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Case Report

Osteoarticular Melioidosis in Anhui, China: A Case Report and Literature Review

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Abstract

Melioidosis is endemic primarily in tropical and subtropical regions but is rarely encountered and often misdiagnosed in non-endemic settings. We report a case of *Burkholderia pseudomallei* osteomyelitis with concomitant septic arthritis in Anhui Province, China. The patient was a 71-year-old male farmer whose main predisposing factor was recently diagnosed type 2 diabetes mellitus. *Burkholderia pseudomallei* was recovered from intraoperative purulent material; whole-genome sequencing supported species identification and assigned the isolate to sequence type 51 (ST51), and phylogenetic analysis revealed close genetic relatedness to isolates from Southeast Asia. Three surgical procedures and sequential antimicrobial therapy were followed by short-term clinical improvement. Oral trimethoprim–sulfamethoxazole was continued after intravenous treatment. At two months, the patient had no recurrent fever and showed satisfactory wound healing, but treatment completion and post-treatment outcomes were unavailable. Phylogenetic analysis placed the clinical isolate near selected Southeast Asian isolates, but neither genomic relatedness nor the absence of recent travel established the source of infection. To place this case in context, we systematically reviewed studies of osteoarticular melioidosis and pooled proportions of clinical characteristics and outcomes. Seventeen studies were included. Osteoarticular involvement was present at some point during the illness in 14% of patients with melioidosis, and among patients with osteoarticular disease, diabetes was present in 81% [95% confidence interval (CI), 74–87%], surgery was performed in 71% (95% CI, 57–82%), and death occurred in 15% (95% CI, 10–23%). Septic arthritis alone was more frequent than osteomyelitis alone (65% versus 22%), and the femur and knee were the most commonly involved sites (31% and 51%). This case highlights the importance of obtaining appropriate cultures, assessing surgical source control, and interpreting treatment duration and early improvement cautiously in osteoarticular melioidosis.

Keywords: melioidosis; *Burkholderia pseudomallei*; osteomyelitis; septic arthritis; whole-genome sequencing; ST51

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1. Introduction

Melioidosis is caused by the environmental bacterium *Burkholderia pseudomallei* (*B. pseudomallei*) and is endemic primarily in Southeast Asia and northern Australia [1]. The global incidence is estimated at approximately 165,000 cases annually [2], and the mortality rate

can reach 80% without effective antimicrobial treatment [3]. In China, most reported cases have occurred in the southern provinces of Hainan, Guangdong, Guangxi, and Fujian [4]. However, locally acquired cases have also been reported in Anhui and Jiangxi [5], and cases without a reported travel history have been described in Chongqing [6]. These observations highlight the need for clinical awareness beyond traditionally recognized endemic regions. The location of Anhui Province relative to traditionally recognized melioidosis-endemic regions in China is shown in Figure 1.

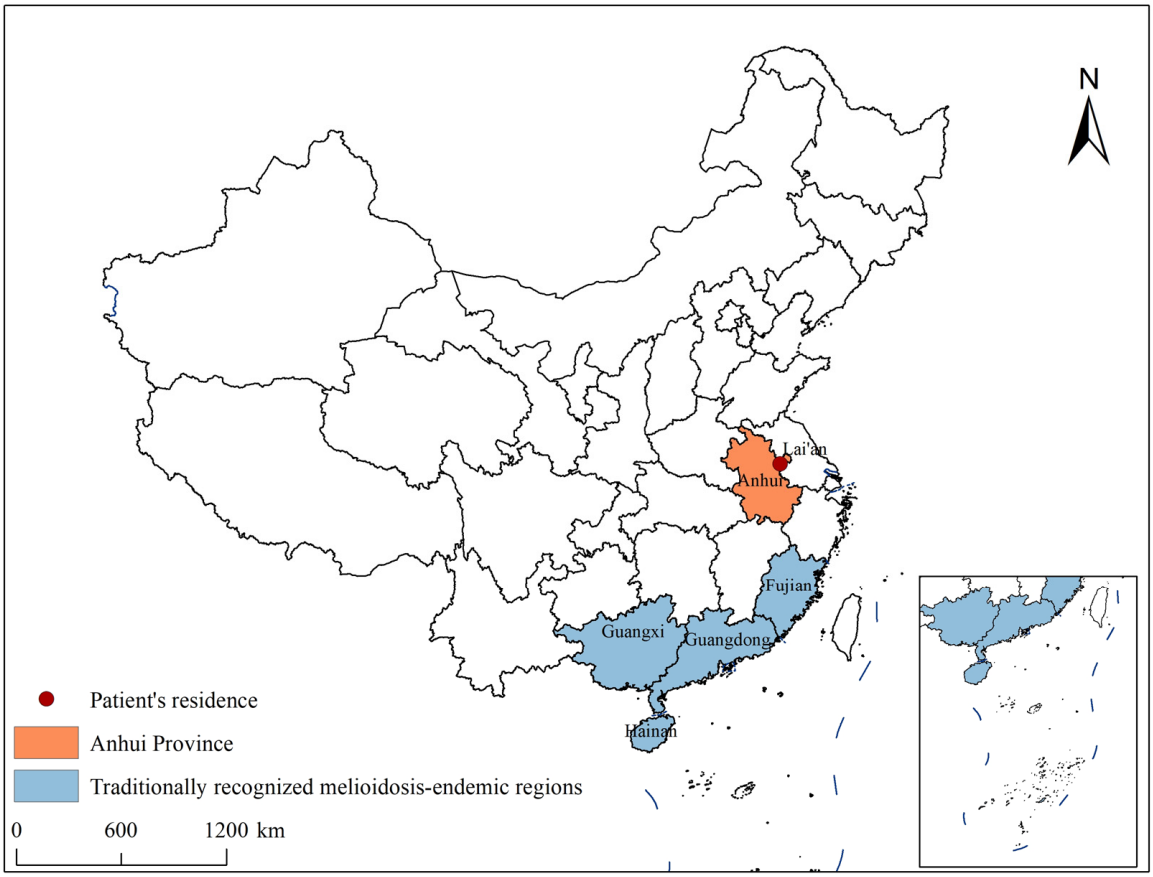


Figure 1. Geographic location of the patient's residence in relation to traditionally recognized melioidosis-endemic regions in China. Hainan, Guangdong, Guangxi, and Fujian are shaded blue; Anhui Province, in which the case was diagnosed, is shaded orange; and the red dot marks Lai'an County, the patient's place of residence.

Osteomyelitis and septic arthritis are less common manifestations of melioidosis and can be difficult to recognize because their clinical and imaging findings are nonspecific. We report distal tibial osteomyelitis with concomitant septic arthritis of the ankle caused by *B. pseudomallei* in a patient from Lai'an County, Anhui Province, China. We describe the clinical course, antimicrobial susceptibility, and genomic findings of this case, and we systematically review cohort studies of osteoarticular melioidosis to summarize the comorbidity, presentation and anatomical site, surgical and antimicrobial treatment, and outcomes. The patient's clinical course is summarized in Figure 2.

