Heliyon 10 (2024) e34024

Contents lists available at ScienceDirect

Heliyon

journal homepage: www.cell.com/heliyon

Research article

Characteristics and risk factors for death in HIV-positive talaromycosis marneffei patients with sepsis

Mengyan Wang [a], Xiaotian Dong [c], Hu Wan [a], Binhai Zhang [a], Lele Yu [a], Wenyan Yu [b], Yan Zhang [b], Kenv Pan [b], Miaochan Wang [b], Aifang Xu [b], Yujiao Jin [b,*]

[a] Department II of Infectious Diseases, Hangzhou Xixi Hospital, Hangzhou Sixth People's Hospital, Hangzhou, China
[b] Department of Clinical Laboratory, Hangzhou Xixi Hospital, Hangzhou Sixth People's Hospital, Hangzhou, China
[c] Department of Clinical Laboratory, The First Affiliated Hospital of Zhejiang University School of Medicine, Zhejiang University, Zhejiang, 310003, China

ARTICLE INFO

Keywords:
HIV
Talaromyces marneffei
Sepsis
Prognosis
Bone marrow

ABSTRACT

Objectives: This case-control study aimed to analyze the characteristics and risk factors for death in HIV-positive Talaromycosis marneffei (TSM) patients with sepsis.
Methods: We retrospectively reviewed 173 AIDS patients diagnosed with TSM infection from January 1, 2013, to December 1, 2023, at Hangzhou Xixi Hospital. We collected and analyzed clinical characteristics, laboratory findings, bone marrow cytology results, treatment, and prognosis.
Results: Out of 173 AIDS-TSM patients, 92 had sepsis while 81 did not. AIDS-TSM patients with sepsis have a higher in-hospital mortality rate (19.6 %) than non-sepsis patients (0 %). The SOFA score showed a significant association with in-hospital mortality in AIDS-TSM patients with sepsis (OR = 1.583, 95 % CI: 1.183–2.118, P = 0.002), indicating an almost linear relationship. After adjusting for the SOFA score, only hemoglobin (Hb) (OR = 0.971, 95 % CI: 0.943–1.000, P = 0.046), international normalized ratio (INR) (OR = 22.33, 95 % CI: 1.84–270.90, P = 0.015), and C-reactive protein (CRP) (OR = 1.014, 95 % CI: 1.001–1.027, P = 0.039) remained significantly associated with in-hospital mortality. The Receiver Operating Characteristic (ROC) curve of the SOFA score, INR, and CRP showed moderately good predictive performance for in-hospital mortality, while Hb had a low predictive performance. The Area Under Curve (AUC) values were 0.834, 0.820, 0.776, and 0.669, respectively.
Conclusions: AIDS-TSM patients with sepsis have a higher mortality rate. Moreover, the SOFA score, along with Hb, INR, and CRP, are the risk factors for death in AIDS-TSM patients with sepsis.

1. Introduction

Talaromyces marneffei (TSM), known as Penicilliosis marneffei previously, is a thermally dimorphic fungus, mainly prevalent in South and Southeast Asia [1], especially in Thailand, India, Vietnam, and southern China [2]. TSM, as an opportunistic pathogen,

* Corresponding author. Department of Clinical Laboratory, Hangzhou Xixi Hospital, Hangzhou Sixth People's Hospital, Hengbu Street No. 2, Hangzhou, 310023, Zhejiang, China.
E-mail address: doctorjinyujiao@163.com (Y. Jin).

https://doi.org/10.1016/j.heliyon.2024.e34024
Received 30 January 2024; Received in revised form 26 June 2024; Accepted 2 July 2024
Available online 4 July 2024

mainly affects immunodeficient individuals such as those infected with HIV and spreads by spores that enter the human body through the respiratory tract or direct contact [3]. The incidence of TSM infection is also increasing in the HIV-negative population, such as patients using immunosuppressive drugs and chemotherapy and after solid and bone marrow transplantations [4,5].

Talaromyces marneffei infections can be divided into disseminated and focal types by invading organs and sites related to the monocyte–macrophage reticuloendothelial system [6]. Focal-type infections are usually confined to the invasion site and are predominantly characterized by primary symptoms. Common clinical manifestations of disseminated Talaromyces marneffei include fever, respiratory signs, anemia, weight loss, skin lesions, lymphadenopathy, and hepatosplenomegaly resulting from involving multiple tissues and organs [7]. Approximately 17,300 T. marneffei infection cases are diagnosed yearly, and the reported mortality rate is up to 30 % [8]. In the HIV-positive population, the risk of mortality is still increased without timely diagnosis and effective antifungal treatment [9]. In China, the prevalence of TSM among HIV patients ranged from 0.2 % to 26.5 % [10]. The highest prevalence is estimated at 15.0 % in South China, and the prevalence is estimated at 0.3 % in Southwest China [11].

