ORIGINAL ARTICLE

Intra-abdominal Abscesses due to Melioidosis: Clinical Course and Outcomes

Siriluck Anunnatsiri MD[1], Ploenchan Chetchotisakd MD[1]

[1] Division of Infectious Diseases and Tropical Medicine, Department of Medicine, Faculty of Medicine, Khon Kaen University, Khon Kaen, Thailand

Background: Intra-abdominal abscesses are the third common presentation of melioidosis in Thailand; however, knowledge about the long-term outcomes after received the appropriate therapy are limited.

Objective: To evaluate the clinical course and outcomes of patients with intra-abdominal abscesses due to melioidosis (IAAM).

Materials and Methods: The authors retrospectively reviewed the data of adult patients who had culture-confirmed melioidosis and presence of intra-abdominal abscesses detected by ultrasonography (US) or computerized tomography (CT) of abdomen between January 2011 and June 2017.

Results: 74 of 356 culture-confirmed melioidosis cases were enrolled with mean (SD) age of 52.4 (12.5) years; 75.7% were male, and nearly 90% of cases had comorbidities. The median duration of illness was 30 days (IQR 13 to 55). Abdominal pain or tenderness was detected in 40.5% of cases. Splenic abscess (70.3%) was the most common presentation of IAAM, followed by liver abscess (58.1%), and 32.4% of cases had hepatosplenic abscesses. Splenic abscess was significantly higher presented with multiple lesions than liver abscess (p=0.016). Size of abscess in liver was significantly larger than in the spleen (p<0.001) and internal septation was significantly more common in liver than spleen (p<0.001). Mean (SD) fever clearance time was 11.97 (11.04) days and in-hospital mortality was 13.5%. Median (IQR) time of abscesses resolution was 14 (12.57 to 28.86) weeks. Median (IQR) duration of eradication treatment was 20.9 (20 to 25.6) weeks.

Conclusion: Intra-abdominal abscesses were presented in about one-fifth of melioidosis, which clinical presentation may be subtle. Abdominal US or CT scan surveillance in patients suspected melioidosis and particularly septicemic or disseminated melioidosis was suggested. Splenic abscess and/or liver abscess should raise the suspected melioidosis in endemic areas. Abdominal imaging should be performed around 3-month after co-trimoxazole eradicative treatment to determine feasibility of drug discontinuation.

Keywords: Melioidosis; Intra-abdominal abscesses; Thailand

J Med Assoc Thai 2023;106(Suppl.1):S12-8

Website: http://www.jmatonline.com

Melioidosis is an infectious disease caused by Gram-negative bacterium, *Burkholderia pseudomallei*, which is endemic in Southeast Asia, northern Australia, and the Indian subcontinent[1]. Transmission is commonly by direct inoculation, inhalation of aerosolized bacteria, and ingestion of contaminated food and water with bacteria. Clinical manifestations of melioidosis varies from acute fulminating septicemia to chronic localized infection. The most frequent clinical presentations are community-acquired pneumonia and septicemia[1]. Other common clinical presentation is abscess in several organs such as liver, spleen, prostate, kidney, parotid gland, skin/soft tissue. Splenic and liver abscesses are the third common presentation of melioidosis in Thailand whereas prostatic abscess is more common than hepatosplenic abscesses in northern Australia[1]. The previous studies in intra-abdominal abscesses due to melioidosis (IAAM) have been case reports and the large trials emphasized on clinical presentation and radiographic characteristics of the abscesses[2-8]. There is lack of knowledge about the long-term clinical outcomes after received the appropriate antimicrobial therapy. This information may be factors determining the appropriate intervention, duration of antibiotic treatment, and risk of disease recurrence. The objective of the present study was to evaluate the clinical course and outcomes of patients with IAAM focusing on the resolution of abscesses after receiving treatment.

Materials and Methods

This was a retrospective study conducted in the Srinagarind Hospital, a 1,500-bed tertiary care university hospital, located in northeastern Thailand, between January 2011 and June 2017. All adult patients (aged >18 years) with culture-confirmed melioidosis and presence of intra-

Correspondence to:

Chetchotisakd P.

Department of Medicine, Faculty of Medicine, Khon Kaen University, Khon Kaen 40002, Thailand.

