Infective endocarditis in the Lao PDR: Clinical characteristics and outcomes in a developing country

Mariana Mirabel a, b, c,⁎, Sayaphet Rattanavong d, Khamthavy Frichitthavong e, Vang Chu e, Pany Kesone e, Phonvilay Thongsith d, Xavier Jouven a, b, c, Pierre-Edouard Fournier f, David A.B. Dance d, g, Paul N. Newton d, g, 1

Abstract

Introduction: Data on infective endocarditis (IE) in Southeast Asia are scarce. Objectives: To describe the clinical epidemiology of IE in Lao PDR, a lower middle-income country.

Methods: A single centre retrospective study at Mahosot Hospital, Vientiane. Patients aged over 1 year of age admitted 2006–2012 to Mahosot Hospital with definite or possible IE by modified Duke criteria were included.

Results: Thirty-six patients fulfilled the inclusion criteria; 33 (91.7%) had left-sided IE. Eleven (30.6%) had definite IE and 25 (69.4%) possible left-sided IE. Median age was 25 years old [IQR 18–42]. Fifteen patients (41.7%) were males. Underlying heart diseases included: rheumatic valve disease in 12 (33.3%), congenital heart disease in 7 (19.4%), degenerative valve disease in 3 (8.3%), and of unknown origin in 14 (38.9%) patients. Native valve IE was present in 30 patients (83.3%), and prosthetic valve IE in 6 patients (16.7%). The most frequent pathogens were Streptococcus spp. in 7 (19.4%). Blood cultures were negative in 22 patients (61.1%). Complications included: heart failure in 11 (30.6%), severe valve regurgitation in 7 (19.4%); neurological event in 7 (19.4%); septic shock or severe sepsis in 5 (13.9%); and cardiogenic shock in 3 patients (8.3%). No patient underwent heart surgery. Fourteen (38.9%) had died by follow-up after a median of 2.1 years [IQR 1–3.2]; and 3 (8.3%) were lost to follow-up.

Conclusions: Infective endocarditis, a disease especially of young adults and mainly caused by Streptococcus spp., was associated with rheumatic heart disease and had high mortality in Laos.

© 2014 The Authors. Published by Elsevier Ireland Ltd. This is an open access article under the CC-BY license (http://creativecommons.org/licenses/by/3.0/).

1. Introduction

Infective endocarditis (IE) is a rare but severe disease that still has a high mortality, even in those with access to tertiary centres. The epidemiology of IE has recently significantly changed across North America and Europe in affecting an increasingly ageing population with comorbidities. Presentation is nowadays often acute, characterized by high rates of Staphylococcus aureus infection, cardiac complications, and embolic events [1–3]. Guidelines for prevention and management of IE are based on Western-focused studies, with an increasing emphasis on early heart surgery [4–7]. However, data from developing countries are scarce [8–11]. Driven by other epidemiological characteristics, the challenges and treatment options the physician encounters in middle and low-income settings may differ greatly from those described in the medical literature.

We describe the clinical characteristics of IE in patients admitted to a tertiary teaching hospital, in Vientiane, the Lao PDR (Laos), a lower middle-income country, and examined their long-term outcomes.

2. Methods

2.1. Objectives

The main objective was to describe the characteristics of patients admitted with IE to a tertiary centre in Laos, a lower middle-income country.

http://dx.doi.org/10.1016/j.ijcard.2014.11.184
0167-5273/© 2014 The Authors. Published by Elsevier Ireland Ltd. This is an open access article under the CC-BY license (http://creativecommons.org/licenses/by/3.0/).

⁎ Corresponding author at: Paris Cardiovascular Research Centre, Inserm U970, 56 rue Leblanc, 75737 Paris CEDEX 15, France.
E-mail address: mariana.mirabel@inserm.fr (M. Mirabel).
This author takes responsibility for all aspects of the reliability and freedom from bias of the data presented and their discussed interpretation.
Patients aged over 1 year admitted from January 2006 to January 2012 to Mahosot Hospital with definite or possible IE according to the modified Duke criteria were included in the study [12]. Mahosot Hospital (17,960 N, 102,612 E); Vientiane, is a primary-ternary care teaching hospital, with 400 beds including cardiology wards that provide cardiac surgery, mostly by visiting teams, and infectious disease wards. The hospital has a thoracic echocardiography; trans-oesophageal echocardiography is used by visiting surgical teams. Blood cultures were performed using standard procedures and antibiotic susceptibility patterns determined using Clinical and Laboratory Standards Institute (CLSI) methods [13].