Over the past 20 years, TSM has progressed from a rare disease to a common co-infection in HIV patients, and studies have confirmed that TSM can increase the mortality rate of HIV patients, which is a severe threat to human life and health [8]. A number of studies have analyzed factors associated with poor prognosis of HIV-positive TSM patients [7,12–17]. However, there is a lack of research on the prognosis of severe HIV/AIDS patients with TSM. Sepsis is a life-threatening organ dysfunction that results from a dysregulated host response to infection, reflecting the severity of the infection. Therefore, the purpose of this retrospective case-control study was first to study the clinical and laboratory results, treatment, and prognosis of HIV-positive TSM patients with sepsis. Furthermore, we conducted a further evaluation of risk factors associated with death in HIV-positive TSM patients with sepsis. Considering the most severe patients with trilineage reduction and hemolysis, we also specifically analyzed the bone marrow cytology characteristics of HIV-positive TSM patients, which were not reported before.

2. Materials and methods

2.1. Study population

This retrospective case-control study included AIDS patients diagnosed with *Talaromyces marneffei* infection from January 1, 2013, to December 1, 2023, admitted to the Department of Infectious Diseases at Hangzhou Xixi Hospital. Hangzhou Xixi Hospital, located in Zhejiang Province, is a major infectious specialty tertiary teaching hospital responsible for complex and complicated HIV-infected cases assigned by the government. Inclusion criteria were as follows: (i) age $\geq$18 years; (ii) HIV infection confirmed by Centers for Disease Control and Prevention (CDC) definitions; (iii) a precise diagnosis of T.M infection by a culture positive of *T. marneffei* from patients' specimens including sputum, alveolar lavage fluid, blood, bone marrow, and lymph nodes. Cultures of clinical specimens were established on Sabouraud's dextrose agar at 25 °C and 37 °C. Patients with other immune deficiencies (including malignancy and congenital immunodeficiency) and with other opportunistic infections such as tuberculosis and Pneumocystis were excluded. This study was approved by The Ethics Committee of Hangzhou Xixi Hospital (2023065).

2.2. Data collection and definition

Data extracted from the medical records included demographic information (sex and age), clinical characteristics (symptoms and signs), laboratory findings (a complete blood count, serum biochemistry, hemagglutination index, C-reactive protein (CRP), specimen culture, and lymphocyte subset analysis were conducted at admission), results of bone marrow aspirates, chest CT scan, SOFA score adapted from Vincent et al. (including PaO2/FiO2, platelets, bilirubin, MAP, Glasgow Coma Scale and Creatinine assessment) [18], treatment, and clinical outcomes. Sepsis diagnoses in this study were based on the Sepsis 3.0 criteria, which require a SOFA score of $\geq$2 points and a documented or suspected infection [19]. All procedures and methods were performed per the relevant international guidelines and regulations to reduce the subjects' physical discomfort. Continuous data were missing at a frequency of $<$5 %, and were replaced by the mean or median value in the analysis. Variables with missing values of $>$20 % were not imputed. This study first analyzed the characteristics of AIDS-TSM patients with sepsis, then performed a case-control study to assess risk factors for in-hospital death. The primary outcome was in-hospital death, and the exposure factors were the SOFA score and the first laboratory indicators upon admission.

2.3. Statistical analysis

Data following a normal distribution were expressed as the mean $\pm$ SD and compared using the *t*-test. For non-normal distributions, the Wilcoxon rank-sum test was used. Categorical variables, presented as percentages, were compared using the Chi-square test or Fisher's exact test, as appropriate. The logistic regression model assessed the relationship between variables and sepsis patient mortality. Restricted cubic spline analyses were performed to evaluate the linearity of associations between the SOFA score and mortality of sepsis patients. The Receiver Operating Characteristic curve (ROC) was utilized to demonstrate the predictive performances of variables on sepsis patient mortality by calculating the Area Under the ROC (AUC). Data analyses were performed using R 4.1.2 (The R Foundation) software. *P*-values less than 0.05 were considered significant.

3. Results

This study ultimately included a total of 173 HIV patients with TSM, of which 92 had sepsis, and 81 did not. Among the sepsis patients, 18 died in the hospital, as shown in the flowchart (Fig. 1).

The primary demographic, clinical, and laboratory characteristics of all enrolled patients are summarized in Table 1, stratified by sepsis. On average, the participants were 36.6 ± 11.4 years old, with about 91.3 % being male. The HIV RNA positivity rate was 87.3 % (131/150). Blood culture had a positivity rate of 86.6 % (149/172), and bone marrow culture had a rate of 58.1 % (18/31). The most common symptoms were fever (87.3 %), digestive issues (86.7 %), respiratory symptoms (48.0 %), and skin lesions (22.0 %). Imidazole was the most frequently used anti-fungal drug, accounting for 85.5 % of usage. Sepsis patients have a higher in-hospital mortality rate (19.6 %) than non-sepsis patients (0 %). 18.5 % of sepsis patients developed septic shock. Participants in the sepsis group had significantly higher values for neutrophil-lymphocyte ratio (NLR), international normalized ratio (INR), D-dimer, CRP, alanine aminotransferase (ALT), aspartate aminotransferase (AST), AST/ALT, lactate dehydrogenase (LDH), total bilirubin (TBIL), alkaline phosphatase (ALP), and SOFA score and lower values for hemoglobin (Hb), blood platelet (PLT), fibrinogen (FIB), and albumin (ALB), compared to those in the non-sepsis group.