Phone: +66-43-363664, **Fax:** +66-43-348349

Email: ploencha@kku.ac.th

How to cite this article:

Anunnatsiri S, Chetchotisakd P. Intra-abdominal Abscesses due to Melioidosis: Clinical Course and Outcomes. J Med Assoc Thai 2023;106: S12-8.

DOI: 10.35755/jmedassocthai.2023.S01.13752

abdominal abscesses detected by ultrasonography (US) or computerized tomography (CT) of abdomen were included. Exclusion criteria was incomplete medical data record. Patient information were reviewed and retrieved from the medical records and hospital computerized system. These data included demographic data, organ involvement of intra-abdominal abscesses, other sites of melioidosis infection, radiologic characteristics of intra-abdominal abscesses, management, and outcomes. The authors defined the term of intra-abdominal abscesses as abscesses in solid organs in abdominal cavity including liver abscess, splenic abscess, pancreatic abscess, adrenal abscess, ovarian abscess, renal abscess, and prostatic abscess. Distribution of melioidosis was classified as: 1) disseminated septicemia (positive blood culture with >1 noncontiguous focal infections); 2) non-disseminated septicemia (positive blood culture with or without 1 focal infection); 3) multifocal localized (negative blood culture with >1 noncontiguous focal infections); and 4) localized (negative blood culture with 1 focal infection). Two authors were dependently reviewed the radiographic characteristics (organ with abscesses, size and internal septation) and if the results of review were discordant, we made the discussion to receive the conclusion of findings.

The present study was reviewed and approved by the Khon Kaen University Ethic Committee for Human Resource based on the Declaration of Helsinki and the ICH Good Clinical Practice Guidelines. The protocol number was HE601202.

Statistical analysis

Sample size was not calculated due to no prior study determining time to resolution of IAAM after treatment that was the major outcome of interest in the present study. Data analyses were performed using IBM SPSS Statistics for Windows, version 26.0 (IBM Corp., Armonk, NY, USA). The categorical variables were presented as frequency and proportion. The continuous variables were showed as mean with standard deviation (SD) or median with interquartile range (IQR), as appropriate. A univariate analysis and multiple logistic regression analysis, using the backward likelihood ratio selection method were used to evaluate the significant factors related to persistent abscess after 12 weeks of eradication phase of melioidosis treatment; the results being presented as the odds ratio (OR) with a 95% confidence interval (95% CI). Those variables significant at the 10% level in univariate analysis or clinically relevant were included in the multiple logistic regression model. The p-value less than 0.05 were considered statistically significant.

Results

There were 356 culture-confirmed melioidosis patients

Table 1. Demographic data of patients with intra-abdominal abscesses due to melioidosis

Variables	n=74 cases
Gender	
Male	56 (75.7%)
Female	18 (24.3%)
Age; mean±SD, years	52.4±12.5
Underlying diseases	65 (87.8%)
Diabetes mellitus	50 (67.6%)
Chronic liver disease	14 (18.9%)
Chronic kidney disease	9 (12.2%)
Previous melioidosis	7 (9.5%)
Thalassemia	4 (5.4%)
Others*	7 (9.5%)
Duration of illness; median (IQR), days	30 (13 to 55)
Fever	69 (93.2%)
Organomegaly (liver or spleen)	36 (48.6%)
Abdominal pain/tenderness	30 (40.5%)
Septic shock	13 (17.6%)
Visceral organ involvement	
Splenic abscess	52 (70.3%)
Liver abscess	43 (58.1%)
Prostatic abscess	4 (5.4%)
Pancreatic abscess	2 (2.8%)
Renal abscess	1 (1.4%)
Ovarian abscess	1 (1.4%)
Adrenal gland abscess	1 (1.4%)
Hepatosplenic abscesses	24 (32.4%)
Character of abscess	
Spleen, n=52	
Single: Multiple	10 (19.2%): 42 (80.8%)
Size (cm)	
<2 cm	43 (82.7%)
2 to 5 cm	6 (11.5%)
>5 cm	3 (5.8%)
Internal septation	5 (9.6%)
Liver, n=43	
Single: Multiple	18 (41.9%): 25 (58.1%)
Size (cm), n=42	
<2 cm	7 (16.7%)
2 to 5 cm	15 (35.7%)
>5 cm	18 (47.6%)
Right: Left: Both	18 (41.9%): 9 (20.9%): 16 (37.2%)
Internal septation, n=42	29 (69%)
Prostate, n=4	
Single: Multiple	2 (50%): 2 (50%)
Size (cm.)	
2.5 cm	2 (50%)
>5 cm	2 (50%)
Internal septation	3 (75%)
Rupture of abscess	7 (9.5%)

Table 1. Cont.