The clinical significance of positive cultures was determined by a team of physicians at the time of the result based on factors that included organism identity and the number of samples growing the same organism. We tested (acute and convalescent) sera for antibodies to Coxiella burnetii, Legionella pneumophila, Bartonella quintana and Bartonella henselae by indirect immunofluorescence assay (IFA) as previously described [14]. Specific antibodies to Brucella melitensis and Mycoplasma pneumoniae were detected with an immunoenzymatic antibody test and the Platelia M. pneumoniae IgM kit (Bio-Rad, Marnes-la-Coquette), respectively. When the results of the tests described above were negative, we performed Western blot against Bartonella species antigens, as described [15-16].

Infected consent was given by the patient or the next of kin at the time of the blood culture as part of a study of the aetiology of septicemia. Ethical clearance was provided by the Ethical Review Committee of the Faculty of Medical Sciences, National University of Laos (Vientiane, Laos) and the Oxford University Tropical Ethics Research Committee (Oxford, United Kingdom). The authors of this manuscript all have certified that they comply with the Principles of Ethical Publishing.

### 2.2. Study population, study site and microbiological tests

The hospital charts of patients with a clinical diagnosis or suspicion of IE were retrospectively reviewed by two of the authors (MM and SR). Patients were identified through the Echocardiography Laboratory logbooks and the blood culture database of the Microbiology Laboratory. For each patient, the following data were collected: demographics; symptoms and signs, including details of comorbidities such as diabetes, treatments with steroids, excess alcohol consumption, IV drug use, and HIV infection. Supplementary data were collected through the hospital charts and the echocardiography logbooks: heart valve disease and its aetiology; history of cardiac surgery; IE complications as severe valve dysfunction, heart failure (including cardiogenic shock), septic shock or severe sepsis, neurological complication, and arterial embolism. Definitions of IE complications were based on contemporary guidelines [4]. The type of echocardiography (trans thoracic, trans-oesophageal or both), valve involved, vegetation detected, and its maximum length were recorded. Patients with both left- and right-sided IE were assigned to the left-sided group. Those with native valve IE and prosthetic valve IE were assigned to the latter. The choice of valve affected was based upon the presence of at least moderate valve disease or a prosthetic valve.

Outcomes measures were: in-hospital mortality, status when discharged (alive, unwell, moribund), relapse, and long-term mortality. Follow-up was undertaken as a cross sectional study by contacting the patient and/or his/her next of kin. If the patient was lost to follow-up, the date of the latest attendance to the clinic was recorded.

### 3. Statistical analyses

The results are reported as median and interquartile range (IQR) or as numbers and percentages. Categorical variables were compared using chi-square test or Fisher’s exact test, and continuous variables using Student t-test or Wilcoxon rank sum test, as appropriate. Significance was defined as p-values less than 0.05. Statistical analyses were performed using STATA SE/12.1 (StataCorp LP, College Station, TX).

### 4. Results

After review of 110 patients’ hospital charts, 36 fulfilled the modified Duke criteria for IE and were included in the study; 31 (30.6%) had definite IE and 25 (69.4%) possible IE (Table 1). Median age was 25 years old [IQR 18–42]. Fifteen patients (41.7%) were males. Thirty-three of 36 patients (91.7%) had left-sided IE. Five (13.9%) patients were diabetic, 2 (5.6%) were on steroids, and 1 (2.8%) admitted excessive alcohol consumption. No patient was on chronic replacement renal therapy. No IV drug users or HIV positive patients were identified. Underlying heart diseases included rheumatic valve disease in 12 (33.3%), congenital heart disease in 7 (19.4%) and degenerative valve disease in 3 (8.3%) patients. Eight (22.2%) patients had no evidence of underlying valve disease, and data was missing for 6 (16.7%). Infective endocarditis afflicted a prosthetic valve in 6 (16.7%) patients. The presence of a vegetation, abscess or fistula allowed to formally diagnose mitral valve IE in 11 (30.6%), aortic valve IE in 9 (25%) and both the mitral and aortic valves in 2 patients (5.6%). Further 5 patients were diagnosed with mitral, 2 with aortic and mitral valve, and one with aortic valve IE based on the severity of valve regurgitation or the presence of a prosthetic valve, giving a total of 16 (44.4%) mitral, 10 (27.8%) aortic valve, and 4 (11.1%) combined aortic and mitral valve IE. One patient (2.8%) had unrepaird ventricular septal defect (VSD) IE with vegetations both on the VSD and the tricuspid valve. One patient had unrepaired tetralogy of Fallot with no vegetation and was diagnosed with left-sided IE. One patient had mild mitral regurgitation with a neurological defect but no vegetation on TTE and was classified as having left-sided IE. One patient presented with vegetation on pulmonary ductus arteriosus. Two patients did not undergo TTE during their hospital stay.

