

ORIGINAL RESEARCH

A Retrospective Cohort Analysis to Assess Prevalence of Persistent Bacteraemia in Patients with a Non-Staphylococcal Infective Endocarditis at a Tertiary Care Hospital

¹Mohit Sikka, ²Vivek Tripathi, ³Ravindra Keshavrao Nitturker

^{1,2}Assistant Professor, ³Associate Professor, Department of General Medicine, L.N. Medical College & Research Centre, Bhopal, Madhya Pradesh, India

Correspondence:

Vivek Tripathi

Assistant Professor, Department of General Medicine, L. N. Medical College & Research Centre, Bhopal, Madhya Pradesh, India

Email: vitaltrip@hotmail.com

Received: 15 July, 2022

Accepted: 24 August, 2022

ABSTRACT

Background: Traditionally, prolonged courses (4 to 6 weeks) of intravenous antibiotics have been recommended for *Staphylococcus aureus* bacteremia, largely because of concerns that infective endocarditis or other complications, such as deep infection foci or metastatic infections. The present study was conducted to assess prevalence of persistent bacteraemia in patients with non-staphylococcal infective endocarditis.

Materials & Methods: A retrospective cohort study was conducted to assess prevalence of persistent bacteraemia in patients with non-staphylococcal infective endocarditis. Demographic data and clinical history were taken. Blood cultures were incubated. All statistical analyses were performed by using R software environment.

Results: A total 540 records were screened. Of these, 90 patients were eligible for inclusion. Of 90 patients, 77.77% (70 patients) received antimicrobial therapy effective against the causative microorganism within 24 h of the first culture. Out of 70 patients, only 5 (4.4%) had a positive blood culture after 2 days of effective antimicrobial therapy, meeting the definition of persistent bacteraemia: 3 patients (7.1%) with prosthetic valve endocarditis and 2 with native valve endocarditis. 4 out of 5 patients with persistent bacteraemia had *Enterococcus faecalis* endocarditis, the other 1 had endocarditis by non-HACEK-gram-negative bacteria.

Conclusion: The present study concluded that prevalence of persistent bacteraemia in patients with non-staphylococcal infective endocarditis was 7.14%.

Keywords: Persistent Bacteraemia, Non-Staphylococcal Infective Endocarditis, Antimicrobial Therapy.

INTRODUCTION

Infectious endocarditis is the inflammation of the endocardium, the inner lining of the heart, as well as the valves that separate each of the four chambers within the heart. It is primarily a disease caused by bacteria and has a wide array of manifestations and sequelae.¹ *Staphylococcus aureus* bacteremia (SAB) is one of the most common serious bacterial infections, with an associated mortality of about 30%. SAB may persist in some patients despite several days of antibiotic therapy, a phenomenon called persistent

bacteremia. Persistent bacteremia accounts for 6%–38% of all episodes of SAB, is particularly common in endovascular infections, and is associated with poor clinical outcomes.² Persistent bacteremia after a 48-hour course of antibiotic therapy is uncommon among patients with non-staphylococcal infective endocarditis (IE), according to findings published in the International Journal of Cardiology.³ Persistent bacteraemia is a marker of uncontrolled infection and may lead to changes in patient management, like the duration of antimicrobial treatment, valve replacement surgery or drainage of metastatic infectious foci.³ Current international and national guidelines for the treatment of patients with infective endocarditis (IE) recommend drawing follow-up blood cultures (FUBCs) every 24 to 48 h after the start of antimicrobial therapy, until sterilization of the bloodstream has been documented.^{4,5} The present study was conducted to assess prevalence of persistent bacteraemia in patients with a non-staphylococcal infective endocarditis.