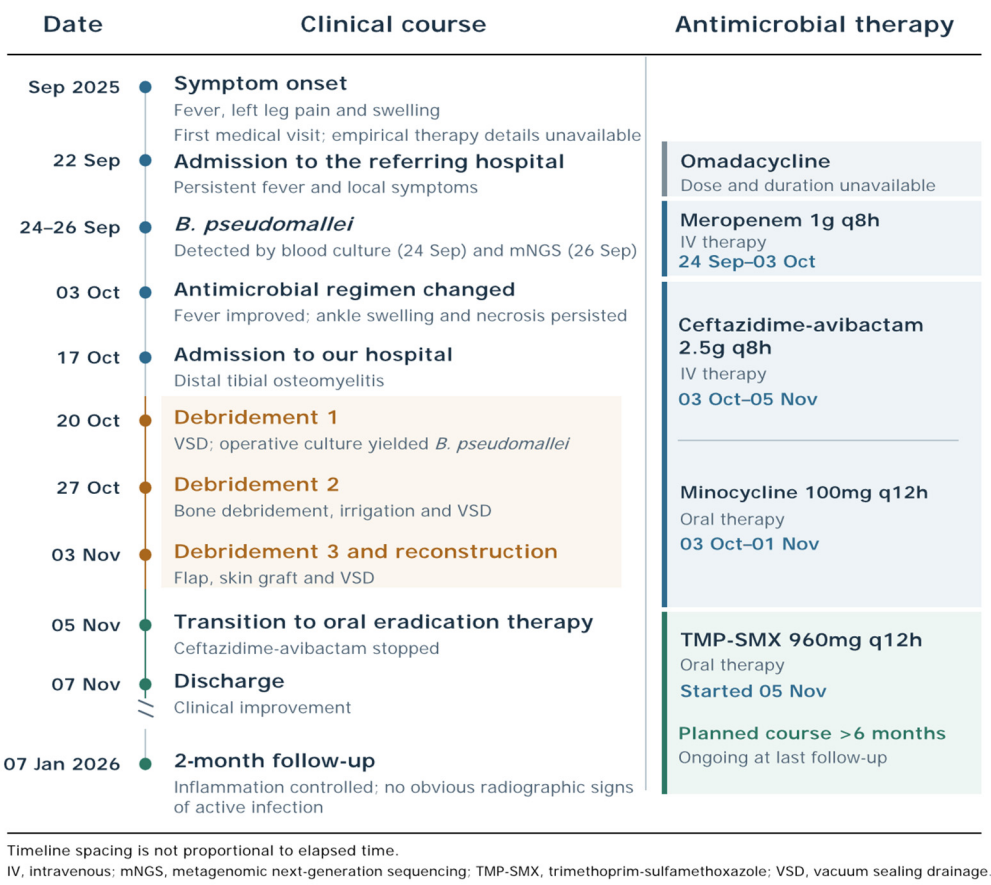


Figure 2. Clinical course and antimicrobial treatment of a patient with osteoarticular melioidosis. The left timeline summarizes diagnostic, surgical, and follow-up events, and the right column shows systemic antimicrobial therapy. Dates refer to 2025 unless otherwise indicated, and spacing is schematic. *B. pseudomallei*, *Burkholderia pseudomallei*; IV, intravenous; mNGS, metagenomic next-generation sequencing; TMP–SMX, trimethoprim–sulfamethoxazole; VSD, vacuum sealing drainage.

2. Case Presentation

2.1. Presentation and Initial Assessment

A 71-year-old male farmer was admitted to our hospital on 17 October 2025 with more than one month of fever and progressive swelling and pain in the left lower extremity. His early symptoms included recurrent fever, nausea, and fatigue. Omadacycline administered at a referring hospital did not produce clinical improvement. Blood culture at that hospital reportedly yielded *B. pseudomallei*, which was also detected by metagenomic next-generation sequencing (mNGS). The isolate was reported to be susceptible to ceftazidime. Intermittent fever persisted after 10 days of meropenem (1 g every 8 h), and treatment was changed to ceftazidime–avibactam (2.5 g every 8 h; ceftazidime 2 g plus avibactam 0.5 g) plus minocycline (100 mg every 12 h), after which clinical improvement was reported. He was subsequently transferred to our hospital for further management.

Type 2 diabetes mellitus (DM) had been diagnosed at the referring hospital approximately two weeks before transfer, and insulin had been started for glycemic control. He reported a previous ankle sprain but no associated skin breach or specific exposure to contaminated soil or water. He also reported no recent travel to Southeast Asia or to regions of China traditionally considered endemic for melioidosis.

On admission, his temperature was 36.9 °C, heart rate was 92 beats/min, and blood pressure was 138/69 mmHg. Examination revealed bilateral lower-extremity edema, marked swelling of the left ankle, and a focal dark-red skin lesion with breakdown (Figure 3A).

Laboratory tests showed severe anemia (hemoglobin, 66 g/L), leukopenia (white blood cell count, 3.32×10^9/L), thrombocytopenia (platelet count, 60×10^9/L), an elevated high-sensitivity C-reactive protein level (42.08 mg/L), an erythrocyte sedimentation rate of 70 mm/h, and hypoalbuminemia. The glycated hemoglobin (HbA1c) level was 6.34%.

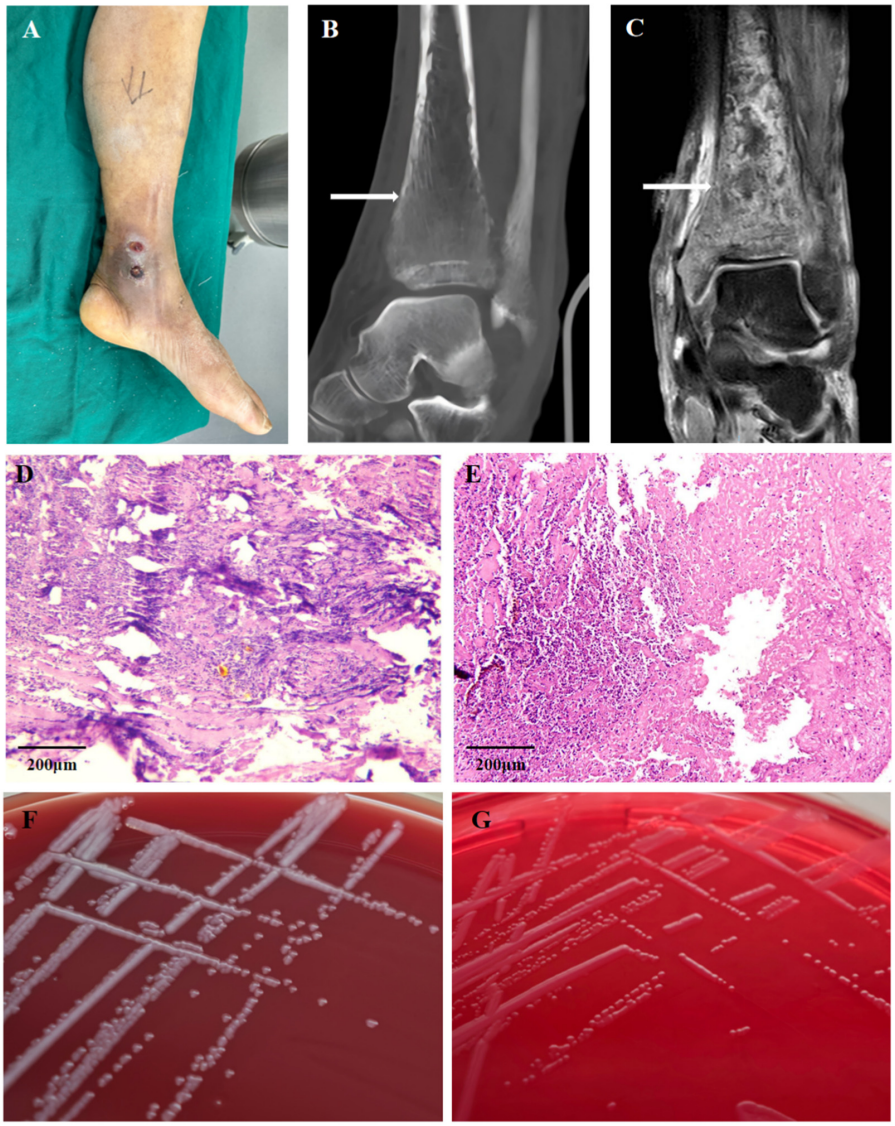


Figure 3. Clinical, imaging, histopathological, and microbiological findings in a patient with distal tibial osteomyelitis caused by *B. pseudomallei*. (**A**) Left ankle swelling, erythema, and focal skin breakdown. The markings visible on the skin are preoperative surgical site markings. (**B**) Non-contrast computed tomography showing osteolytic destruction and cortical disruption of the distal tibia, most prominent around the medial malleolus. (**C**) Coronal proton density-weighted fat-suppressed magnetic resonance image showing abnormal distal tibial marrow signal, with adjacent marrow and soft-tissue edema, synovial thickening, and joint effusion. White arrows in (**B**,**C**) indicate the distal tibial lesion. (**D**,**E**) Hematoxylin and eosin-stained intraoperative tissue sections showing inflammatory cell infiltration, abscess formation, and necrosis; scale bars, 200 μm. (**F**,**G**) Colonies of the isolate recovered from intraoperative purulent material after subculture at 37 °C for 24 h: creamy-white, circular, smooth, moist, convex colonies measuring approximately 1–2 mm without evident hemolysis on blood agar (**F**), and pale pink, circular, smooth colonies with entire margins on MacConkey agar (**G**). Colony morphology alone is insufficient for species identification; the isolate was presumptively identified as *B. pseudomallei* by whole-genome sequencing.