Investigations included TTE in 34 (94.4%) patients. All patients had at least one set of blood cultures. One (2.8%) patient underwent brain CT scan. None underwent transoesophageal examination. At the date when blood cultures were drawn, symptoms had been present for 7 days (median [IQR 2–21]). Blood cultures were negative in 22 out of 36 patients (61.1%, missing data in one case), of whom 4 had definite IE and 18 possible IE. One patient with blood culture negative IE had evidence for B. henselae infection. Pathogens were isolated on blood cultures from 13 (36.1%) patients: Streptococcus spp. in 7/13 (Streptococcus pyogenes in 2, Streptococcus oralis in 1, Streptococcus mutans in 1, Streptococcus anginosus in 1, and Streptococcus gordonii in 2), followed by Escherichia coli in 3, Enterococcus faecalis in 1, Staphylococcus aureus in 1/13 (2.7%), and coagulase negative staphylococci in 1/13 (in a patient with a prosthetic aortic valve). Serology gave no evidence for C. burnetii, L pneumophila, B. melitensis or M. pneumoniae infection in those with negative blood cultures. The antimicrobial susceptibilities of the organisms isolated were largely as expected for the species concerned. All seven Streptococcus spp. tested for their penicillin minimum inhibitory concentration (MIC) by Etest (bioMérieux, Basingstoke, UK) were fully susceptible (MIC ≤ 0.125 mg/L). Both E. coli isolates were fully susceptible to ceftriaxone and gentamicin by disk diffusion testing although both were resistant to ampicillin. Both E. faecalis isolates were susceptible to penicillin or ampicillin (MIC < 4 mg/L) although one showed evidence of high level resistance to gentamicin. Both Staphylococcus spp. had oxacillin MICs < 1 mg/L.

Clinical complications during hospital stay included: heart failure with no shock in 11 (30.6%); severe valve regurgitation in 7 (19.4%); and...
neurological complication in 7 (19.4%); septic shock or severe sepsis in 5 (13.9%); and cardiogenic shock in 3 (8.3%) patients. Among the 11 patients with detailed echocardiography reports, valve obstruction was noted in 4/11; and 2/11 presented with large vegetations (i.e. >10 mm as the longest dimension), abscess or fistula on TTE.

The initial antibiotic regimen given was available for 25 out of 36 patients, among whom 10 received a combination of ceftriaxone and gentamicin; 5 ceftriaxone alone; 4 a combination of penicillin and gentamicin; 1 a combination of ampicillin and gentamicin; 1 penicillin alone; 1 cloxacillin alone; 1 a combination of clindamycin and gentamicin; 1 a combination of cloxacillin and rifampicin; and 1 a combination of ceftriaxone, gentamicin and doxycycline.

No patient underwent surgery either during the acute phase or after completion of antibiotic treatment. The median length of hospital stay was 16 days [IQR 9–21].

Nine (25.0%) patients died during their hospital stay whilst 14 (38.9%) had died by follow-up after a median of 2.1 years [IQR 1–3.2]. Three (8.3%) patients were lost to follow-up. Among the 10 patients discharged unwell, 6 were dead at follow-up, 3 were alive, and 1 was lost to follow-up. Five patients (13.9%) experienced IE relapse requiring readmission. Causes of death were available in 6 out of 14 cases: heart failure in 3 patients; shock in 1 patient; gastrointestinal bleed in 1 patient; and ventricular fibrillation and acute renal failure in the remaining patient. The only factor associated with long-term mortality on univariate analysis was greater age (p = 0.02) (Table 2).

5. Discussion

We describe the first series of patients with IE in Laos. Patients were mostly young with mainly rheumatic heart disease as their underlying condition and rare comorbidity. The main causative agents were Streptococcus spp., but blood cultures remained negative in over half the patients. No patient underwent transoesophageal echocardiography as a routine diagnostic tool. Hospital stay was relatively short and the rate of relapses was high. Due to lack of resident cardiac surgeons, surgery could not be performed in the presence of clear indications such as heart failure or cardiogenic shock. Mortality was extremely high, reaching ~39% at 2 years follow-up.

