The rate of septic shock is high (20.6%).

- Abscess manifestations occur in multiple organs: lung, spleen, liver, kidney, skin, muscle, brain, salivary glands.

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