2.2. Diagnosis and Treatment

Non-contrast computed tomography (CT) of the left ankle showed multifocal areas of decreased bone density involving the distal tibia and fibula, talus, and calcaneus, with the most extensive destruction in the distal tibia (Figure 3B). Associated findings included periarticular soft-tissue swelling and focal skin breakdown. Magnetic resonance imaging (MRI) of the left ankle demonstrated distal tibial marrow abnormalities consistent with osteomyelitis, marrow edema in the distal fibula and tarsal bones, synovial thickening, joint effusion, and periarticular soft-tissue inflammation; a localized abscess was suspected (Figure 3C). The clinical, imaging, and microbiological findings supported melioidosis with distal tibial osteomyelitis and adjacent soft-tissue infection. Concomitant ankle septic arthritis was clinically suspected because of pain, swelling, synovial thickening, and joint effusion. However, no synovial fluid analysis or joint-specific microbiological confirmation was available. Ceftazidime–avibactam 2.5 g every 8 h plus minocycline 100 mg every 12 h was continued.

On hospital day 4 (20 October 2025), the patient underwent left ankle debridement and negative-pressure drainage. Local irrigation with meropenem was also used postoperatively at the discretion of the surgical team. There is no published evidence for the efficacy of this procedure, and no conclusion about its effect can be drawn from this case. Intraoperative cultures yielded *B. pseudomallei*, whereas concurrent blood cultures were negative. A second procedure was performed on hospital day 11 (27 October 2025). Extensive purulence and necrotic tissue extended into the distal tibia; a cortical window was created to remove the affected tissue. Histopathological examination showed inflammatory cell infiltration, abscess formation, and necrosis (Figure 3D,E).

The isolate recovered from intraoperative purulent material (Figure 3F,G) underwent broth microdilution susceptibility testing. Results were interpreted using Clinical and Laboratory Standards Institute (CLSI) M45 criteria where organism-specific breakpoints were available (Table 1). The isolate was susceptible to ceftazidime, imipenem, amoxicillin–clavulanate, trimethoprim–sulfamethoxazole (TMP–SMX), tetracycline, and doxycycline. Meropenem and minocycline minimum inhibitory concentrations (MICs) were 1 mg/L and ≤1 mg/L, respectively; no susceptibility categories were assigned because CLSI M45 does not provide *B. pseudomallei*-specific clinical breakpoints for these agents. Ceftazidime–avibactam 2.5 g every 8 h plus minocycline 100 mg every 12 h was continued postoperatively. Once the isolate was shown to be susceptible to ceftazidime, single-agent ceftazidime was appropriate; however, it was not available in our hospital, and ceftazidime was therefore continued as the ceftazidime–avibactam combination. Avibactam has no activity against *B. pseudomallei* and added nothing to treatment, its inclusion reflecting drug availability rather than a therapeutic rationale. Ceftazidime–avibactam should not be regarded as a preferred agent for melioidosis, and CLSI M45 defines no interpretive category for the combination.

A third procedure, comprising further debridement and flap reconstruction, was performed on hospital day 18 (3 November 2025). Oral TMP–SMX was initiated on hospital day 20 (5 November 2025) at a dose of 160 mg trimethoprim and 800 mg sulfamethoxazole per dose every 12 h. The total duration of intravenous antimicrobial therapy was 43 days: meropenem was given for 10 days (24 September to 3 October), followed by ceftazidime–avibactam for a further 33 days (3 October to 5 November 2025). He was discharged on 7 November 2025, after 22 days at our hospital, with clinical improvement and instructions to continue oral eradication therapy.

Table 1. Antimicrobial susceptibility of the *B. pseudomallei* isolate.

Antimicrobial Agent	MIC (μg/mL)	Susceptible Breakpoints (μg/mL)	Susceptibility Category
Amoxicillin/clavulanate	8/4	≤8/4	S
Ceftazidime	≤1	≤8	S
Imipenem	≤1	≤4	S
Tetracycline	≤4	≤4	S
Doxycycline	≤4	≤4	S
Trimethoprim/sulfamethoxazole	≤2/38	≤2/38	S
Meropenem	1	–	Not interpreted
Minocycline	≤1	–	Not interpreted

Abbreviations: S, susceptible; MIC, minimum inhibitory concentration; CLSI, Clinical and Laboratory Standards Institute. MICs were determined by broth microdilution and interpreted using CLSI M45, 3rd edition, where applicable. Only susceptible-category thresholds are shown. No categorical interpretation was assigned to meropenem or minocycline. For combination agents, paired MIC values indicate the concentrations of the two components in the order listed.

At the two-month post-discharge follow-up on 7 January 2026, he remained on oral TMP–SMX, had no recurrent fever, and showed satisfactory wound healing. The planned eradication course was more than six months. Treatment completion, post-treatment recurrence, and long-term ankle function had not been documented at the last available assessment.

2.3. Genomic Analysis

Whole-genome sequencing (WGS) of the clinical isolate recovered during surgery was performed by Shanghai Biozeron Biotechnology Co., Ltd. (Shanghai, China) on a NovaSeq X Plus platform (Illumina, San Diego, CA, USA) using 150 bp paired-end reads. After standard library preparation, sequencing generated 4,163,224 read pairs (2 × 150 bp), corresponding to 1.25 Gb of raw data and 1.14 Gb of clean data. The percentage of clean bases with a Phred quality score of at least 30 (Q30) was 90.11%, and the mean genome coverage was approximately 162×. Reads were processed using Trimmomatic v0.36 (SLIDINGWINDOW:4:15; MINLEN:75) [7], assembled using SPAdes v3.9.0 with multiple k-mer values [8], and further processed with GapCloser v1.12 [9]. The final assembly was 7,040,885 bp (guanine–cytosine content, 68.2%) comprising 123 scaffolds (N50, 122,463 bp; N rate, 0.01%).

FastANI v1.34 [10] confirmed the isolate as *B. pseudomallei* (99.85% average nucleotide identity (ANI) with ATCC 23343; GCF_001182285.1) [11], which supported the species assignment based on the ≥95% ANI species threshold [12]. Multilocus sequence typing (MLST) was performed in silico using the assembled genome. The seven housekeeping genes of *B. pseudomallei* (*ace*, *gltB*, *gmhD*, *lepA*, *lipA*, *narK*, and *ndh*) [13] were extracted and queried against the *B. pseudomallei* MLST database hosted on PubMLST [14]. The clinical isolate was identified as sequence type 51 (ST51), with no novel alleles or sequence types.

Phylogenetic analysis was performed using CSI Phylogeny v1.4 [15], which implements whole-genome single-nucleotide polymorphism (SNP) calling and maximum-likelihood tree construction using FastTree [16]. In total, 48 genomes were included: the clinical isolate obtained in this study (labeled "This Study" in Figure 4) and 47 *B. pseudomallei* reference genomes retrieved from the National Center for Biotechnology Information (NCBI) (Table S1). The genome of *B. pseudomallei* K96243 (NCBI RefSeq assembly accession GCF_000011545.1) [17] was used as the mapping reference. After filtering, 3,549,671 reliable positions were shared across genomes, corresponding to 87.12% of the reference, and 49,512 high-quality SNPs were obtained. The maximum-likelihood tree was visualized and annotated in Interactive Tree Of Life (iTOL) [18]. The clinical isolate grouped with se-

lected Southeast Asian isolates in this dataset (Figure 4). This relationship indicates genetic similarity within the sampled genomes but does not establish the location of acquisition or a transmission route.

