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Bartonella quintana Endocarditis: A Systematic Review of Individual Cases

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Background. *Bartonella quintana* is a louse-borne bacterium that remains a neglected cause of endocarditis in low-resource settings. Our understanding of risk factors, clinical manifestations, and treatment of *B. quintana* endocarditis are biased by older studies from high-income countries.

Methods. We searched Pubmed Central, Medline, Scopus, Embase, EBSCO (CABI) Global Health, Web of Science and international trial registers for articles published before March 2023 with terms related to *Bartonella quintana* endocarditis. We included articles containing case-level information on *B. quintana* endocarditis and extracted data related to patient demographics, clinical features, diagnostic testing, treatment, and outcome.

Results. A total of 975 records were identified, of which 569 duplicates were removed prior to screening. In total, 84 articles were eligible for inclusion, describing a total of 167 cases. Infections were acquired in 40 different countries; 62 cases (37.1%) were acquired in low- and middle-income countries (LMICs). Disproportionately more female and pediatric patients were from LMICs. More patients presented with heart failure (n = 70/167 [41.9%]) than fever (n = 65/167 [38.9%]). Mean time from symptom onset to presentation was 5.1 months. Also, 25.7% of cases (n = 43/167) were associated with embolization, most commonly to the spleen and brain; 65.5% of antimicrobial regimens included doxycycline. The vast majority of cases underwent valve replacement surgery (n = 154/167, [98.0%]). Overall case fatality rate was 9.6% (n = 16/167).

Conclusions. *B. quintana* endocarditis has a global distribution, and long delays between symptom onset and presentation frequently occur. Improved clinician education and diagnostic capacity are needed to screen at-risk populations and identify infection before endocarditis develops.

Keywords. trench fever; poverty; louse; cardiac.

Bartonella quintana is a louse-borne bacterium that remains a neglected cause of bacteremia and endocarditis in low-resource settings [1–3]. *B. quintana* is transmitted by body lice, although rare transmission related to head lice has recently been described [4]. Due to the link with pediculosis, infection with *B. quintana* is associated with inadequate access to running water and suitable housing, with documented outbreaks in refugee camps and homeless shelters [1, 5, 6].

The first description of human disease due to *B. quintana* was reported in 1915 among World War I soldiers, causing a relapsing febrile illness historically known as trench fever [7]. It is estimated that 1 million cases of trench fever occurred during the war [8]. Eighty years later, *B. quintana* was determined to be a cause of culture-negative endocarditis among homeless individuals in high-income countries (HIC) with the first case published in 1993 [9, 10]. In 2023, *Bartonella* serologic titer greater than 1:800 was added as a major criterion in the diagnosis of infective endocarditis [11].

Bartonella species, and *B. quintana* specifically, have been identified as a common cause of bacteremia and endocarditis on the African continent [3, 12]. In a multicenter study of febrile illness, *Bartonella* species were among the first and second most common bacterial causes of fever in Madagascar and Burkina Faso, respectively [12]. Recent publications suggest that *B. quintana* may be the second most common cause of endocarditis in South Africa, and may be a common cause of endocarditis in Ethiopia [3, 13]. In a single study from France, mortality due to *B. quintana* endocarditis exceeded 10%, even with recommended antimicrobial therapy and valvular replacement surgery [14].

Despite *B. quintana*'s historical significance and contemporary prevalence, extensive knowledge gaps limit our understanding of this pathogen's most severe clinical manifestation. Clinical data on *B. quintana* endocarditis are limited to case reports and case series, with few prospective cohorts, no systematic reviews and no randomized controlled trials. Multiple

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factors contribute to *B. quintana*'s neglect. *B. quintana* is a fastidious, intra-erythrocytic gram-negative bacillus [15]. The bacterium does not grow on routine 5-day blood culture and predominantly requires molecular and serologic techniques or prolonged culture with specialized methods for identification [1]. *B. quintana* causes subacute bacteremia that may last longer than 18 months and therefore temporal delays occur between acute infection and disease-related mortality [1, 2, 16]. This delay may interfere with identifying *B. quintana* as the cause of severe disease, as endocarditis may manifest months to years after initial infection [1]. Furthermore, the few cohort studies of fever that include *Bartonella* testing are often limited by selection bias, as the disease necessitates lice infestation and thus conditions of severe privation: returning travelers are unlikely to experience conditions of extreme poverty associated with body lice infestation. Risk factors for *B. quintana* infection, such as homelessness and poverty, are simultaneously barriers to diagnosis and care.