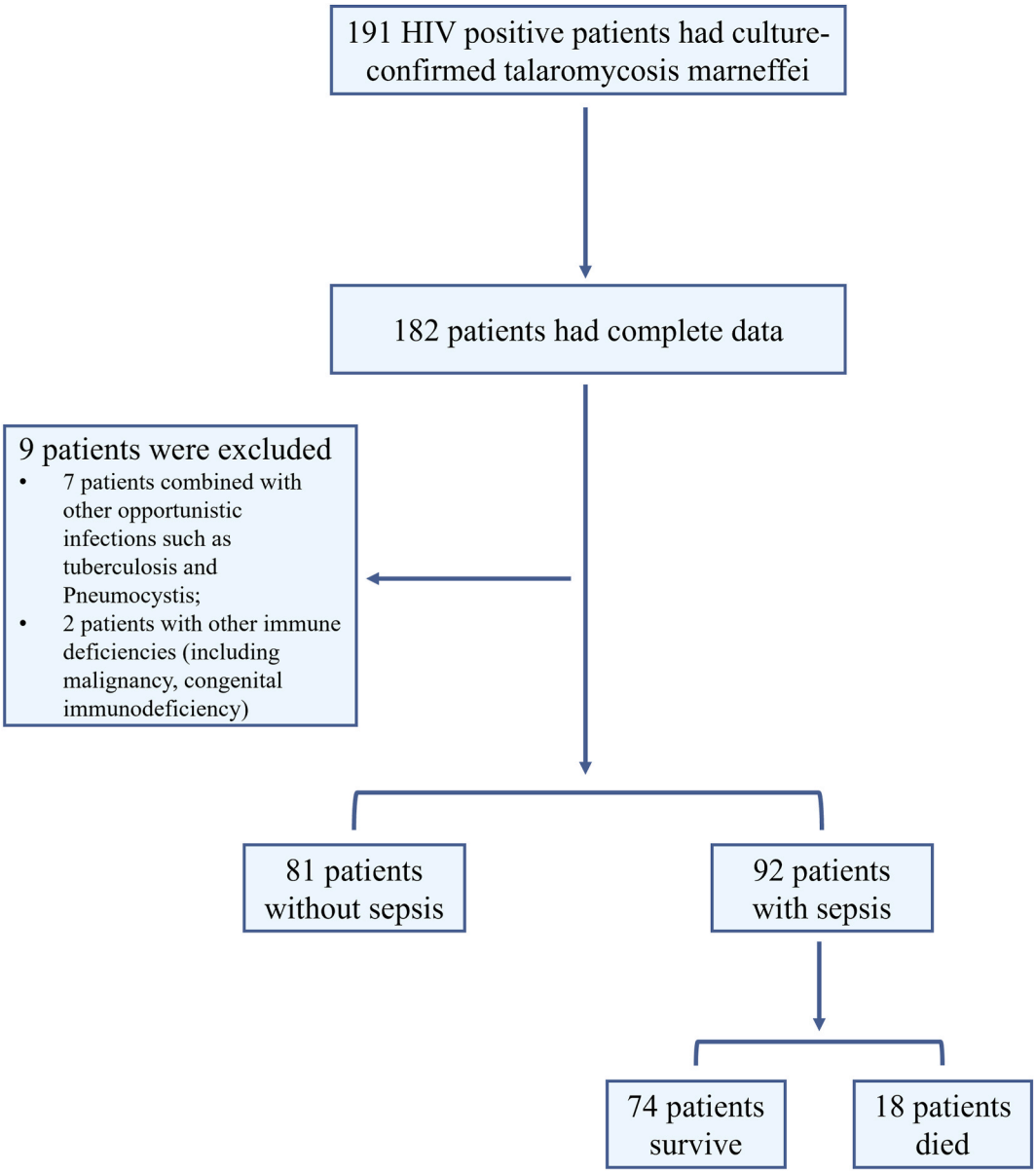

Fig. 1. The flowchart of this study.

Table 1
The basic demographic, clinical, and laboratory characteristics of included patients.