Variables	n=74 cases
Other organ involvement	58 (78.4%)
Blood	35 (47.3%)
Lung	22 (29.7%)
Skin and soft tissue	18 (24.3%)
Bone and joint	13 (17.6%)
Others**	10 (13.5%)
Distribution of melioidosis	
Disseminated septicemia	21 (28.4%)
Non-disseminated septicemia	14 (18.9%)
Multifocal localized	23 (31.1%)
Localized	16 (21.6%)

*Other underlying diseases: HIV (2), Cancer (3), Received prednisolone (1), Systemic lupus erythematosus (1)

**Other organ involvement: Lymph node (6), Deep neck infection (2), pericardium (1), mycotic aneurysm (1)

during the study period. Of these, 78 cases (21.9%) had intra-abdominal abscesses and 74 cases (94.9%) were included into the study. Demographic data of the patients is shown in Table 1. The mean (SD) age was 52.4 years (12.5) and about three-quarters of the patients were male. Nearly 90% of patients had preexisting diseases; diabetes mellitus was the most common followed by chronic liver disease and chronic kidney disease. The median duration of illness before diagnosis of melioidosis was 30 days (IQR 13 to 55). The most common symptom was fever; abdominal pain or tenderness was detected in 40.5% of cases.

Splenic abscess (70.3%) was the most common presentation of IAAM, followed by liver abscess (58.1%), and 32.4% of cases had hepatosplenic abscesses. The other intra-abdominal organs involved with melioidosis were prostate (4%), pancreas (2.8%), kidney, ovary, and adrenal gland (1.4% each). Splenic abscess was significantly higher presented with multiple lesions than liver abscess (p=0.016). Size of abscess in liver was significantly larger than in the spleen (p<0.001) and internal septation in the abscess was significantly more common in liver than spleen (p<0.001). Right lobe of the liver was predominant site of liver abscess (41.9%), however bilateral lobes of liver were involved up to 37.2%. Rupture of abscess into the intraabdominal cavity (liver and splenic abscesses one case each) or extended to abdominal wall (3 cases of liver abscess) or subcapsular space (2 cases of splenic abscess) was found in 7 cases (9.5%). Apart from intra-abdominal abscesses, most patients (78.4%) were documented other sites of infection which nearly half (47.3%) of the patients had septicemia and others included: lung (29.7%) and skin/soft tissues (24.3%).

Management and outcomes of the patients were summarized in Table 2. Most patients received initial parenteral antibiotic treatment (97.3%) with either ceftazidime or meropenem, which a median (IQR) duration of treatment was 17 (14 to 27) days. Nearly 40% of patients received combination treatment with co-trimoxazole. 36.5% of patients received abscess drainage. Mean (SD) fever clearance time was 11.97 (11.04) days and in-hospital mortality was 13.5%. Of 74 cases, 61 cases (82.4%) received eradicative treatment, mostly with co-trimoxazole alone or co-trimoxazole with doxycycline (95.1%) however only 42 cases (56.8%) had available complete treatment data. Of these, a median (IQR) duration of eradicative treatment was 20.9 (20 to 25.6) weeks. Approximately two-third of the patients required drainage of the abscesses, mostly by percutaneous technique. Forty-three cases (58.1%) had available abdominal US or CT scan follow-up during treatment but 31 cases (41.9%) had follow-up abdominal imaging until abscess clearance, of these, median (IQR) time of abscess resolution was 14 (12.57 to 28.86) weeks.