MATERIALS & METHODS

A retrospective cohort study was conducted to assess prevalence of persistent bacteraemia in patients with non-staphylococcal infective endocarditis in the Department of General Medicine, L. N. Medical College & Research Centre, Bhopal, Madhya Pradesh, India. Before the initiation of the study ethical approval was taken from the Ethical committee of the institute and informed consent was taken from the patients. All adult patients with a definite diagnosis of non-staphylococcal IE were included in the study. Patients with staphylococcal endocarditis, blood-culture negative endocarditis and patients without at least one follow-up blood culture were excluded from the study. Demographic data and clinical history was taken. Blood cultures were incubated using the BACTEC (Becton-Dickinson) and BacT/ALERT (Biomérieux) systems, according to manufacturer's instructions and local protocols. Blood cultures were incubated for a minimum of five day. The index culture was defined as the first blood culture demonstrating clinically significant bacteraemia. A FUBC was defined as a blood culture drawn after the index culture. FUBCs up to 7 days after the index culture was collected and recorded the last day with a positive FUBC. Fever was defined as a temperature of 38 °C or higher. We defined the time to resolution of fever as the interval between the start of appropriate antimicrobial therapy and the first of three consecutive days with a temperature <38 °C. Persistence of fever was defined as time to resolution of fever of seven days or more. Antimicrobial therapy was considered effective if the antimicrobial agent had in vitro activity against the cultured micro-organism. We defined persistent bacteraemia as any blood culture growing the same microorganism as the index culture ≥ 48 h after start of effective antimicrobial treatment. Thus, patients with a positive culture within 48 h but a negative culture thereafter were classified as not having persistent bacteraemia. Patients with a negative culture after 48 h but a positive culture at 72 h were classified as having persistent bacteraemia. This 48-h cut-off after start of antimicrobial treatment is in line with recommendations for defining persistent bacteraemia for *S. aureus* bacteraemia. All statistical analyses were performed by using R software environment (R3.6.0, R: A language and environment for statistical computing).

RESULTS

A total 540 records were screened. Of these, 90 patients were eligible for inclusion. Of 90 patients, 77.77% (70 patients) received antimicrobial therapy effective against the causative microorganism within 24 h of the first culture. Out of 70 patients, only 5 (4.4%) had a positive blood culture after 2 days of effective antimicrobial therapy, meeting the definition of persistent bacteraemia: 3 patients (7.1%) with prosthetic valve endocarditis and 2 with native valve endocarditis. 4 out of 5 patients with persistent bacteraemia had *Enterococcus faecalis* endocarditis, the other 1 had endocarditis by non-HACEK-gram-negative bacteria.

Table 1: Prevalence of persistent bacteraemia in patients with a non-staphylococcal infective endocarditis

Prevalence of persistent bacteraemia	N(%)
Prosthetic valve endocarditis	3(4.28%)
Native valve endocarditis	2(2.85%)
Total	5(7.14%)

Table 2: Prevalence of persistent bacteraemia per microorganism.

Causative bacteria	N
Viridans group streptococci	0
β -haemolytic streptococci	0
Streptococcus pneumonia	0
Enterococcus faecalis	4
Enterococcus faecium	0
HACEK-group	0
Cutibacterium acnes	0
Other bacteria	1

DISCUSSION

Clinically, infective endocarditis may present with a myriad of signs and symptoms, and clinicians should consider this diagnosis in any patient with risk factors who present with fever or sepsis of unknown origin.⁶ Patients will often describe the insidious onset of fevers, chills, malaise, and fatigue that generally prompts medical evaluation within the first month. Fever, typically defined as a temperature over 38.0 degrees C (100.4 degrees F), was found in over 95% of all patients in a large, multi-national prospective cohort study.⁷

A total 540 records were screened. Of these, 90 patients were eligible for inclusion. Of 90 patients, 77.77% (70 patients) received antimicrobial therapy effective against the causative microorganism within 24 h of the first culture. Out of 70 patients, only 5 (4.4%) had a positive blood culture after 2 days of effective antimicrobial therapy, meeting the definition of persistent bacteraemia: 3 patients (7.1%) with prosthetic valve endocarditis and 2 with native valve endocarditis. 4 out of 5 patients with persistent bacteraemia had Enterococcus faecalis endocarditis, the other 1 had endocarditis by non-HACEK-gram-negative bacteria.