These data highlight the marked differences in IE epidemiology between developing and wealthy countries. The demographic characteristics, high frequency of underlying rheumatic heart disease and microbiological aetiology are consistent with reports from other developing countries [9,17–20,36].

Rheumatic heart disease, a neglected disease of poverty, remains the most common underlying condition. However, prevention programmes reduce the burden of the disease. Control of rheumatic heart disease can be achieved through cost-effective, register-based, primary and secondary prevention programmes that deliver penicillin [21]. Congenital heart disease was the second most frequent underlying aetiology, probably because of the inclusion of children in our series.

The high frequency of streptococcal species in the Lao patients probably in part reflects poor oral health [22], suggesting the interest of promoting dental hygiene education and awareness. Over half the patients had negative blood cultures. This finding is consistent with other series from developing countries [8,9,11,19]. Over the counter antibiotics are available in Laos and self-medication is common [23], and may have contributed to the low frequency of positive blood cultures, although the retrospective design of our study did not allow this to be assessed. Some of the pathogens identified, such as E. coli and S. pyogenes, have been described as causing IE but are rare in industrialised country case series [24,25]. On the basis of the results of this series, initial empirical treatment of patients with suspected endocarditis with ceftriaxone and gentamicin would be appropriate in Laos, adjusted on the basis of susceptibilities if an organism is grown.

Access to imaging techniques was relatively low, with no transoesophageal echocardiography performed. Only a minority of patients (1 out of 7) with clinical neurological complications underwent a brain CT scan. Contrary to international guidelines [4,5], cephalosporins were frequently the first line of treatment, because of the logistic difficulties of providing repeated infusions of penicillin. Median length of stay was 16 days, suggesting that many patients did not receive a minimum of 14 days of intravenous treatment, likely responsible for the high rate of relapses (13.9%).

Access to cardiac surgery remains limited in Laos. No patient in this series underwent cardiac surgery either during acute IE or after completion of antibiotic treatment.

Outcomes were poor with approximately 39% of patients dead at follow-up. These findings are worrying considering the clinical characteristics of the disease: young patients with streptococcal infections, and barely any comorbid conditions. Indeed, viridans streptococcal IE has been documented as having a good prognosis when compared to other causative microorganisms [1]. Younger age also should be associated with higher chances of survival according to other series [1,26]. The deadly toll in this series is consistent with reports from other developing countries [18,19,27,28].

In contrast to our findings, Thuny and colleagues recently outlined the tremendous progress achieved in the management of IE in wealthy countries [7]. Mortality is as low as 8.2% in some high-volume centres [29]. Early surgery has become a mainstay in the therapy of complicated IE [4,5,30]. Such improvement is nonetheless largely restricted to the wealthy world. In many developing countries, limited access to health facilities, lack of adequate diagnostic tools such as transthoracic and transoesophageal echocardiography, inadequate laboratory facilities to perform trustworthy blood cultures and susceptibility testing and insufficient skilled staff hamper early reliable diagnoses. Antibiotics are not necessarily appropriate or of good quality [23,31]. The treatment course is commonly interrupted prematurely as patients cannot afford the parenteral antibiotics, inpatient charges and family income loss associated with prolonged hospitalisation. These results suggest the need for prospective studies assessing reasons for early discharge in developing countries and what engagement strategies may help to reduce this. Importantly, access to cardiac surgery is limited in most low- and lower-middle income countries. For instance, surgical facilities are restricted to only 15 out of 55 African states, often supported by visiting teams from Europe or North America [32].

Prevention of rheumatic heart disease and access to dental health services may reduce the incidence of IE worldwide. Considerable investment in national referral centres for access to diagnosis, inexpensive, good quality, antibiotics and resources to support patients with long-term therapy and offset income loss are likely to be vital in reducing the burden of this curable neglected infectious disease.
6. Strength and limitations

This study is one of the very few reports on IE from Southeast Asian developing countries [18,33–35]. It provides valuable data on the clinical characteristics of IE in Laos. Although retrospective, follow-up data was available in the majority of patients providing long-term mortality rates. Access to diagnostic techniques was limited hence patients with possible IE were included in the study. This study has a number of limitations. The sample size was relatively small and therefore predictors of mortality could not be thoroughly assessed. The inclusion of children in our series may have overrepresented, in comparison to sectors of mortality could not be thoroughly assessed. The inclusion of limitations. The sample size was relatively small and therefore predictions to increasing diagnostic and therapeutic capacities need to be addressed in developing countries.