Characteristics	Total (n = 173)	Sepsis (n = 92)	Non-sepsis (n = 81)	P value
Age (year)	36.6 ± 11.4	37.4 ± 11.9	35.7 ± 10.7	0.322
Male, n (%)	158 (91.3 %)	87 (94.6 %)	71 (87.7 %)	0.107
CD4/CD8	0.06 (0.02, 0.10)	0.06 (0.02, 0.10)	0.05 (0.02, 0.11)	0.938
CD4 count (/μL)	10 (3, 27)	7 (3, 24)	15 (4, 28)	0.130
HIV RNA positive, n (%)	131 (87.3 %)	68 (87.2 %)	63 (87.5 %)	0.953
Blood culture positive, n (%)	149 (86.6 %)	83 (91.2 %)	66 (81.5 %)	0.061
Bone morrow culture positive, n (%)	18 (58.1 %)	10 (62.5 %)	8 (53.3 %)	0.722
Symptoms				
Fever, n (%)	151 (87.3 %)	80 (87 %)	71 (87.7 %)	0.891
Respiratory, n (%)	83 (48.0 %)	44 (47.8 %)	39 (48.1 %)	0.966
Digestive, n (%)	150 (86.7 %)	80 (87 %)	70 (86.4 %)	0.917
Skin lesions, n (%)	38 (22.0 %)	23 (25 %)	15 (18.5 %)	0.304
Laboratory				
NLR	10.6 (5.8, 18.1)	11.9 (6.7, 19.2)	9.0 (5.0, 14.9)	0.055
Hb (g/L)	97.8 ± 23.1	93.3 ± 21.6	103.0 ± 23.8	0.006
PLT (10^9/L)	117 (73, 199)	76 (43, 100)	193 (131, 276)	0.000
INR	1.1 (1.1, 1.2)	1.1 (1.1, 1.3)	1.1 (1.1, 1.2)	0.009
FIB (mg/dL)	3.3 ± 1.4	2.8 (1.9, 3.6)	3.9 (2.9, 4.5)	<0.001
D-dimer (mg/L)	6.7 (2.4, 20.3)	14.2 (5.1, 33.1)	3.8 (2.2, 6.6)	<0.001
CRP (mg/L)	60.8 (32.2, 96.4)	72.5 (42.1, 120.3)	47.0 (25.0, 72.3)	<0.001
ALB (g/L)	26.9 ± 6.4	25.4 ± 5.6	28.6 ± 6.8	0.001
ALT (U/L)	36 (22, 67)	45 (27, 78)	28 (18, 58)	0.003
AST (U/L)	87 (46, 153)	110 (77, 244)	54 (32, 93)	<0.001
AST/ALT	2.4 (1.6, 3.4)	2.9 (2.1, 4.2)	1.8 (1.3, 2.6)	<0.001
LDH (U/L)	445 (288, 687)	578 (339, 888)	333 (253, 485)	<0.001
TBIL (μmol/L)	9.7 (6.6, 14.4)	12.1 (8.9, 20.0)	7.5 (5.5, 10.8)	<0.001
ALP (U/L)	111 (75, 210)	142 (84, 235)	92 (66, 155)	0.003
Cr (μmol/L)	67 (57, 78)	69 (57, 84)	66 (57, 75)	0.160
Treatment				
Polyene, n (%)	16 (9.2 %)	13 (14.1 %)	3 (3.7 %)	0.018
Imidazole, n (%)	148 (85.5 %)	75 (81.5 %)	73 (90.1 %)	0.108
Triazole, n (%)	7 (4.0 %)	2 (2.2 %)	5 (6.2 %)	0.344
SOFA score	2 (1, 3)	3 (2, 4)	1 (0, 1)	0.000
Septic shock, n (%)	17 (9.8 %)	17 (18.5 %)	–	–
Death, n (%)	18 (10.4 %)	18 (19.6 %)	0 (0 %)	0.000

Abbreviations: NLR, neutrophil-lymphocyte ratio; Hb, hemoglobin; PLT, blood platelet; INR, international normalized ratio; FIB, fibrinogen; CRP, C reactive protein; ALB, albumin; ALT, alanine aminotransferase; AST, aspartate aminotransferase; LDH, lactate dehydrogenase; TBIL, total bilirubin; ALP, alkaline phosphatase; Cr, creatinine; SOFA, sequential organ failure assessment.

A total of 31 patients underwent bone marrow biopsy, with the morphological manifestations of their bone marrow presented in Table 2. Among these patients, 6 cases (19.4 %) showed phagocytes engulfing TSM in bone marrow smears (Fig. 2A). The proliferation activity accounted for 87.1 % of the granulocytic system, 71.0 % of the erythrocytic system, and 74.2 % of the megakaryocyte system. Hemophagocytic cells were observed in 11 cases, making up 35.5 % of the patients (Fig. 2B). Granulocytic, erythrocytic, and megakaryocytic dysplasia were found in 67.7 %, 58.1 %, and 9.7 % of the cases, respectively. Additionally, 15 cases (48.4 %) displayed internuclear bridging (Fig. 2C).

We conducted a further evaluation of the risk factors associated with death in sepsis patients. The demographic, clinical, and laboratory characteristics of sepsis patients are shown in Table S1, stratified by death. Compared to the survival group, the SOFA score of the death group was significantly higher (6 vs. 3, $P < 0.001$), and the proportion of septic shock was higher (44.4 % vs. 12.2 %, $P = 0.005$). After incorporating both the SOFA score and septic shock into the binary Logistic regression, only the SOFA score remained

Table 2
Bone marrow morphological findings.

	n (%)
Granulocytic hyperplasia	27 (87.1 %)
Erythrocytic hyperplasia	22 (71.0 %)
Megakaryocyte hyperplasia	23 (74.2 %)
Granulocytic dysplasia	21 (67.7 %)
Erythrocytic dysplasia	18 (58.1 %)
Internuclear bridging	15 (48.4 %)
Megakaryocyte dysplasia	3 (9.7 %)
TSM	6 (19.4 %)
Hemophagocytic cells	11 (35.5 %)

Abbreviations: TSM, Talaromyces marneffei.