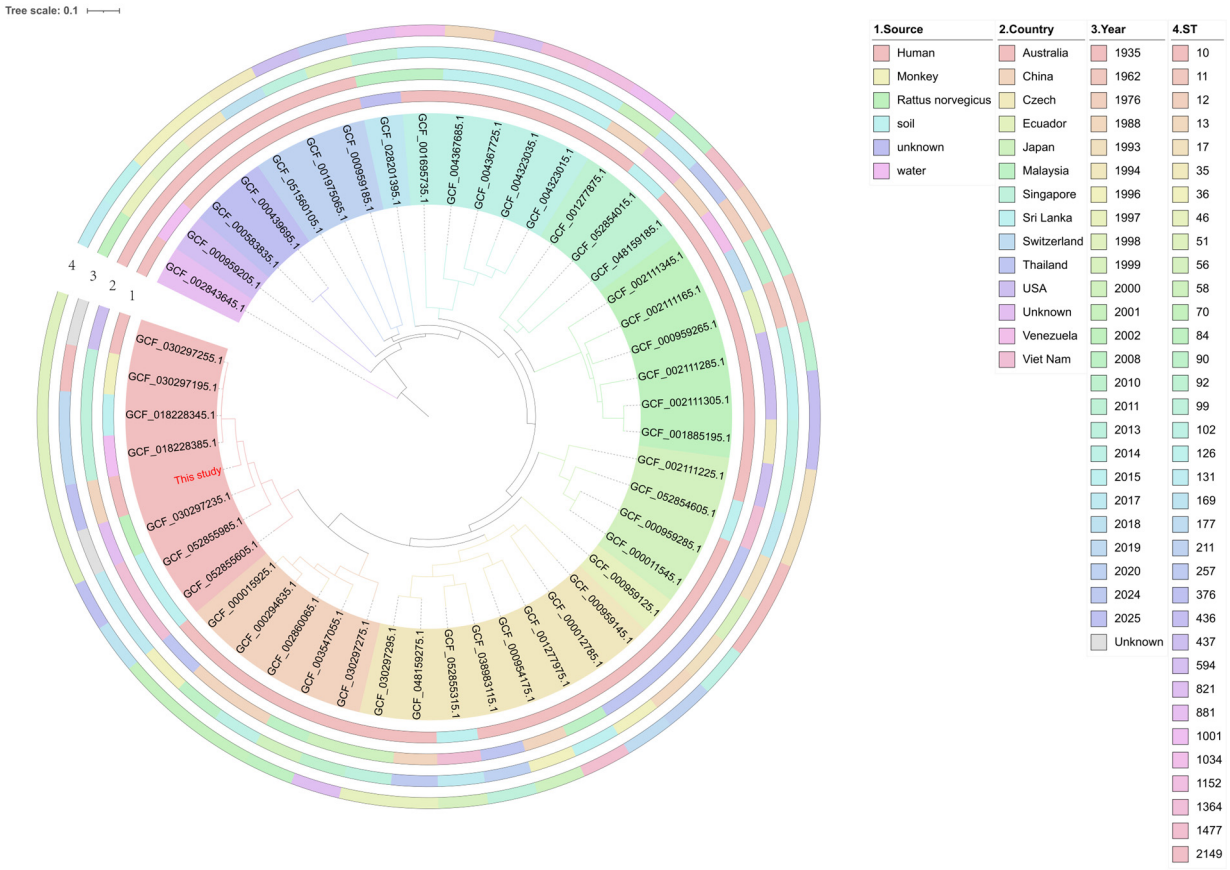


Figure 4. Whole-genome single-nucleotide polymorphism (SNP)-based maximum-likelihood phylogeny of *B. pseudomallei*. The clinical isolate is shown in red alongside reference genomes retrieved from the National Center for Biotechnology Information database; reference genome accession numbers and metadata are listed in Table S1. The four annotation rings indicate, from the innermost to the outermost, isolation source, country, year, and sequence type (ST) determined by multilocus sequence typing (MLST). The scale bar represents 0.1 nucleotide substitutions per site.

2.4. Environmental Investigation

To explore a possible environmental source, soil and water were sampled around the patient's residence in Lai'an County on 9 December 2025. Sites were selected after a structured interview covering farming activities, the recalled ankle injury, and contact with wet soil or surface water, and comprised the yard, adjacent farmland, and the site of the injury, all within approximately 50 m of the residence. At each of the 20 sites, two soil samples were taken at 30 cm depth (40 samples); six water samples were collected from the household tap, an irrigation ditch, and standing water nearby. Samples were transported at ambient temperature, protected from light, and processed within 24 h.

Processing followed the consensus recommendations for environmental sampling of *B. pseudomallei* [19]. Ten grams of each soil sample (or 10 mL of each water sample) was inoculated into 10 mL of Ashdown broth and incubated at 40 °C for 48 h. Enrichment cultures were streaked onto Ashdown's agar and incubated at 40 °C for up to 7 days. Plates were examined daily for colonies typical of *B. pseudomallei* (purple, flat, dry, and wrinkled). DNA was extracted from each enrichment broth using the FastPure Stool/Soil DNA Extraction Kit (Vazyme Biotech, Nanjing, China) according to the manufacturer's

instructions. The extracts were examined by TaqMan real-time PCR targeting *orf2* within the type III secretion system 1 gene cluster, using the primers and probe described by Novak et al. [20], with Premix Ex Taq (Probe qPCR; Takara Bio, Kusatsu, Japan) on a QuantStudio 3 Real-Time PCR System (Applied Biosystems, Waltham, MA, USA). Any colony of typical morphology would have been confirmed by the same assay. Sterile water blanks and a no-template control were included in each batch.

B. pseudomallei was neither recovered by culture nor detected by PCR in any of the 40 soil or six water samples. A single negative survey of this size does not establish that a site is free of *B. pseudomallei*, and these results therefore do not exclude a local reservoir.

3. Methods

3.1. Systematic Review-Search Strategy

This systematic review was conducted in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) 2020 statement [21]. PubMed/MEDLINE and Web of Science were searched from database inception to 5 November 2026. The strategy combined terms for the organism ("*Burkholderia pseudomallei*" OR "melioidosis") with terms for osteoarticular involvement ("osteomyelitis", "septic arthritis", "osteoarticular", "musculoskeletal", "bone and joint", "spondylodiscitis", "spondylitis", and "discitis"). PubMed and MEDLINE were searched through their respective interfaces (PubMed and EBSCOhost); records retrieved from both were pooled and de-duplicated so that each record was counted once. The complete database-specific strategies are provided in Table S2.

3.2. Eligibility Criteria

Studies were eligible if they (i) were full-text English-language reports of observational cohorts drawn from general melioidosis populations or specifically investigating osteoarticular melioidosis, with a defined source population, recruitment period, and longitudinal clinical observation; (ii) included patients with melioidosis confirmed by culture, with or without a validated molecular assay; (iii) reported osteomyelitis, native-joint septic arthritis, or both, diagnosed clinically with supporting imaging, operative, pathological, or microbiological evidence; and (iv) provided an extractable numerator and corresponding valid denominator for at least one variable or outcome. Clinical variables comprised comorbidity, presentation, and anatomical site. Management and outcome variables comprised surgical and antimicrobial treatment, death, and recurrence.

Reports were excluded if they were single case reports, selectively assembled case series, narrative reviews or editorials without primary data, conference abstracts without extractable data, or animal or in vitro studies. When two or more reports from the same source described overlapping periods, the most recent report providing the most complete data for each outcome was retained.