7. Conclusion

Infective endocarditis has a high mortality rate in Laos, especially affecting young adults with rheumatic heart disease and mainly caused by Streptococcus spp. Ways to reduce the burden of disease through rheumatic heart disease prevention, promotion of oral health, and treatment options by increasing diagnostic and therapeutic capacities need to be addressed in developing countries.

Conflict of Interest

No conflict of interest to declare.

Acknowledgements

We are very grateful to the directors and staff of Mahosot Hospital, especially of the Cardiology Ward and Microbiology Laboratory for their support and assistance. We thank Rattanaphone Pheutsavanh, Manivanh Vongsouvath, Mayfong Mayxay, Viengmon Davong and Latsaniphone Bouthisavong for their help.

PNN and DADB are funded by the Wellcome Trust of Great Britain (Grant No. 089275/Z/09/Z) that also supported the clinical microbiology diagnostic research.

References

[1] D.R. Murdoch, G.R. Corey, B. Hoen, et al., Clinical presentation, etiology, and outcome of infective endocarditis in the 21st century: the International Collaboration on Endocarditis-Prospective Cohort Study, Arch. Intern. Med. 169 (5) (2009) 463–473.
[2] C. Selton-Suty, M. Celard, V. Le Moang, et al., Preeminence of Staphylococcus aureus in infective endocarditis: a 1-year population-based survey, Clin. Infect. Dis. 54 (9) (2012) 1230–1239.
[3] D.H. Bor, S. Woolhandler, R. Nardin, J. Bruch, D.J. Himmelstein, Infective endocarditis in the U.S., 1998–2005: a nationwide study, PLoS One 8 (3) (2013) e60033.
[4] G. Habib, B. Hoen, P. Tornos, et al., Guidelines on the prevention, diagnosis, and treatment of infective endocarditis (new version 2009): the Task Force on the Prevention, Diagnosis, and Treatment of Infective Endocarditis of the European Society of Cardiology (ESC), Endorsed by the European Society of Clinical Microbiology and Infectious Diseases (ESCMID) and the International Society of Chemotherapy (ISC) for Infection and Cancer, Eur. Heart J. 30 (19) (2009) 2369–2413.
[5] L.M. Baddour, W.R. Wilson, A.S. Bayer, et al., Infective endocarditis: diagnosis, antimicrobial therapy, and management of complications: a statement for healthcare professionals from the Committee on Rheumatic Fever, Endocarditis, and Kawasaki Disease, Council on Cardiovascular Disease in the Young, and the Councils on Clinical Cardiology, Stroke, and Cardiovascular Surgery and Anesthesia, American Heart Association: endorsed by the Infectious Diseases Society of America, Circulation 111 (23) (2005) e394–e434.
[6] D.H.J. Kang, Y.J. Kim, S.H. Kim, et al., Early surgery versus conventional treatment for infective endocarditis, NEJM 366 (26) (2012) 2466–2473.
[7] F. Thuny, D. Grisoli, F. Collart, G. Habib, D. Raoult, Management of infective endocarditis: challenges and perspectives, Lancet 379 (9819) (2012) 965–975.
[8] R.S. Math, G. Sharma, S.S. Kothari, et al., Prospective study of infective endocarditis from a developing country, Am. Heart J. 162 (4) (2011) 633–638.
[9] A. Letais, E. Boughzala, N. Kaabia, et al., Epidemiology of infective endocarditis in Tunisia: a 10-year multicenter retrospective study, Int. J. Infect. Dis. 11 (5) (2007) 430–433.
[10] Y. Cetinkaya, M. Akova, H.E. Akalin, et al., A retrospective review of 228 episodes of infective endocarditis where rheumatic valvular disease is still common, Int. J. Antimicrob. Agents 18 (1) (2001) 1–7.
[11] M.B. Ndiaye, M. Diao, A. Kane, et al., Infective endocarditis in cardia setting in Dakar: descriptive study about 39 cases, Pan Afr. Med. J. 7 (2010) 12.
[12] J.S. Li, D.J. Sexton, N. Mick, et al., Proposed modifications to the Duke criteria for the diagnosis of infective endocarditis, Clin. Infect. Dis. 30 (4) (2000) 633–638.