Table 2. Management and outcomes

Characteristics	n (%)
Parenteral treatment	72 (97.3)
Appropriate parenteral therapy	71 (98.6)
Ceftazidime	67 (94.4)
Meropenem	33 (46.5)
Cefoperazone-sulbactam	7 (9.9)
Coadministration treatment with co-trimoxazole	28 (39.4)
Duration of parenteral treatment; median (IQR), days	17 (14 to 27)
Received eradicative treatment; n=61	
Co-trimoxazole	52 (85.2)
Co-trimoxazole + doxycycline	6 (9.8)
Amoxicillin-clavulanate	3 (4.9)
Duration of eradicative treatment; median (IQR), weeks, n=42	20.9 (20 to 25.6)
Drainage	27 (36.5)
Percutaneous drainage	16 (59.3)
Open drainage	3 (11.1)
Both percutaneous and open drainage	3 (11.1)
Splenectomy	3 (11.1)
Hepatectomy	1 (3.7)
Number of drainages	
1 time	16 (63)
2 times	6 (37)
Outcome	
Fever clearance time; mean±SD, days	11.97±11.04
Time to abscess resolution; median (IQR), weeks; n=31	14 (12.57 to 28.86)
In-hospital mortality	10 (13.5)
Recurrence	3 (4.1)

The univariate analysis identified 2 significant factors related to having residual abscesses after 12 weeks of

Table 3. Univariate and multivariate analysis for factors related to persistent intra-abdominal abscesses due to melioidosis after 12 weeks of eradicative phase of treatment (n=43)

Factors	Unadjusted OR (95% CI)	p-value	Adjusted OR (95% CI)	p-value
Age	0.993 (0.947 to 1.041)	0.758	-	-
Male	1.692 (0.361 to 7.943)	0.505	-	-
Duration of illness (days)	1.036 (1.001 to 1.073)	0.046	1.053 (1.000 to 1.109)	0.051
Diabetes mellitus	0.320 (0.065 to 1.589)	0.164	-	-
Chronic liver diseases	0.702 (0.138 to 3.578)	0.671	-	-
Chronic renal diseases	0.396 (0.051 to 3.080)	0.376	-	-
Previous melioidosis	1.922 (0.286 to 12.928)	0.502	-	-
Melioidosis septicemia	0.140 (0.025 to 0.779)	0.025	-	-
Liver abscess	2.413 (0.666 to 8.744)	0.180	-	-
Multiple liver abscesses	2.708 (0.529 to 13.855)	0.232	-	-
Size of liver abscess				
<2 cm	Reference		-	-
2 to 5 cm	1.800 (0.210 to 15.407)	0.592	-	
>5 cm	15.000 (0.983 to 228.896)	0.051	-	-
Septation in abscess	2.080 (0.391 to 11.061)	0.390	-	-
Splenic abscess	2.292 (0.516 to 10.18)	0.276	-	-
Multiple splenic abscesses	0.900 (0.139 to 5.811)	0.912	-	-
Hepatosplenic abscesses	3.273 (0.891 to 12.026)	0.074	-	-
Duration of parenteral antibiotic treatment (days)	0.996 (0.954 to 1.041)	0.869	-	-
Coadministration co-trimoxazole during initial phase treatment	0.438 (0.121 to 1.576)	0.206	-	-
Drainage of abscess	2.917 (0.666 to 12.764)	0.155	-	-

Adjusted by 7 covariates: duration of illness, septicemia, having diabetes mellitus, co-trimoxazole combination initial parenteral treatment, drainage of abscess, duration of parenteral antibiotic treatment, and liver with splenic abscesses.

eradicative phase of melioidosis treatment: prolonged duration of illness (OR: 1.036, 95% CI: 1.001 to 1.073) and septicemia (OR: 0.14, 95% CI: 0.025 to 0.779). Prolonged duration of illness trend toward a factor associated with residual abscesses after 12-week of treatment by multivariate regression analysis after adjusted by 7 covariates included: duration of illness, septicemia, having diabetes mellitus, co-trimoxazole combination initial parenteral treatment, drainage of abscess, duration of parenteral antibiotic treatment, and liver with splenic abscesses (Table 3). Three cases (4.1%) had melioidosis recurrence.

Discussion

Intra-abdominal abscesses were presented in about one-fifth of melioidosis in the present study. Splenic abscess was more common than liver abscess, and hepatosplenic abscesses were frequently found. Visceral abscesses in melioidosis mostly occurred secondary from bacteremia or a part of dissemination resulting in multiple abscesses. Large abscess with internal septation, mostly required drainage, occurred more common in liver than spleen.