3.3. Selection and Data Extraction

Records were exported and de-duplicated. Titles and abstracts were screened independently by two reviewers (Y.W. and Y.D.), and the full text of every potentially eligible record was then assessed against the criteria by the same two reviewers. Disagreements were resolved by a third reviewer (J.L.) when consensus was not reached. Reasons for exclusion at full-text stage were documented and are summarized.

Data were extracted independently by the two reviewers into a standardized form, and discrepancies were checked against the source article. The form captured study setting and country, design, study period, total number of melioidosis patients, number with osteoarticular involvement, age and sex, predisposing conditions, anatomical site, diagnosis evidence,

antimicrobial regimens and durations, surgical procedures, and reported outcomes with follow-up.

3.4. Study Quality Assessment

The descriptive clinical data from the included osteoarticular populations were appraised using the 10-item Joanna Briggs Institute (JBI) Critical Appraisal Checklist for Case Series [22] by two reviewers (Y.W. and Y.D.). In cases of disagreement, the opinion of a third reviewer (J.L.) was requested. Items addressed eligibility criteria, reliable measurement and identification of the condition, consecutive and complete inclusion, demographic and clinical reporting, outcomes or follow-up, study setting, and statistical analysis. Each item was recorded as yes (Y), no (N), unclear (U), or not applicable (NA). Each Y response was assigned 1 point, and each N or U response was assigned 0 points. Items rated as NA were excluded from the denominator [23]. The summary percentage was calculated by dividing the number of Y responses by the number of applicable items and multiplying by 100. No items were rated as NA in this review. Studies were categorized as having high (≥70%), moderate (≥50% to <70%), or low (<50%) methodological quality, using the thresholds reported in a previous review [24].

3.5. Statistical Analysis

Analyses were performed in R version 4.6.1 (R Foundation for Statistical Computing, Vienna, Austria) with the meta package. Two levels of denominator were distinguished throughout: proportions describing the clinical spectrum of osteoarticular disease (comorbidity, presentation and anatomical site, treatment, death, and recurrence) used as denominator the patients with osteoarticular involvement in each cohort, whereas the proportion of melioidosis patients with osteoarticular involvement used as denominator all culture-confirmed melioidosis patients in that cohort. Proportions were pooled on the logit scale with a random-effects model and reported with 95% confidence intervals (CIs). Heterogeneity was quantified with τ^2 and I^2. Sensitivity analyses comprised leave-one-out estimation, in which each study was omitted in turn and the pooled estimate recalculated. Publication bias was examined with funnel plots and Egger's regression test.

4. Results

4.1. Study Selection

The searches retrieved 322 records (PubMed/MEDLINE 214, and Web of Science 108). After removal of 87 duplicates, 235 records were screened by title and abstract. Full texts were sought for 90 reports; 10 could not be retrieved, leaving 80 reports for eligibility assessment. Of these, 63 reports were excluded because they had no eligible original cohort data ($n = 1$), had an ineligible design ($n = 27$), involved an ineligible pathogen ($n = 3$) or diagnosis ($n = 1$), did not permit separation of relevant data ($n = 18$), lacked a determinable numerator or denominator ($n = 6$), overlapped with retained reports without an eligible additional dataset ($n = 6$), or were not published in English ($n = 1$). Seventeen reports were included in the review and quantitative synthesis (Figure 5).

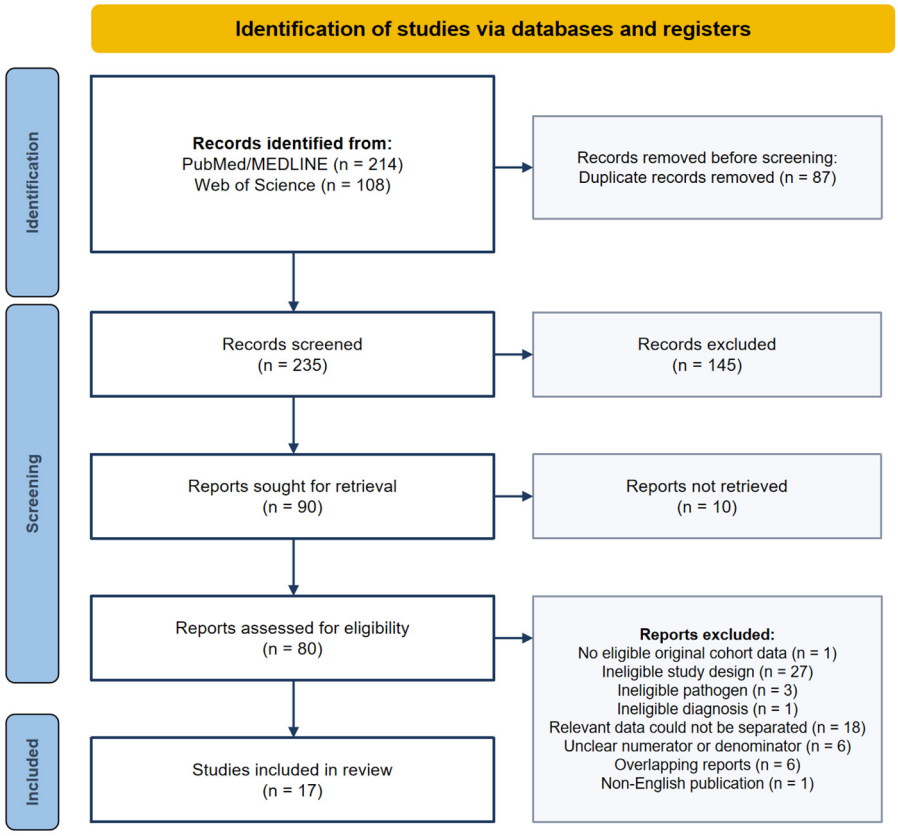


Figure 5. PRISMA flow diagram.

4.2. Characteristics of the Included Cohorts

Seventeen cohorts were included (Table 2), published between 2000 and 2026 and recruiting over a period extending from October 1989 to February 2024. Thirteen were from South and Southeast Asia (seven from India, three from Thailand, and one each from Sri Lanka, Malaysia, and Brunei), three from northern Australia, and one from southern China. All were cohort studies with general melioidosis and dedicated osteoarticular populations. The number of patients with osteoarticular involvement ranged from 4 to 122, and the 17 cohorts together contributed 584 patients.

The age range was 29 to 70 years, with a male predominance. Melioidosis was confirmed by culture in every cohort, and three added a molecular method [25–27]. Antimicrobial susceptibility was reported by seven cohorts. Isolates were susceptible to ceftazidime and meropenem, with individual reports of amoxicillin–clavulanate resistance [27] and of ciprofloxacin and gentamicin resistance [28]. Intravenous intensive therapy was ceftazidime or a carbapenem in every cohort that specified a regimen, given for about two weeks in most cohorts and for four to eight weeks in those that described osteoarticular treatment in detail [29–31]. It was followed by oral trimethoprim–sulfamethoxazole, with or without doxycycline, for three to six months. Surgery was reported by 11 cohorts. Procedures ranged from aspiration and image-guided drainage to arthrotomy, bone debridement and spinal instrumentation. Mortality was reported by most cohorts, recurrence by seven, and the duration of follow-up by only five, in which it ranged from one to ten years.

Table 2. Summary of the characteristics of the included studies.