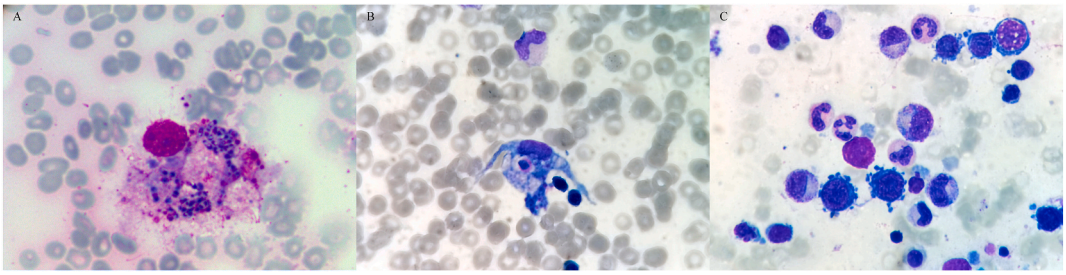

Fig. 2. Bone marrow smear in Wright-Giemsa staining of Talaromyces marneffei (TSM) infection. (A) Visible phagocytes engulfing TSM; (B) Visible hemophagocytic cells; (C) Visible internuclear bridging.

associated with the hospital mortality rate (OR = 1.583, 95 % CI: 1.183–2.118, P = 0.002) (Table S2). The restricted cubic spline demonstrated an almost linear relationship between the SOFA score and in-hospital mortality after adjusting for septic shock (Fig. 3).

We then performed univariate and multivariate Logistic analysis of in-hospital mortality in sepsis patients based on laboratory indicators (Table 3). In univariate Logistic regression, high levels of NLR, INR, CRP, AST, AST/ALT, LDH, TBIL, and Cr, as well as low levels of Hb and PLT, were significantly associated with in-hospital mortality in sepsis patients. After adjusting the SOFA score, only Hb (OR = 0.971, 95 % CI: 0.943–1.000, P = 0.046), INR (OR = 22.33, 95 % CI: 1.84–270.90, P = 0.015), and CRP (OR = 1.014, 95 % CI: 1.001–1.027, P = 0.039) remained significantly associated with in-hospital mortality.

The ROC curve was further performed to assess the predictive efficiency of the SOFA score, Hb, INR, and CRP on in-hospital mortality of sepsis patients (Fig. 4). The result showed SOFA score (AUC = 0.834, 95%CI: 0.731–0.936), INR (AUC = 0.820, 95% CI: 0.709–0.930), and CRP (AUC = 0.776, 95%CI: 0.654–0.898) had moderately good predictive performances, where Hb (AUC = 0.669, 95%CI: 0.522–0.816) had low predictive performance. According to the maximum Youden index, the optimal cut-off values for the SOFA score, Hb, INR, and CRP are 3.5, 66.5 g/L, 1.37, and 73.1 mg/L, respectively. The corresponding sensitivity and specificity for these values were 77.8 % and 77.0 %, 38.9 % and 91.9 %, 58.8 % and 90.4 %, 86.7 % and 60.0 %, respectively.

4. Discussion

In our study, 92 patients had sepsis of 173 HIV patients with TSM, of which 18 died. The in-hospital mortality rate was 10.4 %. 18.5 % of sepsis patients developed septic shock. We found SOFA scoring has excellent predictive power in HIV-TSM patients with sepsis. Furthermore, bone marrow morphology analysis is of great significance for the clinical diagnosis of AIDS complicated with TSM infection.

Our study systematically assessed the clinical and laboratory results, bone marrow cytology characteristics, treatment, and

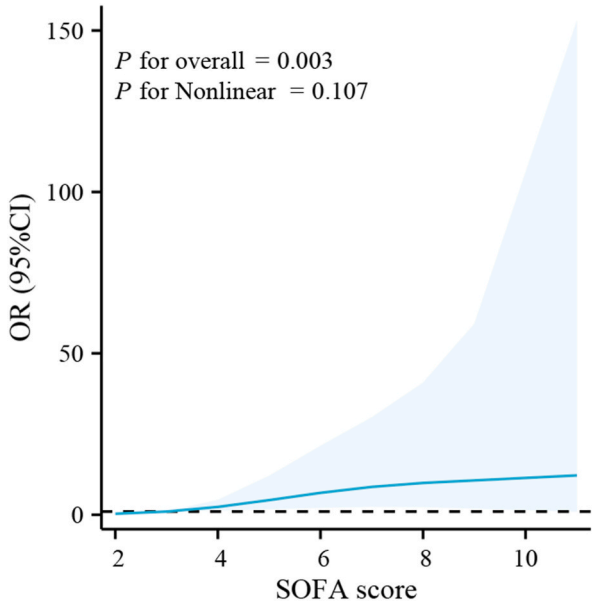

Fig. 3. The restricted cubic spline depicts the relationship between the SOFA score and in-hospital mortality of sepsis patients. The data were adjusted for septic shock. The curve line and shaded areas illustrate the estimated values and their corresponding 95 % confidence intervals. SOFA, sequential organ failure assessment.

Table 3
Logistic regression to assess the association of laboratory indicators with in-hospital mortality.