The objective of this systematic review was to examine the epidemiology, clinical manifestations, diagnosis, treatment and outcomes of *B. quintana* endocarditis cases to inform evidence-based guidelines.

METHODS

Systematic Literature Search Strategy

We searched databases in PubMed Central, Medline, Scopus, Embase, Web of Science, EBSCO Global Health and Cochrane Central Register of Controlled Trials (CENTRAL) and the trial registers www.ClinicalTrials.gov and https://trialsearch.who.int/Default.aspx from database inception to 1 March 2023 to identify publications containing specific search terms (Figure 1). We searched for titles and abstracts using the following search string: {(*Bartonella quintana* OR *Rochalimaea quintana* OR *Rickettsia quintana* OR Trench fever) AND (Endocarditis)}. Additionally, we searched reference lists of selected publications and conducted a Google search of the grey literature to identify other reported cases not published elsewhere. No language restrictions were placed, though search terms were run in English. This review followed the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines for conducting and reporting systematic literature reviews and was registered in the International Prospective Register of Systematic Reviews (PROSPERO; identifier CRD42023404504) [17, 18].

Search terms for title, abstract, references, and MeSH index:

(*Bartonella quintana* OR *Rochalimaea quintana* OR *Rickettsia quintana* OR Trench fever)

AND

Endocarditis

Figure 1. Search strategy for PubMed specifically is listed here. Terms and strategies for other databases modified slightly based on each database's searchable fields. Abbreviation: MeSH, medical subject headings.

Study Selection

We evaluated any publication containing human case-level data on *B. quintana* endocarditis (Supplementary Appendix 1). This included randomized controlled trials, prospective cohort studies, retrospective cohort studies, case series, case reports, observational epidemiological studies and brief communications. Laboratory confirmation of *B. quintana* infection to species level was required for inclusion in this review. Author report of endocarditis was sufficient for inclusion. Echocardiography findings were recorded but not required. Due to serological cross reactivity with other *Bartonella* species, *Chlamydia,* and *Coxiella*, cases of *Bartonella* endocarditis diagnosed by serology alone and not identified to species level were excluded from the main analysis and described separately (Supplementary Appendix 2) [19]. The same applied to cases identified to *Bartonella* genus using molecular techniques. Reports of *B. quintana* endocarditis confirmed to species level but without case-level data were excluded from the main analysis and described separately (Supplementary Appendix 3). Information on antimicrobial type, duration and total number of different antimicrobials administered was recorded but not necessary for inclusion. Country of likely acquisition was based on author determination or, if not stated, then location of presumed risk factors for *B. quintana* infection was ascribed.

Article Review

The title and abstract of each article identified in the search were screened by 2 individuals (C. B., N. G.) to determine whether the article qualified for full-text review. Articles that were included after title/abstract screening were subsequently reviewed in full by 2 independent reviewers (C. B., N. G.) for eligibility and inclusion. Discrepancies in reviewer decisions were resolved by discussion with a third reviewer. Certain case series included cases of *B. quintana* endocarditis that met inclusion criteria as well as cases that did not.

Data Extraction

Information was extracted manually from included articles by one author (C. B.) using Microsoft Excel (2019, version 16.72) and verified by a second author (N. G.) who flagged incongruities. Discrepancies were resolved through group discussion. For each reference, we extracted the study type, country of the first author's institution, and number of patients. We collected:

- Epidemiologic information: patient demographics, location of exposure, housing status, and ectoparasitosis.

- Clinical information: symptomatology, affected valve(s), vegetation size, embolization, immunologic sequalae, comorbidities including substance use disorders, human immunodeficiency virus (HIV) infection, and pre-existing valvular abnormalities, clinical outcome and antimicrobial-related adverse effects.
- Diagnostic information: serology, molecular testing, and culture results.
- Treatment-related information: antimicrobial regimen, duration of antimicrobial treatment, and surgical interventions.

We avoided repeating individual cases by consolidating descriptions of the same case described in different articles into one case record. Living in a refugee camp qualified as being homeless due to common risk factors such as lack of running water. Living in a single-room-occupancy (SRO) or in prison counted as being housed. The following clinical outcomes were considered: all-cause mortality, survival, and loss-to-follow-up. The cases were divided based on the country of acquisition into low and middle-income countries (LMIC) and HICs, as defined by Organisation for Economic Co-operation and Development (OECD) [20]. Data were pooled to facilitate a single analysis.

Statistical Analysis

Descriptive analyses were conducted using R version 4.2.2 software (2022-10-31).

Fisher exact test was used to analyze categorical variables, and 2-tailed *t*-tests were used to compare means of numerical values that were normally distributed. $P \leq .05$ was considered statically significant.