Study (Year)	Country	Design, Study Period	OA/Melioidosis Cohort, *n*	Mean/Median Age or Range, y	Male, *n*	Diabetes, *n*	Surgery/Procedures, *n*	Antimicrobial Treatment (Intensive → Eradication)	Microbiological Evidence and Susceptibility	Follow-Up, y	Mortality, *n*	Recurrence, *n*	JBI
Currie et al. (2000) [29]	Australia	Cohort, October 1989–September 1999	19/252	NR	NR	NR	NR	IV CAZ or MEM/IPM ≥14 days (some OA ≥8 weeks) → oral TMP–SMX or DOX ≥3 months	Culture; AST NR	NR	1	NR	10
Mukhopadhyay et al. (2008) [32]	India	Cohort, September 2005–July 2007	4/25	29–40	4	2/4	NR	IV MEM or CAZ → oral TMP–SMX; duration NR	Culture; AST NR	NR	0	NR	9
Teparrakkul et al. (2008) [33]	Thailand	Cohort, February 2002–May 2005	86/679	NR	NR	NR	Aspiration, arthrotomy or incision and drainage (64)	IV CAZ median 13 days → oral (agent NR) median 127 days	Culture; AST NR	1–4	27	NR	10
Pande et al. (2011) [34]	Brunei	Cohort, August 2001–November 2007	8/48	31–55	7	5	Percutaneous knee washout (4), open elbow washout (1), tibial fenestration / curettage (3)	IV CAZ + AMC or MEM 2–4 weeks → oral AMC, TMP–SMX or DOX 6 months	Culture; AST NR	NR	0	1	9
Vidyalakshmi et al. (2012) [35]	India	Cohort, January 2005–December 2010	21/95	NR	NR	15	NR	IV CAZ 2 weeks → oral TMP–SMX + DOX + CHL 12–20 weeks (CHL first 8 weeks only)	Culture; AST NR	NR	0	NR	9
Arockiaraj et al. (2016) [28]	India	Cohort, January 2009–December 2014	4/NR	58–65	4	4	Subcutaneous abscess aspiration (1), CT-guided biopsy (1), US-guided psoas abscess drainage (2)	IV CAZ 2 weeks → oral TMP–SMX + DOX 20 weeks	Culture; CAZ/DOX susceptible, CIP/GEN resistant	2	0	NR	7
Corea et al. (2016) [25]	Sri Lanka	Cohort, 2006–March 2014	6/32	31–61	5	5	NR	NR	Culture, PCR/MALDI–TOF; AMC susceptible	NR	1	NR	8
Teparrukkul et al. (2017) [36]	Thailand	Cohort, 1 January 2012–31 December 2014	74/NR	53	42	65	Open arthrotomy and washout (53)	NR	Culture; AST NR	1	25	NR	10
Tang et al. (2019) [37]	Malaysia	Cohort, January 2013–December 2017	6/46	NR	NR	NR	NR	IV CAZ or MEM; durations NR	Culture; CAZ/IPM 100%, TMP–SMX 97.1% susceptible	NR	NR	NR	8
Perumal et al. (2020) [38]	India	Cohort, January 2007–December 2016	25/342	47	23	20	Abscess incision/drainage, arthrotomy, bone decompression/curettage (26)	IV CAZ → oral DOX and/or TMP–SMX; durations incomplete	Culture; AST NR	1–10	NR	0	8

Table 2. *Cont.*

Study (Year)	Country	Design, Study Period	OA/Melioidosis Cohort, *n*	Mean/Median Age or Range, y	Male, *n*	Diabetes, *n*	Surgery/Procedures, *n*	Antimicrobial Treatment (Intensive → Eradication)	Microbiological Evidence and Susceptibility	Follow-Up, y	Mortality, *n*	Recurrence, *n*	JBI
Gupta et al. (2021) [39]	India	Cohort, 2018–2020	11/NR	49.8	9	9	Therapeutic debridement (6)	IV MEM or CAZ (± oral TMP–SMX) 2–6 weeks → oral TMP–SMX 1–7 months	Culture; MEM/CAZ/TMP–SMX susceptible	NR	1	1	10
Wu et al. (2021) [26]	China	Cohort, 2010–2019	44/334	50.8	41	38	Drainage/debridement (18)	IPM, CAZ, MEM and TMP–SMX; duration NR	Culture, molecular; CAZ/IPM/AMC 100%, TMP–SMX 97.7% susceptible	NR	9	3	9
Vithiya et al. (2024) [40]	India	Cohort, December 2014–February 2024	22/100	20–70	21	20	Arthrotomy/debridement (7), spinal fixation (2), soft-tissue drainage (4)	IV CAZ or MEM 1–3 weeks → oral TMP–SMX or DOX 6 months	Culture; MEM susceptible; CAZ/DOX/TMP–SMX susceptible increased exposure	1–7	4	NR	9
Dadwal et al. (2024) [30]	Australia	Cohort, 1 January 1998–1 June 2023	39/477	52	27	31	Initial SA arthroscopy (14), open arthrotomy (9), open OM surgery (7)	IV CAZ or MEM 4.6–6.3 weeks → oral TMP–SMX 4.9–6.2 months	Culture; AST NR	NR	1	8	10
Chittrakarn et al. (2024) [41]	Thailand	Cohort, January 2002–December 2022	81/478	56	49	76	Any joint intervention, open arthrotomy or aspiration/drainage (81)	IV CAZ or MEM ± TMP–SMX, median 18 days → oral TMP–SMX ± DOX; eradication duration NR	Culture; AST NR	NR	15	3	10
Campbell et al. (2025) [31]	Australia	Cohort, October 1999–September 2023	122/1129	48.7	59	80	OM sampling, incision/drainage or bone debridement, SA arthroscopy/arthrotomy (71)	IV CAZ or MEM 44.4–56.3 days → oral TMP–SMX 155.2–159.5 days	Culture; AST NR	NR	8	20	10
Radhakrishnan et al. (2026) [27]	India	Cohort, September 2004–August 2012	12/34	NR	NR	NR	NR	IV CAZ 2 weeks → oral TMP–SMX + DOX 3 months	Culture, PCR; CAZ susceptible, AMC resistant	NR	NR	NR	10

Abbreviations: AMC, amoxicillin–clavulanate; AST, antimicrobial susceptibility testing; CAZ, ceftazidime; CHL, chloramphenicol; CIP, ciprofloxacin; CT, computed tomography; DOX, doxycycline; GEN, gentamicin; IPM, imipenem; IV, intravenous; JBI, Joanna Briggs Institute; MALDI–TOF, matrix-assisted laser desorption/ionization time-of-flight mass spectrometry; MEM, meropenem; NR, not reported for the specified population; OA, osteoarthritis; OM, osteomyelitis; PCR, polymerase chain reaction; SA, septic arthritis; TMP–SMX, trimethoprim–sulfamethoxazole; US, ultrasound; y, years.

4.3. Pooled Proportions

Fourteen reports contributed to the analysis of osteoarticular involvement among 4071 patients with melioidosis. The random-effects pooled proportion was 14% (95% CI, 11–18%; I^2 = 80.0%) (Figure 6A). Diabetes mellitus was reported by 13 cohorts and was present in 81% (95% CI 74–87%; I^2 = 53.8%) of the 455 patients whose comorbidity status was reported (Figure 6B).