Melioidosis is well recognized infectious disease in area endemicity but may be misdiagnosed in non-endemic regions. The extend of countries with melioidosis endemicity is evident that related to several factors, e.g., increase the population at risk of melioidosis, global warming, and global trade[9]. The disease has a wide range of clinical presentations from acute sepsis with localized or disseminated infection, with high mortality, to chronic illness with abscess formation. Similar to other studies[6,8,10], most melioidosis patients have comorbidities at risk such as poor-controlled diabetes mellitus, chronic liver and kidney diseases, in the present study, these comorbidities were found nearly 90% of cases. Community-acquired septicemic pneumonia is the most common clinical manifestations in patients with melioidosis, accounting for about half[1]. Intra-abdominal abscesses (most commonly liver, splenic, and prostatic abscesses) are also common in melioidosis[1]. Prospective observational study from northeast Thailand which all adult patients with culture-confirmed melioidosis underwent abdominal ultrasonography have reported 33% of cases detected liver and/or splenic abscesses[5]. The present study showed lower rate of IAAM that might be underestimated due to lack of abdominal imaging either US, CT scan, or magnetic resonance imaging (MRI) performance in all cases. Furthermore, difference in time to perform the abdominal imaging and technique may affect the prevalence rate. Most patients presented with an acute infection (less than 2 months of symptoms) with average around one month of illness. Similar to previous study[5], IAAM was commonly silent

as 60 to 70% of cases did not have abdominal symptoms and/or signs suspected having the abscess. In the present study, intra-abdominal abscesses presented as a localized infection around 20% and as a part of dissemination high up to nearly 60%, and about half of them had bacteremia. These findings support the abdominal imaging surveillance for intra-abdominal abscesses in suspected cases of melioidosis and particular in patients presented with septicemic or disseminated melioidosis. The study in Lao revealed that the positive predictive value of visceral abscesses detection by abdominal ultrasonography for melioidosis was high at 93%[11].

Splenic abscess is an uncommon infection which usually results from endocarditis or another source of hematogenous seeding; however, this is a crucial clinical clue for suspected melioidosis in endemicity. The study in Taiwan[12] found that the most common organism causing splenic abscess is *Klebsiella pneumoniae*, followed by *Escherichia coli* and *Salmonella* species, in contrast to Thailand, *B. pseudomallei* is an important pathogen[13]. Among IAAM, splenic abscess was the most common followed by liver abscess, and frequently found hepatosplenic abscesses[2,5]. Although high frequency of multiple, small (<2 cm) abscesses in spleen and liver was detected, the large (>5 cm) liver abscess with internal septation was common. These our findings were consistent with the results of other studies[2,5]. Abscess in other intra-abdominal organs were rare which were revealed in previous several case reports[4,7]. Therefore, presence of splenic abscess or concurrent liver and splenic abscesses, especially multiple small abscesses should raise clinician concern about melioidosis.

Ceftazidime or carbapenems (meropenem, imipenem) is the choice for initial treatment of severe melioidosis which reduces overall mortality by half compared with the 3-drug regimen (chloramphenicol, co-trimoxazole, and doxycycline)[14,15]. In general practice, some physicians prefer to use ceftazidime or carbapenems in combination with co-trimoxazole in patients with visceral abscesses caused by melioidosis as demonstrated in the present study that nearly half of cases received this drug combination during the initial phase of treatment. Combination co-trimoxazole with ceftazidime did not demonstrate survival benefit[10] but the Darwin melioidosis guideline recommends adding co-trimoxazole during initial treatment in cases with cutaneous and soft tissue, osteomyelitis or septic arthritis, central nervous system, and with deep seated collections[16]. The rational underlies this recommendation is the excellent tissue penetration and intracellular activity of co-trimoxazole and the possibility limit the emergence of resistance. Whether this rational affecting the clinical outcomes are unknown. Due to limitation of small sample size and study design, we are unable to determine the clinical benefit of add-on co-trimozaxole to ceftazidime or carbapenems for treatment of IAAM and future research with proper study design are warranted. Duration of intensive phase of parenteral antibiotic treatment is usually at least 10 to 14 days; however, the Darwin guideline recommends at least 2 to 8 weeks depending on severity and site of infection[1,16]. Following initial parenteral antibiotic treatment, oral eradicative treatment with 12 to 20 weeks of co-trimoxazole is very important to decrease the relapse rate as low as 2 to 5%[17,18]. Small abscesses frequently resolve with medical treatment, but adequate drainage of large deep-seated and prostatic abscesses is an essential management to control source of infection. In the present study, almost patients received appropriate initial parenteral (average almost 3 weeks) and oral eradicative (average around 20 weeks) antibiotic treatment. Radiologically guided percutaneous drainage for large liver abscess mostly provided adequate source control although the intervention required more than once in some patients. Fever clearance took time with average up to 12 days and time to abscess resolution was about 3 months. In patients with clinically response to treatment including adequate drainage of large abscess, abdominal US or CT should be performed around 3-month after eradicative treatment with co-trimoxazole. Patient can be discontinued treatment if there is no residual abscess[18]. In-hospital mortality was low (13.5%) but similar recurrent rate (4.1%) of melioidosis compared to previous studies[17,18].