Variable	Crude OR (95 % CI)	P value	Adjusted[a] OR (95 % CI)	P value
NLR	1.037 (1.004–1.072)	0.029	1.029 (0.988–1.071)	0.163
Hb	0.969 (0.945–0.993)	0.012	0.971 (0.943–1.000)	0.046
PLT	0.986 (0.971–1.000)	0.050	0.997 (0.985–1.010)	0.692
INR	95.96 (7.18–1282.52)	<0.001	22.33 (1.84–270.90)	0.015
FIB	0.787 (0.510–1.216)	0.281		
D-dimer	0.991 (0.967–1.015)	0.444		
HCRP	1.019 (1.007–1.030)	0.001	1.014 (1.001–1.027)	0.039
ALB	0.930 (0.842–1.027)	0.150		
ALT	1.006 (0.999–1.013)	0.086		
AST	1.003 (1.001–1.005)	0.015	1.002 (1.000–1.004)	0.089
AST/ALT	1.270 (1.035–1.559)	0.022	1.177 (0.939–1.475)	0.157
LDH	1.001 (1.000–1.001)	0.039	1.001 (1.000–1.001)	0.143
TBIL	1.027 (1.003–1.051)	0.028	1.011 (0.983–1.039)	0.450
ALP	0.999 (0.995–1.002)	0.414		
Cr	1.007 (1.001–1.012)	0.021	1.001 (0.995–1.007)	0.754

Abbreviations: NLR, neutrophil-lymphocyte ratio; Hb, hemoglobin; PLT, blood platelet; INR, international normalized ratio; FIB, fibrinogen; CRP, c reactive protein; ALB, albumin; ALT, alanine aminotransferase; AST, aspartate aminotransferase; LDH, lactate dehydrogenase; TBIL, total bilirubin; ALP, alkaline phosphatase; Cr, creatinine; SOFA, sequential organ failure assessment.
[a] Adjusted for SOFA score.

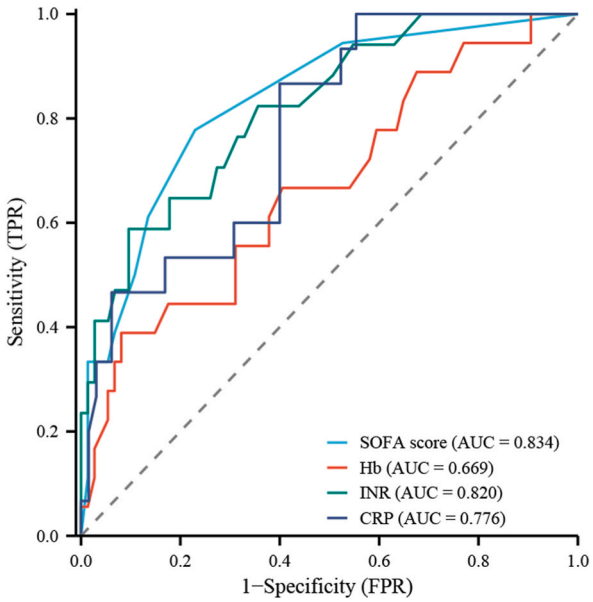

Fig. 4. Receiver operating characteristic (ROC) curve of SOFA score, Hb, INR, and CRP for predicting in-hospital mortality. SOFA, sequential organ failure assessment; Hb, hemoglobin; INR, international normalized ratio; CRP, C reactive protein; AUC, area under curve.

prognosis of TSM infection between with and without sepsis patients. The most characteristic manifestation of TSM is the typical central umbilical cutaneous nodule. However, in this study, only 21.97 % of patients had skin lesions significantly lower than other reports [7,17,20]. 87.28 % of patients had a fever, and fever was the most frequent clinical sign consistent with the results of previous studies [13,14,17], indicating the importance of blood cultures for diagnosis. Significant laboratory abnormalities in our patients included liver inflammation and bone marrow suppression, supporting the spread of TM through the endothelial network. In addition, CD4 T-cell count was <50 cells/L in all patients, suggesting severe immune dysfunction in susceptible individuals. Liver inflammation, bone marrow suppression, and immune dysfunction in TSM patients were consistent with the conclusions of other studies [7,14].

Ying et al. had reported that the positivity in blood culture was only 66.6 % of the patients and the positivity in bone marrow culture was 74.5 %, and combined bone marrow culture with blood culture, the positivity rate increased further to 86.6 %. Their mortality at discharge was 8.0 %, and they thought the lower mortality can be attributed to the use of bone marrow culture for earlier diagnosis and treatment [7]. The positivity rate of bone marrow culture in our study was low. We think this may have something to do with our small sample size. There are relatively few studies on the morphological characteristics of bone marrow in AIDS patients with TSM infection. Considering that bone marrow examination can help the early diagnosis and treatment of TSM patients, a retrospective analysis was performed on 173 AIDS patients with TSM infection, and the morphological characteristics of bone marrow cells in 31

AIDS patients with TSM infection were studied. Previous studies had reported that most of the bone marrow abnormalities associated with HIV infection appear to be related directly to the infection or its complications and not to therapeutic intervention. It is helpful of bone marrow examination in the management of patients infected with HIV in specific clinical situations [21]. This study found that granulocytic, erythrocytic, and megakaryocytic dysplasia in 67.7 %, 58.1 %, and 9.7 %, respectively, which may cause trilineage decreased in peripheral blood. In addition, we found 15 cases (48.4 %) displayed internuclear bridging. Internuclear bridging between erythroblasts resulting from abnormal mitosis is an uncommon cytological feature highly suggestive of myelodysplastic syndrome (MDS) and congenital dyserythropoietic anemia. It was rare as a reactive phenomenon that had been observed in an HIV disease and Burkitt lymphoma patient [22]. There was no study of internuclear bridging reported in HIV TSM patients, and the mechanism is not yet clear. Pan et al. reported talaromycosis-associated secondary hemophagocytic lymphohistiocytosis in HIV patients [23]. And we also observed hemophagocytic cells in 11 cases. Therefore, bone marrow morphology analysis is of great significance for the clinical diagnosis of AIDS complicated with TSM infection. Based on the results of bone marrow, glucocorticoid therapy may contribute to an increase in PLT in patients, as we have suggested in a previous study [24].