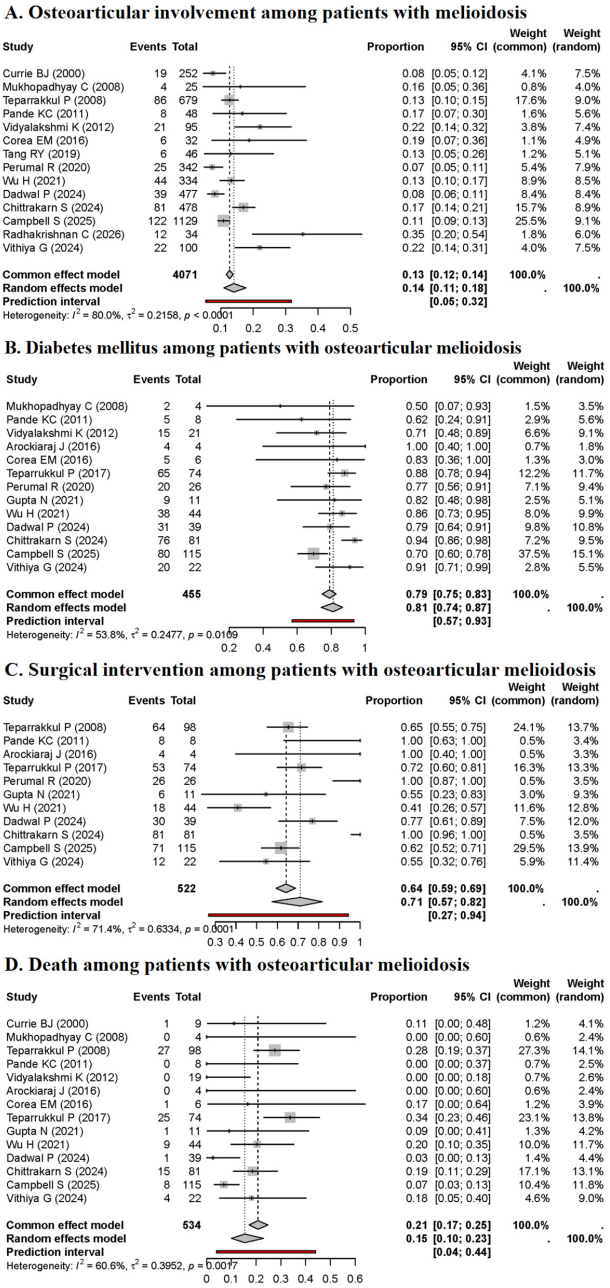


Figure 6. Forest plots of pooled proportions of osteoarticular involvement and associated clinical characteristics and outcomes in melioidosis. (**A**) Proportion of osteoarticular involvement among patients with melioidosis. (**B**–**D**) Proportions of diabetes mellitus (**B**), surgical intervention (**C**), and mortality (**D**) among patients with osteoarticular melioidosis. The source studies are cited in references [25–41]. Each gray square represents the estimate of an individual study, and the horizontal line through it represents the 95% confidence interval. The diamond represents the pooled estimate and its 95% confidence interval, and the vertical reference line indicates the pooled estimate. The red horizontal bar represents the 95% prediction interval.

The phenotype analyses each included 14 cohorts and 525 patients. The pooled proportions for osteomyelitis (OM) alone, septic arthritis (SA) alone, and both manifestations were 22% (95% CI 11–39%; $I^2 = 81.1\%$), 65% (95% CI 42–82%; $I^2 = 89.9\%$) and 15% (95% CI 8–26%; $I^2 = 73.9\%$), respectively (Figure S1). Among 253 patients with OM in eight studies, the tibia was affected in 28% (95% CI 23–34%; $I^2 = 43.6\%$) and the femur in 31% (95% CI 18–48%; $I^2 = 74.7\%$) (Figure S2). The pooled proportions for knee and ankle involvement were 51% (95% CI 47–56%; $I^2 = 23.0\%$) and 21% (95% CI 15–30%; $I^2 = 56.6\%$) of 420 patients with SA in eleven studies (Figure S3). The three phenotype proportions are not additive because OM and SA overlap within patients.

Surgical intervention was reported by 11 cohorts and was performed in 71% (95% CI 57–82%; $I^2 = 71.4\%$) of patients (Figure 6C). Death was reported by 14 cohorts, with a pooled proportion of 15% (95% CI 10–23%; $I^2 = 60.6\%$) among 534 patients (Figure 6D).

4.4. Sensitivity Analyses

Between-study heterogeneity varied across outcomes ($I^2 = 23.0\%$ to 89.9%; $\tau^2 < 0.0001$ to 2.6456 on the logit scale). In a leave-one-out analysis of the proportion of patients with osteoarticular involvement, omission of any single cohort left the estimate between 13% and 15% and I^2 between 76.5% and 81.5%, indicating that no individual cohort determined the pooled estimate or accounted for the heterogeneity (Figure S4).

4.5. Publication Bias

Publication bias was assessed for osteoarticular involvement. The funnel plot showed some visual asymmetry (Figure S5), but Egger's regression test gave no evidence of asymmetry ($p = 0.29$). We therefore found no evidence of publication bias for this outcome.

5. Discussion

This case documents ST51 *B. pseudomallei* distal tibial osteomyelitis with concomitant ankle septic arthritis in an older patient from Anhui Province. Culture and WGS of operative material, supported by imaging and histopathology, established the infectious diagnosis. Repeated surgery and sequential antimicrobial therapy were followed by improvement during ongoing treatment. The main clinical lessons concern recognition of melioidosis where it is infrequently reported, and this case adds clinical, genomic, and treatment data on ST51 osteoarticular melioidosis.

5.1. Clinical Recognition and Diagnosis

Historically, most recognized Chinese cases of melioidosis have occurred in southern provinces [1,42]. Reports from Anhui, Jiangxi, and Chongqing indicate that clinicians in inland regions also need to recognize the disease [5,6]. Such reports may reflect previously unrecognized endemicity, improved detection, or changes in distribution; individual cases cannot distinguish these explanations. For patients with subacute or chronic bone and joint infection, particularly those with diabetes or potential environmental exposure, the absence of recent travel to a recognized endemic area should not exclude melioidosis from the differential diagnosis.

DM is a major predisposing factor for melioidosis, affecting 23–60% of patients [43]. The proportion is higher in osteoarticular disease: in the present review, diabetes was recorded in 81% (95% CI 74–87%) of the 455 patients with osteoarticular involvement in whom comorbidity status was reported. In an Australian cohort that included 39 patients with melioidosis-associated bone and joint infection, diabetes was independently associated with osteoarticular involvement [30]. In our patient, diabetes had been diagnosed during

the current illness, and the elevated HbA1c level suggested that dysglycemia may have preceded the clinical onset of infection.

The patient's occupation as a farmer may suggest opportunities for environmental exposure, but no specific contaminated-soil or water exposure was identified. An ankle sprain without a documented skin breach is not evidence of direct inoculation. Prior bacteremia makes hematogenous spread plausible, while unrecognized inoculation with contiguous extension and secondary bacteremia is another possibility. The sequence of infection and route of acquisition remain undetermined.

Melioidosis has a highly variable clinical spectrum, ranging from localized infection to disseminated disease. Pneumonia is the most common primary presentation, and internal organ abscesses are also frequent, whereas osteomyelitis and septic arthritis are relatively uncommon primary manifestations [31,43,44]. In the 20-year prospective study in Australia, osteomyelitis or septic arthritis was the primary presentation in approximately 4% of patients with melioidosis [44]. In the present review, osteoarticular involvement was recorded in 14% (95% CI 11–18%) of 4071 patients with melioidosis across 14 cohorts; this figure refers to involvement at any time rather than to the primary presentation, and is therefore not directly comparable with the 4% reported above. Among patients with osteomyelitis, the pooled proportions of femoral and tibial involvement were 31% (95% CI 18–48%) and 28% (95% CI 23–34%), respectively, and for joint involvement the knee was affected in 51% (95% CI 47–56%) and the ankle in 21% (95% CI 15–30%). Taken together, the pooled estimates place the femur above the tibia and the knee above the ankle, so the femur and the knee were the more frequently involved sites in the published cohorts; because the two bone estimates overlap, that difference should be read as a trend rather than as a ranking.

Osseous melioidosis may be difficult to diagnose because its clinical and radiological features are nonspecific, particularly when clinical suspicion is low [38]. In this case, CT demonstrated distal tibial destruction, while MRI better delineated marrow, joint, and soft-tissue involvement. MRI can facilitate earlier detection of osteoarticular involvement while plain radiographs and CT may reveal no apparent abnormalities [30]. When feasible, representative deep-tissue or bone specimens and synovial fluid should be obtained to improve diagnostic specificity and guide treatment.

Isolation of *B. pseudomallei* remains the diagnostic cornerstone of melioidosis and enables phenotypic susceptibility testing [3]. In this patient, culture and mNGS results from the referring hospital were reported, but the original documentation was incomplete. Recovery of *B. pseudomallei* from operative purulent material provided direct local microbiological evidence, and WGS supported species identification, and MLST based on the genomic data assigned the isolate to ST51. Unlike nucleic acid-based tests, which generally demonstrate the presence of pathogen-derived genetic material but do not establish organism viability [45], culture recovers viable organisms and permits reliable isolate-based phenotypic antimicrobial susceptibility testing, MLST, and WGS-based phylogenetic analysis. mNGS may complement conventional testing after prior antimicrobial exposure [46].