[13] R. Pheutsavanh, S. Phommany, D. Souklouan, et al., Causes of community-acquired bacteremia and patterns of antimicrobial resistance in Vientiane, Laos, Am. J. Trop. Med. Hyg. 75 (5) (2006) 978–985.
[14] P. Houpukian, D. Raoult, Blood culture-negative endocarditis in a reference center: etiologic diagnosis of 348 cases, Medicine 83 (3) (2005) 162–173.
[15] P. Houpukian, D. Raoult, Western immunoblotting for Bartonella endocarditis, Clin. Diag. Lab. Immunol. 10 (1) (2003) 95–102.
[16] P.E. Fournier, F. Thuny, H. Richet, et al., Comprehensive diagnostic strategy for blood culture-negative endocarditis: a prospective study of 819 new cases, Clin. Infect. Dis. 51 (2) (2010) 131–140.
[17] N. Garg, R. Randal, N. Garg, et al., Characteristics of infective endocarditis in a developing country-clinical profile and outcome in 192 Indian patients, 1992–2001, Int. J. Cardiol. 98 (2) (2005) 253–260.
[18] O. Pachirat, P. Chetchotisakd, V. Klangboonkrong, P. Taweesangsuksakul, C. Taipong, M. Loaippont, Infective endocarditis: prevalence, characteristics and mortality in Khon Kaen, 1990–1999, J. Med. Assoc. Thail. 85 (1) (2002) 1–10.
[19] C.F. Koegelenberg, A.F. Doubell, H. Orth, H. Reuter, Infective endocarditis in the Western Cape Province of South Africa: a three-year prospective study, QJM 96 (3) (2003) 217–225.
[20] M. Tariq, M. Alam, G. Munir, M.A. Khan, R.A. Smego Jr, Infective endocarditis: a five-year experience at a tertiary care hospital in Pakistan, Int. J. Infect. Dis. 8 (3) (2004) 163–170.
[21] E. Marijon, M. Mirabel, D.S. Cölermajer, X. Jouven, Rheumatic heart disease, Lancet 379 (9819) (2012) 953–964.
[22] N. Jurgensen, P.E. Petersen, Oral health and the impact of socio-behavioural factors in a cross sectional survey of 12-year old school children in Laos, BMC Oral Health 9 (2009) 29.
[23] M. Khennavong, V. Davone, M. Vongsouvath, et al., Urine antibiotic activity in patients presenting to hospitals in Laos: implications for worsening antibiotic resistance, Am. J. Trop. Med. Hyg. 85 (2) (2011) 295–302.
[24] S. Branger, J.P. Casalta, G. Habib, F. Collard, D. Raoult, Escherichia coli endocarditis: seven new cases in adults and review of the literature, Eur. J. Clin. Microbiol. Infect. Dis. 24 (8) (2005) 537–541.
[25] O. Pachirat, S. Prathani, V. Lulitanond, G. Watt, Echocardiographic features in Streptococcus agalactiae endocarditis: four cases report, J. Med. Assoc. Thail. 97 (1) (2014) 118–122.
[26] E.E. Hill, F. Hervig, P. Claus, S. Vanderschueren, M.C. Herregods, W.E. Peetermans, Infective endocarditis: changing epidemiology and predictors of 6-month mortality: a prospective cohort study, Eur. Heart J. 38 (2) (2007) 196–203.
[27] M.A. Elbery, S. Akdog, M.E. Kalkan, et al., A multicenter study on experience of 13 tertiary hospitals in Turkey in patients with infective endocarditis, Anatol. J. Cardiol. 13 (6) (2013) 523–527.
[28] M.C. Nunes, C.L. Gelápe, T.C. Ferrari, Profile of infective endocarditis at a tertiary care center in Brazil during a seven-year period: prognostic factors and in-hospital outcome, Int. Infect. Dis. 14 (13) (2010) e2394–e2398.
[29] E. Botelho-Nevers, F. Thuny, J.P. Casalta, et al., Dramatic reduction in infective endocarditis-related mortality with a management-based approach, Arch. Intern. Med. 169 (14) (2009) 1290–1298.
[30] S. Chatterjee, P. Sardar, Early surgery reduces mortality in patients with infective endocarditis: insight from a meta-analysis, J. Infect. Dis. 193 (10) (2006) 1304–1307.
[31] S. Rattanavong, P.-E. Fournier, V. Chu, K. Frichitthavong, P. Kesone, M. Mayxay, M. Mirabel, Newton PN, Bartonella henselae endocarditis in Laos - ‘the unsought will go undetected’, PLoS NTD (2014).