Currently, there is no standard scoring index for TSM patients with severe disease. When we classified these patients into patients with or without sepsis, we found that all patients who died were sepsis patients. Therefore, we used SOFA to stratify these patients and help find risk factors for death in HIV-positive talaromycosis marneffei patients with severe disease. Finally, we validated SOFA has a certain predictive power of death. In addition, we also adjusted SOFA and found the predictive value of death of Hb, INR, and CRP in patients with sepsis. These results suggested that we need to pay attention to inflammation, coagulation, and anemia in patients with severe infection, so aggressive anti-inflammatory therapy, anticoagulation, and blood transfusion may help patients with severe disease. In addition, we did not find a clear difference between the choice of antifungals. In previous studies, low CD4 + T and CD8 + T cell counts, negative G test result, leukocytosis, thrombocytopenia, impaired liver function, impaired renal function, respiratory failure, decreased albumin, a state of Epstein-Barr virus persistence and azole monotherapy have also been found as the risk factors of poor prognosis in HIV-positive patients with TSM infection [7,13,14,17].

Our finding validated that SOFA has a certain predictive power of death in patients with sepsis. We also adjusted SOFA and found the predictive value of death of Hb, INR, and CRP in patients with sepsis. These results can identify severe patients who are at low or high risk of death. In addition, we found the clinical value of bone marrow morphology analysis. This study had several limitations. Firstly, it was a single-center retrospective study conducted at Hangzhou Xixi Hospital in Zhejiang, which is not an endemic area for TSM infection in China. The relatively small number of patients may introduce selection bias, but we strictly controlled the inclusion and exclusion criteria to minimize this. Secondly, information bias might occur due to the study's retrospective nature. To reduce this, we used objective indicators and had multiple team members conducted repeated analyses. Thirdly, we controlled for confounding factors through multivariate logistic regression. However, due to the limited number of deaths in this study, we could include only a few variables in the regression for statistical reasons. Finally, the sample size was relatively small and not pre-calculated. Nevertheless, in patients with AIDS-TSM and sepsis, the SOFA score (main exposure) was significantly associated with in-hospital mortality (outcome), and the narrow confidence interval suggests that the study size was adequate. Therefore, future studies with larger datasets and prospective cohorts are needed for other endemic areas in China.

5. Conclusions

Patients with AIDS-TSM who develop sepsis exhibit a higher mortality rate. The SOFA score is crucial not only for diagnosing sepsis but also for its significant positive correlation with in-hospital mortality rates in septic AIDS-TSM patients. Moreover, Hb, INR, and CRP are additional risk factors for mortality in these patients. Furthermore, bone marrow morphology analysis also plays a significant role in clinically diagnosing AIDS complicated with TSM infection.

Funding

The study was supported by Zhejiang Medical and Health Science and Technology Project, China (2022KY1028).

Data availability statement

Data will be made available on request.

CRediT authorship contribution statement

Mengyan Wang: Writing – review & editing, Writing – original draft, Supervision, Project administration, Methodology, Investigation, Data curation, Conceptualization. **Xiaotian Dong:** Writing – review & editing, Writing – original draft, Methodology, Formal analysis. **Hu Wan:** Writing – review & editing, Validation, Investigation, Data curation. **Binhai Zhang:** Validation, Investigation, Data curation. **Lele Yu:** Validation, Investigation, Data curation. **Wenyan Yu:** Validation, Investigation, Data curation. **Yan Zhang:** Validation, Investigation, Data curation. **Kenv Pan:** Validation, Investigation, Data curation. **Miaochan Wang:** Validation, Investigation, Data curation. **Aifang Xu:** Writing – review & editing, Validation, Funding acquisition. **Yujiao Jin:** Writing – review & editing, Writing – original draft, Methodology, Formal analysis, Data curation, Conceptualization.

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.heliyon.2024.e34024.