5.2. Antimicrobial Therapy and Surgical Source Control

Antimicrobial susceptibility testing showed that the isolate was susceptible in vitro to several agents used in the treatment of melioidosis. Persistent fever after 10 days of meropenem may reflect the longer intensive-phase treatment generally required for osteoarticular melioidosis rather than antimicrobial resistance. Undrained purulence and necrotic bone during the early disease course may have contributed to the suboptimal initial clinical response [30].

Antimicrobial treatment of melioidosis generally consists of an initial intensive phase followed by an eradication phase. Intravenous ceftazidime or meropenem is recommended

as first-line treatment during the intensive phase [43]. For osteomyelitis, the 2024 Darwin guideline recommends at least six weeks of intravenous intensive therapy followed by six months of oral eradication therapy. The starting point for intensive-phase duration depends on the timing and culture results of the most recent drainage or debridement [47].

Surgical management is frequently required in osteoarticular melioidosis. In the present review, 71% (95% CI 57–82%; $I^2 = 71.4\%$) of 522 patients with osteoarticular involvement across 11 cohorts underwent a surgical procedure. Differences in the frequency of combined osteomyelitis and septic arthritis, and in local surgical thresholds are the likely sources of the high heterogeneity. Among patients managed operatively in the Darwin cohort, those with combined osteomyelitis and septic arthritis required more procedures than those with either manifestation alone, highlighting the complexity of achieving adequate source control in combined infection [31]. Septic arthritis usually requires drainage and irrigation, and repeated procedures may be necessary. Although early long-bone osteomyelitis without abscess formation and vertebral osteomyelitis without an epidural abscess may sometimes be managed without surgical debridement, extensive osteomyelitis generally requires aggressive and, when necessary, repeated debridement of necrotic bone [43]. In the present case, the localized infection persisted despite initial antimicrobial therapy but was subsequently controlled through repeated debridement and drainage combined with appropriate antimicrobial treatment. This clinical course underscores the importance of adequate surgical source control as an integral component of the management of osteoarticular melioidosis.

5.3. Genomic Context and Source Attribution

Source attribution remains uncertain. The patient reported no recent travel to traditionally endemic regions, but this does not establish local acquisition or exclude earlier exposure. *B. pseudomallei* was not detected in soil and water sampled near his residence; without evidence that sampling adequately represented the relevant exposure, these negative results cannot exclude an environmental reservoir.

The clinical isolate was assigned to ST51, a sequence type previously reported in Anhui, Jiangxi, and Hainan and in several Southeast Asian countries [5]. However, neither a shared sequence type nor phylogenetic proximity establishes the geographic origin of infection or direct transmission between regions. Further source attribution would require additional isolates and more detailed epidemiological metadata. This case underscores the need to consider melioidosis in regions where it is infrequently reported and to interpret genomic findings alongside epidemiological evidence.

5.4. Limitations

Several limitations of this report should be acknowledged. First, records of the referring hospital's microbiological testing and early treatment were incomplete, limiting assessment of the initial diagnostic evidence and reasons for regimen changes. Second, the patient had no clearly documented environmental exposure, and *B. pseudomallei* was not recovered from environmental samples collected near his residence; therefore, the source of infection could not be definitively determined. Third, only a single clinical isolate was analyzed. The phylogenetic findings depended on the selection and representativeness of the reference genomes and were subject to sampling bias inherent to publicly available databases. Consequently, these findings cannot establish a specific transmission route or direction of spread. Fourth, the intensive-phase regimen included ceftazidime–avibactam, which is not a first-line agent for melioidosis and was used because single-agent ceftazidime was unavailable; the case should not be read as supporting this combination. Fifth, follow-up was limited to two months; longer follow-up is needed to assess the risk of relapse, particularly

given the prolonged eradication therapy required for osteoarticular melioidosis. Sixth, the systematic review was restricted to English-language reports, and some potentially eligible full texts could not be retrieved. Differences in study populations, diagnostic scope, and outcome reporting, together with between-study heterogeneity, limit the generalizability of the pooled estimates.

6. Conclusions

Melioidosis should be considered in compatible bone and joint infections in regions where it is infrequently reported, particularly in patients with diabetes or potential environmental exposure. In this case, operative cultures established the diagnosis of *B. pseudomallei* osteomyelitis with concomitant septic arthritis. Repeated debridement and sequential antimicrobial therapy were followed by improvement during ongoing treatment. Genomic analysis identified ST51 but did not establish the source of infection. In a systematic review of 17 cohorts, osteoarticular involvement was present at some point during the illness in 14% of patients with melioidosis; among patients with osteoarticular disease, diabetes was present in 81%; surgery was performed in 71%; and death occurred in 15%. Septic arthritis alone was more frequent than osteomyelitis alone (65% versus 22%), and the femur and knee were the most commonly involved sites (31% and 51%). Early diagnosis, established by culture and supported by molecular and imaging findings, together with guideline-concordant antimicrobial therapy and adequate surgical source control, is the principal determinant of a favorable outcome in osteoarticular melioidosis.

Supplementary Materials: The following supporting information can be downloaded at: https://www.mdpi.com/article/10.3390/tropicalmed11120344/s1. Table S1. Reference genomes and metadata used in the phylogenetic analysis. Table S2. Search strategy. Figure S1. Forest plots of the pooled proportions of osteomyelitis (A), septic arthritis (B), and combined bone and joint involvement (C) among patients with osteoarticular melioidosis. Figure S2. Forest plots of the pooled proportions of tibial (A) and femoral (B) involvement among patients with osteoarticular melioidosis complicated by osteomyelitis. Figure S3. Forest plots of the pooled proportions of knee (A) and ankle (B) involvement among patients with osteoarticular melioidosis complicated by septic arthritis. Figure S4. Leave-one-out sensitivity analysis of the pooled proportion of osteoarticular involvement among patients with melioidosis. Figure S5. Funnel plot for the assessment of the pooled proportion of osteoarticular involvement among patients with melioidosis.

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Institutional Review Board Statement: The report was conducted in accordance with the Declaration of Helsinki and approved by the Institutional Ethics Committee of the First Affiliated Hospital of Nanjing Medical University (approval no. 2022-SR-554; 9 November 2022).

Informed Consent Statement: Informed consent was obtained from the subject involved in the study.

Data Availability Statement: The data presented in this study are available on request from the corresponding author.

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

Abbreviations

The following abbreviations are used in this manuscript:

AMC	amoxicillin–clavulanate
ANI	average nucleotide identity
AST	antimicrobial susceptibility testing
CAZ	ceftazidime
CHL	chloramphenicol
CI	confidence interval
CIP	ciprofloxacin
CLSI	Clinical and Laboratory Standards Institute
CT	computed tomography
DM	diabetes mellitus
DNA	deoxyribonucleic acid
DOX	doxycycline
GEN	gentamicin
HbA1c	glycated hemoglobin
IPM	imipenem
iTOL	interactive Tree Of Life
IV	intravenous
JBI	Joanna Briggs Institute
MALDI–TOF MS	matrix-assisted laser desorption/ionization time-of-flight mass spectrometry
MEM	meropenem
MIC	minimum inhibitory concentration
MLST	multilocus sequence typing
mNGS	metagenomic next-generation sequencing
MRI	magnetic resonance imaging
NR	not reported in the available extracted data
NCBI	National Center for Biotechnology Information
OA	osteoarthritis
OM	osteomyelitis
PCR	polymerase chain reaction
PRISMA	Preferred Reporting Items for Systematic Reviews and Meta-Analyses
Q30	Phred quality score of at least 30
SA	septic arthritis
SNP	single-nucleotide polymorphism
SPAdes	St. Petersburg genome assembler
ST	sequence type
ST51	sequence type 51
TMP–SMX	trimethoprim–sulfamethoxazole
US	ultrasound
VSD	vacuum-sealing drainage
WGS	whole-genome sequencing

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