Quality Assessment for Included Studies

Every included case of *B. quintana* endocarditis was assessed for quality using the JBI critical appraisal checklist for methodological quality and potential bias (Supplementary Appendixes 4 and 5) [21]. Each case was evaluated by 2 reviewers (C. B., N. G.). Cases of *B. quintana* endocarditis without sufficient epidemiologic, clinical, diagnostic, and treatment information to meet JBI criteria were excluded from the main analysis and presented separately (Supplementary Appendix 5).

RESULTS

Search Results

We identified 972 articles through the database search, 2 supplementary articles through article reference examination and 1

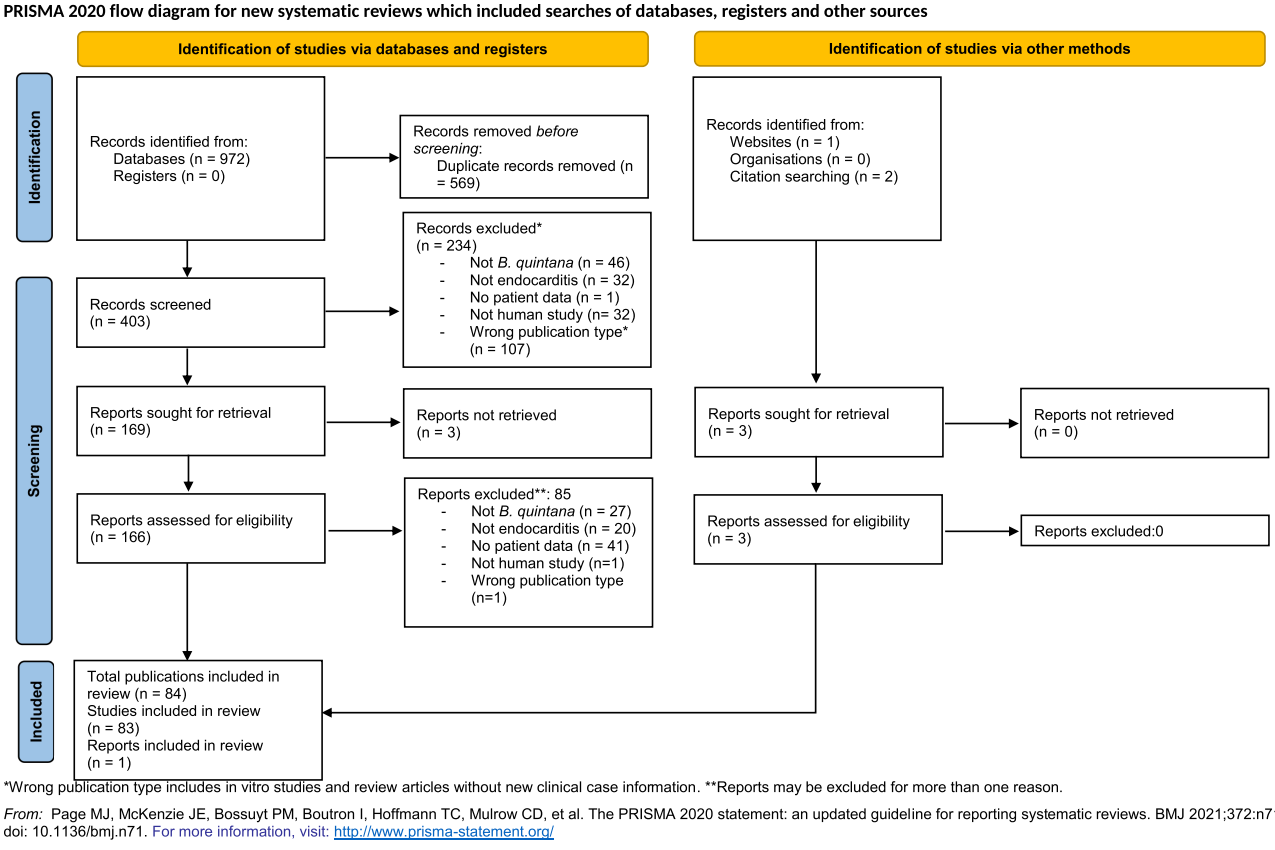

Figure 2. PRISMA 2020 flow diagram for new systematic reviews which included searches of databases, registers and other sources. Abbreviation: PRISMA, Preferred Reporting Items for Systematic Reviews and Meta-Analyses.