The resolution of IAAM could guide the duration of eradicative treatment. Based on the result from a recent randomized, controlled study, 12-week of co-trimoxazole is adequate for oral eradicative treatment in cases with no evidence of active melioidosis[18]. In our analysis, the authors found a prolonged course of illness trended toward associated with a persistence of IAAM at 12-week of eradicative treatment therefore early diagnosis and proper management could shorten the duration of treatment and reduce risk of drug adverse effects.

The present study had some limitations. First, a nature of retrospective study leads to missing of some interested information, selection and recall bias. Some patients were transferred to other hospital during the treatment and some clinicians did not perform follow-up abdominal US or CT for evaluate the resolution of abscess. Second, the difference in performance of abdominal US and CT and time to perform these imaging might result in misclassification bias. Not all cultured-confirmed melioidosis patients were investigated the intra-abdominal abscesses by CT scan therefore some patients may under detection of microabscesses. Third, limitation of sample size to evaluate the factors related to a persistence of IAAM at 12-week of eradicative treatment resulted in underpower to determine several interesting

factors that had associated trend.

Conclusion

Intra-abdominal abscesses were common presentation of melioidosis in endemic areas, which clinical symptoms and/or signs may be subtle. Abdominal imaging (US or CT scan) surveillance for intra-abdominal abscesses in patients presented with septicemic or disseminated melioidosis was advised. Splenic abscess and hepatosplenic abscesses should raise the suspected melioidosis. Drainage of large liver abscess or collection was required, and percutaneous drainage was effective and safe. Abdominal US or CT scan should be performed around 3-month after co-trimoxazole eradicative treatment to determine feasibility of drug discontinuation. Early diagnosis and appropriate management could improve clinical outcomes.

What is already known in this topic?

In melioidosis studies conducted in Thailand, visceral abscesses (splenic and/or liver abscesses, mostly multiple abscesses and clinically silent) is the third common clinical presentation of melioidosis[5,10,14,15]. Patients usually had concomitant septicemia. Findings on CT images, e.g., honeycomb appearance and the necklace sign, have been reported in melioidosis liver abscesses but multiple, small hypodense lesions with or without internal septation are common in splenic abscesses caused by melioidosis[19]. Apart from appropriate antibiotic treatment, adequate drainage of large liver abscess is required.

What this study adds?

Clinical outcomes of patients with IAAM were scarce, mostly limited to mortality. The present study added on the information regarding to fever clearance time, time to abscess resolution, and factors associated with persistence of intra-abdominal abscesses after 12-weeks of eradicative treatment with co-trimoxazole. These could assist the physicians to evaluate, monitor, and provide the proper management of these patients.

Acknowledgements

The authors thank the Department of Medicine, Faculty of Medicine, Khon Kaen University for publication support.

Conflicts of interest

The authors declare no conflict of interest.