A recent study among patients with streptococcal bacteraemia found that 12.5% (5/40) of patients with streptococcal IE had persistent bacteraemia.⁸

In another retrospective cohort study that also did not take timing of antimicrobial therapy into account, only 3% (3/86) of patients with streptococcal bacteraemia had persistent bacteraemia, compared to 20% (20/102) of patients with enterococcal bacteraemia.⁹

van der Vaart TW et al did a retrospective analysis of all patients diagnosed with definite non-staphylococcal endocarditis according to the modified Duke Criteria in two university hospital endocarditis registries. Of the included 159 patients 70 (44%) had prosthetic valve endocarditis (PVE). A median number of two [IQR 1–3] FUBCs were taken during the first week, with 134/159 (84%) having at least one FUBC in the first four days. Seven patients (4.4%) had persistent bacteraemia 48 h after start of antibiotic treatment: 5/70 patients (7.1%) with PVE and 2/89 (2.2%) with native valve endocarditis. Among 97 patients with streptococcal IE, nine patients with HACEK IE and six patients with Cutibacterium IE, no persistent bacteraemia was observed. Enterococcus faecalis was the causative microorganism in five patients with persistent bacteraemia, the other two had non-HACEK Gram-negative endocarditis.³

CONCLUSION

The present study concluded that prevalence of persistent bacteraemia in patients with a non-staphylococcal infective endocarditis was 7.14%.

REFERENCES

1. Yallowitz AW, Decker LC. Infectious endocarditis. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2022 Jan. 2022 Apr 28.
2. Chong YP, Park SJ, Kim HS, Kim ES, Kim MN, Park KH, Kim SH, Lee SO, Choi SH, Jeong JY, Woo JH, Kim YS. Persistent *Staphylococcus aureus* bacteremia: a prospective analysis of risk factors, outcomes, and microbiologic and genotypic characteristics of isolates. *Medicine (Baltimore)*. 2013 Mar;92(2):98-108. doi: 10.1097/MD.0b013e318289ff1e. PMID: 23429353; PMCID: PMC4553980.
3. van der Vaart TW, Stuifzand M, Boekholdt SM, et al. The prevalence of persistent bacteraemia in patients with a non-staphylococcal infective endocarditis, a retrospective cohort study. *Int J Cardiol*.2022;367:49-54. doi:10.1016/j.ijcard.2022.08.038
4. L.M. Baddour, W.R. Wilson, A.S. Bayer, V.G. Fowler Jr., I.M. Tleyjeh, M.J. Rybak, et al., Infective endocarditis in adults: diagnosis, antimicrobial therapy, and management of complications: a scientific statement for healthcare professionals from the American Heart Association, *Circulation*. 132 (15) (2015) 1435–1486.
5. Authors/Task Force M, G. Habib, P. Lancellotti, M.J. Antunes, M.G. Bongiorni, J. P. Casalta, et al., 2015 ESC Guidelines for the management of infective endocarditis: The Task Force for the Management of Infective Endocarditis of the European Society of Cardiology (ESC)Endorsed by: European Association for Cardio-Thoracic Surgery (EACTS), the European Association of Nuclear Medicine (EANM), *Eur. Heart J*. 36 (44) (2015) 3075–3128.
6. Cahill TJ, Prendergast BD. Infective endocarditis. *Lancet*. 2016 Feb 27;387(10021):882-93.
7. Murdoch DR, Corey GR, Hoen B, Miró JM, Fowler VG, Bayer AS, Karchmer AW, Olaison L, Pappas PA, Moreillon P, Chambers ST, Chu VH, Falcó V, Holland DJ, Jones P, Klein JL, Raymond NJ, Read KM, Tripodi MF, Utili R, Wang A, Woods CW, Cabell CH., International Collaboration on Endocarditis-Prospective Cohort Study (ICE-PCS) Investigators. Clinical presentation, etiology, and outcome of infective endocarditis in the 21st century: the International Collaboration on Endocarditis-Prospective Cohort Study. *Arch Intern Med*. 2009 Mar 09;169(5):463-73.
8. E.A. Siegrist, M. Wungwattana, L. Azis, P. Stogsdill, W.Y. Craig, K.E. Rokas. Limited clinical utility of follow-up blood cultures in patients with streptococcal bacteremia: an opportunity for blood culture stewardship. *Open Forum Infect Dis*. 2020 Nov 7;7(12):ofaa541. doi: 10.1093/ofid/ofaa541. eCollection 2020 Dec.
9. J.B. Wiggers, W. Xiong, N. Daneman, Sending repeat cultures: is there a role in the management of bacteremic episodes? (SCRIBE study), *BMC Infect. Dis*. 16 (2016) 286.