additional report through the website search, creating a total of 975 identified articles (Figure 2). In total, 569 duplicate articles were removed, leaving 405 articles for title and abstract screening. After reviewing titles/abstracts and full texts, 84 publications met inclusion criteria: 64 case reports, 19 case series, and 1 outbreak report, describing a total of 167 individual cases of *B. quintana* endocarditis with patient-level information (Supplementary Appendixes 1 and 6). Included articles were published between 1993 and 2022 and originated from 27 countries. Twenty-five publications describing a total of 158 additional cases of possible *B. quintana* endocarditis were excluded due to the absence of species-level confirmation (Supplementary Appendix 2). These 158 cases of endocarditis were predominantly diagnosed by serology alone [22]. Twenty-eight publications describing an additional 203 cases of *B. quintana* endocarditis confirmed to species level were excluded due to the absence of patient-level information (Supplementary Appendix 3). These were predominantly retrospective cohort studies of endocarditis acquired both in HICs and LMICs and analyzed using molecular analysis of stored heart valve tissue [23].

Quality Assessment

Quality assessment using the JBI critical appraisal checklist revealed that 62.7% (84) of publications had sufficient information to be included in the full-text analysis (Supplementary Appendix 5) [21].

Demographics and Epidemiology

Cases of *B. quintana* endocarditis were acquired in 40 different countries (Figure 3, Supplementary Appendices 1 and 6). 62 cases (37.1%) acquired infection in LMICs (Table 1). With the exception of cases from South Africa and Senegal, all other cases acquired in Sub-Saharan Africa and the Horn of Africa were diagnosed in a HIC outside Africa [3, 29, 30]. Mean age was 46.3 years. Seven cases of *B. quintana* endocarditis occurred among children under 18 years of age, of which 6 (85.6%) were acquired in LMICs (Ethiopia, Algeria, Senegal) and 1 was acquired in Northern Canada (Table 2 and Supplementary Appendix 7) [13, 31–33]. Mean age was lower among patients who were infected in LMICs compared to HIC (37.4 vs 49.8, *P* value <.001). 20.9% (n = 35/167) were female. Disproportionately more female cases were reported from LMICs than from high-income countries (HICs) (n = 17/62 [27.4%] vs n = 18/105 [17.1%], *P* value < .121). Significantly more cases of *B. quintana* endocarditis from LMICs were housed compared to those from HICs (n = 40/62 [64.5%] vs N = 26/105 [24.8%], *P* value < .001). Ectoparasitosis was reported among a minority of cases (n = 9/167 [5.4%]), of which 8 described recent body lice infestation and 1 reported remote body lice infestation decades earlier as a child [34].

Clinical Features and Comorbidities

Fever was reported in a minority of *B. quintana* endocarditis cases (n = 65/167 [38.9%]), and more patients presented with symptoms of heart failure (n = 70/167 [41.9%]). Twenty-seven (16.2.%) patients presented with chronic constitutional symptoms (fatigue, weight loss), whereas 22 cases (13.2%) involved renal dysfunction. No cases were associated with bacillary angiomatosis or peliosis. Mean symptom duration prior to presentation was 5.1 months with a standard deviation of 4.2 months, a minimum of 2 weeks and a maximum of 18 months. In addition, 25.7% (n = 43/167) were associated with embolization, most commonly to the spleen (n = 12/43 [27.9%]), brain (n = 10/43 [23.2%]), and peripheral arteries (n = 8/43 [18.6%]). Many patients experienced embolization to multiple anatomic sites [2, 35]. Two cases presented with recurrent intracerebral hemorrhage [33, 36].

Pre-existing valvular abnormalities were reported in 52 cases (31.1%), of which bicuspid aortic valve (n = 12/52 [23.1%]) was the most common aberrancy. There were 5 cases of prosthetic valve endocarditis and 5 cases with preceding rheumatic heart disease. Of the 164 cases where valvular localization was documented, the majority involved the aortic valve alone (n = 94/164 [57.3%]), followed by dual involvement with the aortic and mitral valves (n = 39/164 [23.8%]). Significant valvular destruction was reported in 15 cases (9.1%) with 8 cases of aortic root abscess, 5 cases of valvular perforation, and 2 cases of chordae/coronary cusp rupture. Vegetation size was reported in 40 cases, with a mean largest vegetation diameter of 15.7 millimeters (standard deviation = 9). Immunologic abnormalities were reported in 40 cases, with glomerulonephritis (n = 10/40 [25.0%]) and ANCA-positive vasculitis (n = 4/40 [10.0%]) being the most common syndromes. 9 cases were associated with immunosuppression: 6 individuals lived with HIV and 3 individuals received exogenous immunosuppression. Alcohol use disorder was described in a minority of cases (n = 27/167 [16.2%]) and other substance use was described in 8 cases with 4 cases of injection drug use.