References

1. Gassiep I, Armstrong M, Norton R. Human melioidosis. Clin Microbiol Rev 2020;33:e00006-19.
2. Dhiensiri T, Eua-Ananta Y. Visceral abscess in melioidosis. J Med Assoc Thai 1995;78:225-31.
3. Aphinives C, Pacheerat K, Chaiyakum J, Laopaiboon V, Aphinives P, Phuttharak W. Prostatic abscesses: radiographic findings and treatment. J Med Assoc Thai 2004;87:810-5.
4. Chong VH, Lim KS, Sharif F. Pancreatic involvement in melioidosis. JOP 2010;11:365-8.
5. Maude RR, Vatcharapreechasakul T, Ariyaprasert P, Maude RJ, Hongsuwan M, Yuentrakul P, et al. Prospective observational study of the frequency and features of intra-abdominal abscesses in patients with melioidosis in northeast Thailand. Trans R Soc Trop Med Hyg 2012;106:629-31.
6. Churuangsuk C, Chusri S, Hortiwakul T, Charernmak B, Silpapojakul K. Characteristics, clinical outcomes and factors influencing mortality of patients with melioidosis in southern Thailand: A 10-year retrospective study. Asian Pac J Trop Med 2016;9:256-60.
7. Nernsai P, Sophonsritsuk A, Lertvikool S, Jinawath A, Chitasombat MN. A case report of Tubo-ovarian abscess caused by *Burkholderia pseudomallei*. BMC Infect Dis 2018;18:73.
8. Currie BJ, Mayo M, Ward LM, Kaestli M, Meumann EM, Webb JR, et al. The Darwin Prospective Melioidosis Study: a 30-year prospective, observational investigation. Lancet Infect Dis 2021;21:1737-46.
9. Birnie E, Biemond JJ, Wiersinga WJ. Drivers of melioidosis endemicity: epidemiological transition, zoonosis, and climate change. Curr Opin Infect Dis 2022;35:196-204.
10. Chierakul W, Anunnatsiri S, Short JM, Maharjan B, Mootsikapun P, Simpson AJ, et al. Two randomized controlled trials of ceftazidime alone versus ceftazidime in combination with trimethoprim-sulfamethoxazole for the treatment of severe melioidosis. Clin Infect Dis 2005;41:1105-13.
11. Huson MAM, Kling K, Chankongsin S, Phongluxa K, Keoluangkhot V, Newton PN, et al. Point-of-care ultrasound in the diagnosis of melioidosis in Laos. Am J Trop Med Hyg 2020;103:675-8.
12. Lee CH, Leu HS, Hu TH, Liu JW. Splenic abscess in southern Taiwan. J Microbiol Immunol Infect 2004;37:39-44.
13. Sangchan A, Mootsikapun P, Mairiang P. Splenic abscess: clinical features, microbiologic finding, treatment and outcome. J Med Assoc Thai 2003;86:436-41.
14. White NJ, Dance DA, Chaowagul W, Wattanagoon Y, Wuthiekanun V, Pitakwatchara N. Halving of mortality of severe melioidosis by ceftazidime. Lancet 1989;2:697-701.
15. Simpson AJ, Suputtamongkol Y, Smith MD, Angus BJ, Rajanuwong A, Wuthiekanun V, et al. Comparison of imipenem and ceftazidime as therapy for severe melioidosis. Clin Infect Dis 1999;29:381-7.
16. Sullivan RP, Marshall CS, Anstey NM, Ward L, Currie BJ. 2020 Review and revision of the 2015 Darwin

melioidosis treatment guideline; paradigm drift not shift. PLoS Negl Trop Dis 2020;14:e0008659.
17. Chetchotisakd P, Chierakul W, Chaowagul W, Anunnatsiri S, Phimda K, Mootsikapun P, et al. Trimethoprim-sulfamethoxazole versus trimethoprim-sulfamethoxazole plus doxycycline as oral eradicative treatment for melioidosis (MERTH): a multicentre, double-blind, non-inferiority, randomised controlled trial. Lancet 2014;383:807-14.
18. Anunnatsiri S, Chaowagul W, Teparrukkul P, Chetchotisakd P, Tanwisaid K, Khemla S, et al. A comparison between 12 versus 20 weeks of trimethoprim-sulfamethoxazole as oral eradication treatment for melioidosis: An open-label, pragmatic, multicenter, non-inferiority, randomized controlled trial. Clin Infect Dis 2021;73:e3627-33.
19. Apisarnthanarak P, Thairatananon A, Muangsomboon K, Lu DS, Mundy LM, Apisarnthanarak A. Computed tomography characteristics of hepatic and splenic abscesses associated with melioidosis: a 7-year study. J Med Imaging Radiat Oncol 2011;55:176-82.