References

[1] C. Cao, L. Xi, V. Chaturvedi, Talaromycosis (Penicilliosis) due to Talaromyces (Penicillium) marneffei: insights into the clinical trends of a major fungal disease 60 Years after the discovery of the pathogen, Mycopathologia 184 (6) (2019) 709–720.
[2] A.H. Limper, A. Adenis, T. Le, T.S. Harrison, Fungal infections in HIV/AIDS, Lancet Infect. Dis. 17 (11) (2017) e334–e343.
[3] Y. Li, H. Luo, J. Fan, X. Lan, G. Liu, J. Zhang, et al., Genomic analysis provides insights into the transmission and pathogenicity of Talaromyces marneffei, Fungal Genet. Biol. 130 (2019) 54–61.
[4] J. Wipasa, R. Chaiwarith, K. Chawansuntati, J. Praparattanapan, K. Rattanathammethee, K. Supparatpinyo, Characterization of anti-interferon-γ antibodies in HIV-negative immunodeficient patients infected with unusual intracellular microorganisms, Exp. Biol. Med. 243 (7) (2018) 621–626.
[5] P.P. Lee, M. Lao-Araya, J. Yang, K.W. Chan, H. Ma, L.C. Pei, et al., Application of flow cytometry in the diagnostics pipeline of primary immunodeficiencies underlying disseminated Talaromyces marneffei infection in HIV-negative children, Front. Immunol. 10 (2019) 2189.
[6] K. Pruksaphon, J.D. Nosanchuk, K. Ratanabanangkoon, S. Youngchim, Talaromyces marneffei infection: virulence, intracellular lifestyle and host defense mechanisms, J. Fungi (Basel, Switzerland) 8 (2) (2022).
[7] R.S. Ying, T. Le, W.P. Cai, Y.R. Li, C.B. Luo, Y. Cao, et al., Clinical epidemiology and outcome of HIV-associated talaromycosis in Guangdong, China, during 2011-2017, HIV Med. 21 (11) (2020) 729–738.
[8] F. Wang, R. Han, S. Chen, An overlooked and underrated endemic mycosis-talaromycosis and the pathogenic fungus Talaromyces marneffei, Clin. Microbiol. Rev. 36 (1) (2023) e0005122.
[9] J. Jiang, S. Meng, S. Huang, Y. Ruan, X. Lu, J.Z. Li, et al., Effects of Talaromyces marneffei infection on mortality of HIV/AIDS patients in southern China: a retrospective cohort study, Clin. Microbiol. Infect. 25 (2) (2019) 233–241.
[10] L.H. Zhou, Y.K. Jiang, R.Y. Li, L.P. Huang, C.W. Yip, D.W. Denning, et al., Risk-based estimate of human fungal disease burden, China, Emerg. Infect. Dis. 26 (9) (2020) 2137–2147.
[11] Y. Qin, X. Huang, H. Chen, X. Liu, Y. Li, J. Hou, et al., Burden of Talaromyces marneffei infection in people living with HIV/AIDS in Asia during ART era: a systematic review and meta-analysis, BMC Infect. Dis. 20 (1) (2020) 551.
[12] L. Wu, Y. Pan, K. Xu, Clinical characteristics associated with poor prognosis of acquired immunodeficiency syndrome patients complicated with disseminated talaromycosis marneffei, Infect. Drug Resist. 16 (2023) 7097–7108.
[13] Y. Wang, X. Mo, J. Zhang, Z. Yan, Y. Fang, W. Deng, et al., Clinical features of Talaromyces marneffei infection in HIV-positive and HIV-negative individuals: a retrospective study in southern China, Med. Mycol. 61 (8) (2023).
[14] J. Cen, J. Huang, W. Zeng, M. Pan, Y. Qiu, J. Zhang, Clinical features of HIV positive talaromycosis marneffei patients and development of a risk prediction model, Heliyon 9 (9) (2023) e20068.
[15] M. Shi, J. Lin, W. Wei, Y. Qin, S. Meng, X. Chen, et al., Machine learning-based in-hospital mortality prediction of HIV/AIDS patients with Talaromyces marneffei infection in Guangxi, China, PLoS Neglected Trop. Dis. 16 (5) (2022) e0010388.
[16] J. Klus, V.T. Ly, C. Chan, T. Le, Prognosis and treatment effects of HIV-associated talaromycosis in a real-world patient cohort, Med. Mycol. 59 (4) (2021) 392–399.
[17] J. Sun, W. Sun, Y. Tang, R. Zhang, L. Liu, Y. Shen, et al., Clinical characteristics and risk factors for poor prognosis among HIV patients with Talaromyces marneffei bloodstream infection, BMC Infect. Dis. 21 (1) (2021) 514.
[18] Y. Yang, J. Dong, Y. Li, R. Chen, X. Tian, H. Wang, et al., Development and validation of a nomogram for predicting the prognosis in cancer patients with sepsis, Cancer Med. 11 (12) (2022) 2345–2355.
[19] L. Evans, A. Rhodes, W. Alhazzani, M. Antonelli, C.M. Coopersmith, C. French, et al., Surviving sepsis campaign: international guidelines for management of sepsis and septic shock 2021, Intensive Care Med. 47 (11) (2021) 1181–1247.
[20] M. Larsson, L.H. Nguyen, H.F. Wertheim, T.T. Dao, W. Taylor, P. Horby, et al., Clinical characteristics and outcome of Penicillium marneffei infection among HIV-infected patients in northern Vietnam, AIDS Res. Ther. 9 (1) (2012) 24.
[21] D.S. Karcher, A.R. Frost, The bone marrow in human immunodeficiency virus (HIV)-related disease. Morphology and clinical correlation, Am. J. Clin. Pathol. 95 (1) (1991) 63–71.
[22] J.A. Rojas-Martínez, R.M. Morales-Camacho, Internuclear bridging outside of primary myelodysplasia and congenital dyserythropoietic anemia, Blood 132 (2) (2018) 236.
[23] M. Pan, Y. Qiu, W. Zeng, S. Tang, X. Feng, J. Deng, et al., Talaromycosis-associated secondary hemophagocytic lymphohistiocytosis in nine human immunodeficiency virus-negative patients: a multicenter retrospective study, Infect. Drug Resist. 12 (2019) 3807–3816.
[24] M. Wang, Z. Zhang, J. Yan, J. Shi, S. Liu, H. Wan, The presence of secondary vans syndrome in AIDS patients with Talaromyces marneffei infection, Infect. Drug Resist. 14 (2021) 1265–1271.