Diagnostics

The vast majority of *B. quintana* endocarditis cases confirmed to species level were diagnosed via molecular testing of excised cardiac valves (n = 153/167 [91.6%]). Twenty-five cases (15.0%) were associated with blood cultures positive for *B. quintana,* with a mean time to positivity of 21.4 days. Of the 138 cases where the molecular target was described, 16S rRNA was the most common (n = 70/138 [50.7%]), followed by citrate synthase gene (gltA) (n = 29/138 [21.0%]) and intergenic transcribed spacer gene (ITS) (n = 24/138 [17.4%]). Serology for *B.quintana* IgG was reported for 153 cases, of which all but 1 were positive (n = 152/153 [99.3%]). The most common serologic test was the indirect immunofluorescent antibody test

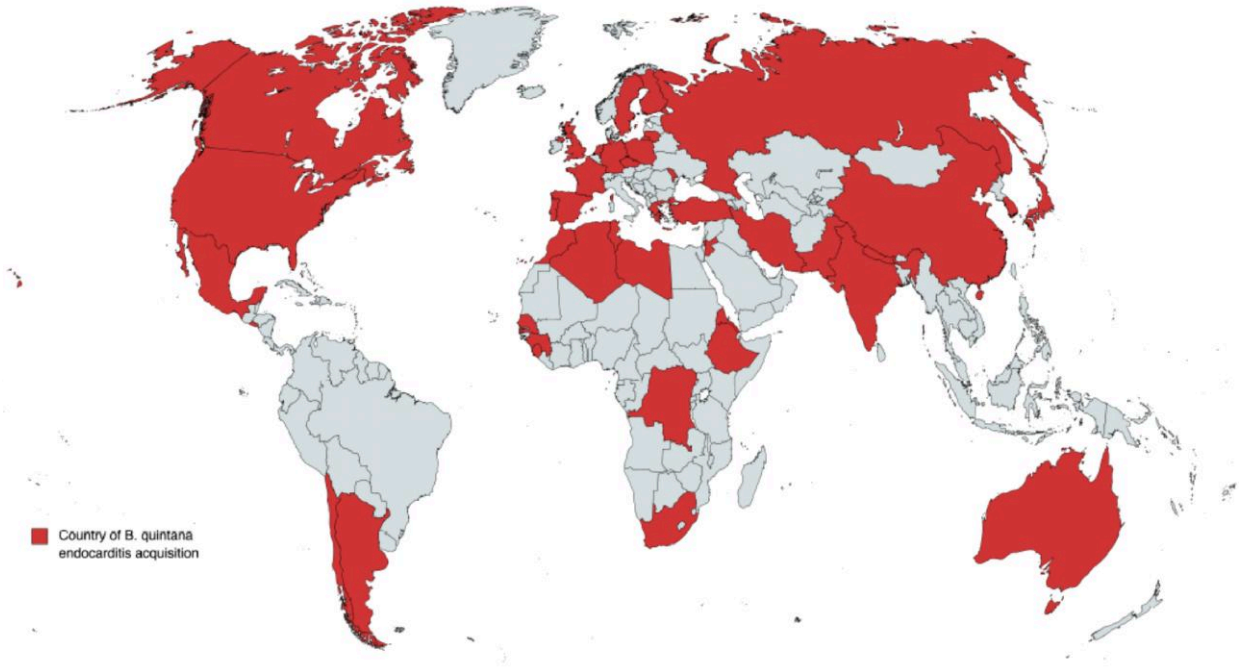

Figure 3. Countries of likely *Bartonella quintana* acquisition among cases of *B. quintana* endocarditis. When 2 countries of likely *B. quintana* acquisition were possible in the original article, both countries were highlighted. This occurred in the following cases: Sierra Leone versus Libya [24], United States versus Nepal [25], Guinea versus France [26], Australia versus Jordan [27]. United States and France were associated with other cases beyond those mentioned above. One case was acquired in Tonga but is not visible due to the country's small geographic area [28]. A full list of country of likely acquisition and associated references are available in Supplementary Appendix 6. References for figure 3 legend.

(IFA) (n = 86/153 [56.2%]), with an average positive titer of 1:2421. The most common cutoff for positivity was assay dependent (1:64 or 1:100). Four cases of polymicrobial endocarditis were identified, with 2 cases of *Streptococcus pneumoniae* and *Staphylococcus aureus* each [2].

Antimicrobial Treatment, Surgical Interventions and Outcomes

Dozens of various empiric antimicrobial regimens were used, but therapy was predominantly narrowed to a combination regimen of doxycycline with either an aminoglycoside (eg: gentamicin) or rifampin after diagnosis was confirmed (n = 73/115 [63.5%]). 65.5% of antimicrobial regimens included doxycycline. 75.7% of regimens included an aminoglycoside Twelve cases (7.2%) could not initiate or continue aminoglycosides due to renal failure. The average duration of antimicrobial therapy was 77.7 days. The vast majority of cases underwent valve replacement surgery (n = 154/167 [98.0%]). Three individuals underwent additional surgery for associated embolization, such as embolectomy/mycotic aneurism coiling.

Overall case fatality rate was 9.6% (n = 16/167); 5 individuals were lost to follow-up. Fatal cases demonstrated more multivalvular involvement (n = 8/16 [50.0%]) than cases that survived (n = 31/105 [29.8%]) (Tables 3 and 4 and Supplementary Appendix 7). Fatal cases were also more likely to be above 65 years of age ($P = .008$), present with fever ($P = .034$), have renal dysfunction ($P = .026$) and not receive valvular replacement surgery ($P = .010$).

DISCUSSION

The existence of *B. quintana* endocarditis in 40 countries, on all continents except Antarctica, with both urban and rural acquisition, indicates that *B. quintana* is an infection with a worldwide presence. Many reports describe *B. quintana* endocarditis as a rare entity [37]. Our description of 370 cases (167 in the main analysis and 203 additional cases excluded due to insufficient patient-level data) suggests that *B. quintana* may be more common than previously suggested. This statement is further corroborated by the fact that the majority of the articles describe single cases without screening close contacts, suggesting a substantial burden of undiagnosed infection across dozens of geographic areas [5, 38].

The existing narrative about risk factors for *B. quintana* acquisition is biased by cases acquired in high-income countries, focusing on urban homelessness, alcohol use, and male sex [1, 39]. Infections acquired in LMICs without these associations are frequently described as having no risk factors [13, 40]. Considering the disproportionate number of female and

Table 1. Comparison of *Bartonella quintana* Endocarditis Cases From Low and Middle-income Countries (LMICs) and High-income Countries (HICs)

	LMIC			HIC				
	N	%	95% CI	N	%	95% CI	RR (95% CI)	*P* Value
Rural	26	41.9	29.5–55.1	6	5.7	2.1–12.0	7.4 (3.2–16.8)	***P* < .001**
Housed	40	64.5	51.3–76.3	26	24.8	16.9–34.1	2.6 (1.8–3.8)	***P* < .001**
Female	17	27.4	16.8–40.2	18	17.1	10.5–25.7	1.6 (.9–2.9)	*P* = .121
Emboli	14	22.6	12.9–35.0	29	27.6	19.3–37.2	0.8 (.5–1.4)	*P* = .583
Pre-valve disease	4	6.5	1.8–15.7	27	25.7	17.7–35.2	0.3 (.1–.7)	***P* = .002**
Death	3	4.8	1.0–13.5	13	11.4	6.1–19.1	0.4 (.1–1.3)	*P* = .172
Total	**62**			**105**			…	…

Rural: cases reported to be acquired from a rural environment. Housed: cases who were housed (rather than houseless). Emboli: cases associated with embolization. Pre-valve disease: cases with pre-existing valvular disease. *P* value from Fisher exact test.

Abbreviations: CI, confidence interval; RR, risk ratio.

Table 2. Pediatric Cases of *Bartonella quintana* Endocarditis

Author	Year	Country	Age	Sex	Valve	Emboli	Surgery	Outcome
Berdagué [1]	1998	Algeria	15	F	AV/MV	Y (lung)	Embolization pulmonary artery, VR	Survived
Posfay [2]	2000	Senegal	13	F	AV/MV	N	VR	Survived
Tasher-1 [3]	2017	Ethiopia	7	F	PV	N	VR, PDA closure	Survived
Tasher-2 [3]	2017	Ethiopia	9	F	AV	Y (brain)	VR, PDA closure	Survived
Tasher-3 [3]	2017	Ethiopia	12	F	MV	N	VR	Survived
Tasher-4 [3]	2017	Ethiopia	16	F	AV	Y (spleen)	VR	Survived
Boodman [4]	2022	Canada	11	M	AV	N	VR	Survived

Age in years.

References for this table are available in Supplementary Appendix 7.

Abbreviations: AV, aortic valve; F, female; M, male; MV, mitral valve; N, no; PV, pulmonary valve; VR, valve replacement; Y, yes.

pediatric cases from LMICs without a history of homelessness or alcohol use disorder, we hypothesize that being from a location in an LMIC where there are barriers to accessing water for routine hygiene is a risk factor for *B. quintana* infection, irrespective of housing and alcohol use. Four cases from HICs without typical risk factors reported working in excavation and waste disposal, suggesting that this work may put one at risk for *B. quintana* infection [41, 42].

B. quintana endocarditis is predominantly a disease affecting native aortic valves, as previously described [1]. Many cases described months of non-specific constitutional symptoms before presenting with valvular insufficiency or embolization [1, 2]. Notably, most cases were afebrile. After this insidious initial presentation, *B. quintana* endocarditis may then cause abrupt clinical decompensation due to cardiac tissue destruction with large vegetations, valvular perforation and aortic root abscesses [37]. The average symptomatology of 5 months before diagnosis reflects a missed opportunity to identify and treat the disease early and prevent catastrophic endovascular outcomes. Early treatment may help reduce the 10% case fatality rate, though prospective studies are needed. Due to *B. quintana's* vague symptomatology and association with auto-antibody production, a few cases were initially misdiagnosed as ANCA-vasculitis or glomerulonephritis [41]. Iatrogenic immunosuppression therapy for these misdiagnoses can have fatal consequences [43].

Considering that only 15% of cases of *B. quintana* endocarditis were associated with blood culture positivity, and that there was a long delay between symptom onset and diagnosis, improvements in diagnostic testing and education are needed to screen at-risk populations and identify bacteremia before the development of endocarditis [1]. The majority of cases were diagnosed by 16S rRNA sequencing of excised cardiac valves, and cases from LMICs were predominantly diagnosed and treated after immigrating to a HIC. *B. quintana* may thus reflect a hidden cause of heart failure in LMICs where access to cardiac surgery and molecular microbiologic testing is limited.

Most cases were treated with a combination of doxycycline and gentamicin. However, a meta-analysis on bartonellosis treatment, not specific to *B. quintana* or endocarditis, failed to find the benefit of gentamicin as the second agent when compared to other antimicrobials, and certain experts recommend rifampin and doxycycline based on anecdotal success [44]. In our study, the survival of 6 *B. quintana* endocarditis cases treated with ceftriaxone and doxycycline suggests that regimens combining doxycycline with another antimicrobial with gram-negative coverage, such as a third-generation cephalosporin, may be effective for *B. quintana* endocarditis [6, 45]. Broadening treatment options may improve clinical outcomes, as many cases of renal toxicity associated with gentamicin were described in this study.

Table 3. Fatal Cases of *Bartonella quintana* Endocarditis

1st Author	Year	Country	Age	Sex	Emboli	Cx	Antimicrobials	Surgery	Time Of Death	Duration Sx
Drancourt [1]	1995	France	43	M	No	Yes	ceftaz + oflo/+netilmicin	VR	4 m post-surg	N/D
Raoult [2]	1996	France	66	F	No	No	ceftriax + gent	VR	N/D	N/D
Raoult [2]	1996	Canada	81	F	No	No	doxy	None	N/D	N/D
Bergmans [3]	1997	Netherlands	74	M	Yes (lung)	No	amp + gent	VR	3 w post-surg	N/D
Guyot [4]	1999	UK	50	M	Yes (lung, skin)	Yes	ceftaz + vanco/ + cipro	None	4 m post-adm	12 m
Znazen [5]	2005	Tunisia	31	M	No	No	None	None	N/D	N/D
Sondermeijer [6]	2006	Morocco	45	M	Yes (brain, spleen)	No	ceftaz	None	1 m post-adm	2 m
Yoda [7]	2008	Japan	66	M	N	Yes	pen/amp-sulbac + vanco	VR	1 m post-surg	1 w
Montcriol [8]	2009	Senegal	50	M	Yes (brain, kidney)	Yes	amox + gent	VR	10 d post-surg	6 m
Alozie [9]	2012	Germany	70	M	Yes (spine)	Yes	rif + ceftriax + vanco + caspo/ gent + doxy	VR	1 m	N/D
Dimopoulos [10]	2012	Greece	26	M	No	No	gent + vanco/gent + doxy	VR	11 d post-adm	N/D
Alaska [11]	2016	USA	51	M	N/D	No	None	None	N/D	N/D
Patel [12]	2019	USA versus Nepal	28	M	No	Yes	gent + doxy	VR	4 m post-adm	6 m
Promer [13]	2020	USA	48	M	Yes (spleen)	No	vanco + aztr + metro/ceftriax + vanco/+ gent + doxy	VR	2 d post-surg	6 m
Boodman [14]	2022	Canada	47	M	Yes (brain)	No	ceftriax + doxy + gent	VR + clip	N/D	N/D
Shepard [15]	2022	USA	66	M	No	No	ceftr + vanco/doxy + rif	VR	12 m post-surg	2 m

Country: country of likely *B. quintana* acquisition.

Abbreviations: +, addition of antimicrobial; adm, after admission; amp, ampicillin; amp-sulbac, ampicillin-sulbactam; aztr, aztreonam; Cx, *B. quintana* growth on blood culture/change in antimicrobial regimen; ceftaz, ceftazidime; ceftriax, ceftriaxone; cipro, ciprofloxacin; doxy, doxycycline; F, female; gent, gentamicin; M, male; metro, metronidazole; N/D, no data; oflo, ofloxacin; pen, penicillin; rif, rifampin; vanco, vancomycin; VR, valve replacement surgery.

Table 4. Comparing Fatal to Non-fatal Cases of *Bartonella quintana* Endocarditis

	Died			Survived				
	N	%	95% CI	N	%	95% CI	RR (95% CI)	*P* value
Age > 65	6	37.5	15.2–64.6	10	9.5	4.6–16.8	**3.9 (1.7–9.3)**	***P* = .008**
Fever	12	75.0	47.6–92.7	48	45.7	36.0–55.7	**1.6 (1.2–2.3)**	***P* = .034**
Emboli	6	37.5	15.2–64.6	37	35.2	26.2–45.2	1.1 (.5–2.1)	*P* = 1.000
Renal dysfct	6	37.5	15.2–64.7	14	13.3	7.5–21.4	**2.8 (1.3–6.3)**	***P* = .026**
Splenomegaly	2	12.5	1.5–38.4	11	10.5	5.4–18.0	1.2 (.3–4.9)	*P* = .682
Multivalvular	8	50.0	24.7–75.4	31	29.5	21.0–39.2	1.7 (1.0–3.0)	*P* = .149
Pre-valve Disease	4	25.0	7.3–52.4	42	40.0	30.6–50.0	0.6 (.3–1.5)	*P* = .284
No surgery	5	31.3	11.0–58.7	7	6.7	2.7–13.3	**4.7 (1.7–13.0)**	***P* = .010**
No gent	7	43.8	19.8–70.1	33	31.4	22.7–41.2	1.4 (.7–2.6)	*P* = .395
No doxy	9	56.3	29.9–80.3	37	35.2	26.2–45.2	1.6 (1.0–2.6)	*P* = .165
Total	**16**			**105**			…	…

Age > 65: age greater than 65 y of age. Fever: presence of fever upon presentation as documented and defined in author's original publication. Emboli: association with embolization. Renal dysfct: renal dysfunction as documented and defined in original publication. Multivalvular: cases of endocarditis affecting multiple cardiac valves. Pre-valve disease: existence of pre-existing valvular abnormalities. No surgery: no valvular replacement surgery. No gent: patients did not receive gentamicin. No doxy: patients did not receive doxycycline. *P* values from Fisher exact test with *P* values < .05 in bold to indicate statistical significance.

Abbreviations: CI, confidence interval; RR, risk ratio.

This systematic review is subject to several limitations. All included articles on *B. quintana* endocarditis with patient-level data were case reports and case series, thus considered low-quality evidence. There was a heterogeneity of clinical data in different studies, with case reports describing more granular data than larger case series. The data may be influenced by publication bias and other forms of bias present in the original studies. Our inclusion criteria created significant bias towards cases diagnosed in HICs with better access to cardiac surgery and molecular diagnostics. Our results may not be generalizable to individuals not undergoing cardiovascular surgery, making it difficult to draw conclusions between surgery and death. The exclusion of articles without case-level information creates further selection bias. Our statistical analyses were performed post hoc, increasing the possibility of false discovery.

This review reveals the lack of high-quality studies on a disease with a global distribution, disproportionately affecting marginalized populations that experience significant diagnostic delays and a substantial case fatality rate despite treatment.

Randomized controlled trials, point-of-care diagnostics and prospective studies are essential to improve our understanding of this neglected disease.

Supplementary Data

Supplementary materials are available at *Clinical Infectious Diseases* online. Consisting of data provided by the authors to benefit the reader, the posted materials are not copyedited and are the sole responsibility of the authors, so questions or comments should be addressed to the corresponding author.

Notes

Disclaimer. The findings and conclusions in this report are those of the authors and do not necessarily represent the official position of the Centers for Disease Control and Prevention (CDC).

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