

Infective Endocarditis in Low- and Middle-Income Countries



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KEYWORDS

• Endocarditis in LMIC • Developing countries • Causes • Management • Challenges

KEY POINTS

- *Staphylococcus* is an increasingly important cause of IE in LMICs, and is the leading cause of IE in UMICs.
- RHD remains the major underlying cardiac pathology of IE in LMICs, identified in almost half of reported cases.
- The rate of microorganism nonidentification is high, reaching up to 60% of IE cases in LMICs, and hampering diagnosis and treatment.
- Rates of access to surgery in UMICs for complicated IE are as high as in HICs, but remain dismal in LMICs.

INTRODUCTION

Infective endocarditis (IE) is a rare, life-threatening disease with a significant mortality and morbidity burden. In-hospital mortality approaches 25%, increasing in patients with cardiac or extracardiac complications.^{1–3} IE also frequently causes debilitating morbidities, such as heart failure, stroke, and renal failure requiring dialysis, which contribute to increased mortality and disability adjusted life-years.^{3–7}

The spectrum of causative microorganisms and underlying risk factors for IE has shifted dramatically in high-income countries (HICs).^{8,9} Staphylococcal IE now predominates. Degenerative valve disease (DVD), prosthetic valves, and other intracardiac devices are the leading underlying cardiac conditions, with little contribution from rheumatic

heart disease (RHD) and congenital heart disease (CHD).

The epidemiology of IE in low- and middle-income countries (LMICs) has been said to resemble that seen in HIC-based studies from the mid-twentieth century, which reported a predominance of IE caused by streptococcal infection, RHD, and CHD as the leading risk factors, and minimal rates of surgical intervention.⁹ Reports from LMICs that mirror this epidemiology and treatment patterns are predominantly from before the turn of this millennium and consequently may not reflect the current state of IE in LMICs.^{10–14}

The prevalence of RHD remains disproportionately high in LMICs, and uncorrected CHD persists in the poorest of these settings because of limited access to cardiac surgery.^{15,16} It is therefore

Disclosure Statement: The authors have nothing to disclose.

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Cardiol Clin 35 (2017) 153–163

<http://dx.doi.org/10.1016/j.ccl.2016.08.011>

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expected that RHD and CHD remain significant underlying cardiac conditions for IE; however, economic improvement in LMIC and upper-middle-income countries (UMIC) has led to medical progress, which may have introduced additional IE risk factors for these populations, and altered the spectrum of causative microorganisms.

This article presents the causes and treatment of IE in LMICs as reported in contemporary studies, defined as studies that primarily report findings from 2000 to 2016. Also discussed is the prevailing challenges to the diagnosis and management of IE in LMICs, and future directions in research are suggested.

METHODS

We searched PUBMED and EMBASE using the keywords “endocarditis,” “IE,” “low income,” “middle income,” and “developing country.” LMICs and HICs were based on 2016 World Bank Income groups classification.¹⁷ Articles were considered relevant if they were original research that described IE epidemiology and management experiences from LMICs from the year 2000 to 2016. When studies reported data from both before and after the year 2000, we excluded studies if most of the experience was from before 2000. We also screened the reference list of the retrieved articles for additional relevant studies.

CAUSES OF INFECTIVE ENDOCARDITIS

Prosthetic valves, DVD and intracardiac devices have replaced RHD as the major underlying cardiac risk factors for IE in HICs.¹ Comorbidities, such as diabetes mellitus, renal failure requiring dialysis, and malignancy, contribute substantially to a growing burden of health care-associated IE (HAIE).^{2,18} Consequently, growing use of long-term intravascular access devices has led to skin bacteria in the form of *Staphylococcus* being the leading cause of IE in HICs.^{1,2,18}

In this section, we review the prevalent underlying cardiac conditions, place of acquisition, and microbial cause of IE in LMICs. A summary of the findings is presented in **Table 1**.

Underlying Cardiac Conditions

RHD is identified as the underlying cardiac pathology in most IE cases, ranging from 28% to 45% in most of our reviewed studies.^{19–24} Nel and Naidoo,²⁵ however, reported a much higher (78%) prevalence of underlying RHD in their study in South Africa, a country where RHD is endemic.²⁶

Overall, this range of underlying RHD in IE represents a decline from the 45% to 80% reported

in earlier (pre-2000) LMIC studies.^{10,11,13,27,28} Compared with HICs, however, these findings are remarkable in that RHD is identified in only 3% of IE cases from HICs.¹ This is likely because the prevalence of RHD is disproportionately high in LMICs,^{29,30} which bear 79% of the global RHD burden.¹⁵

Underlying CHD accounts for 5% to 23% of reported IE cases.^{19,21,23–25,31,32} Math and colleagues²⁰ reported CHD as the leading cause of IE (39%) in northern India in a cardiac surgery center with a large pediatric population, which may account for the higher findings of CHD.

Prosthetic valve IE (PVE) and pacemakers/intracardiac defibrillators are reported in 17% to 44% and 6% to 19% of IE cases in LMICs, respectively.^{19–23,31,32} UMIC studies account for the higher figures in these ranges, which reflects advances in medical technology and higher access to cardiac surgery.^{21,22} Indeed, the largest report of PVE cases from an LMIC comes from Simsek-Yavuz and colleagues,²¹ who reported findings from a referral center in Turkey (an UMIC) in which 141 patients (44%) among 325 IE cases had PVE. A total of 52% of the total patient cohort received surgical intervention, closely approximating the rate seen in HICs.²

DVD contributes little to the IE epidemiology in LMICs, accounting for less than 10% of cases.^{19,21,23,32} Eibey and colleagues,³¹ however, reported a high rate of DVD (23%) in a multicenter retrospective study in Turkey. Mean patient age was 47 years, higher than that typically seen in LMIC studies, which may explain the higher rate of DVD. Overall, unlike in HICs where DVD is the major underlying cardiac disease in native valve IE (NVE), a lower aged mean patient population in LMICs limits its contribution.^{1,8,9,18}

Place of Infection Acquisition

The burden of HAIE is growing in HICs, reported in 30% of IE in recent studies.^{1,2,18} Advances in medical technology, increased indwelling intravascular device use, and increased prevalence of comorbidities, such as end-stage renal disease, contribute to this burden.³³

Two LMIC studies reported on the site of acquisition of IE. Simsek-Yavuz and colleagues²¹ characterized 23% of IE cases as HAIE at a referral center in Turkey, whereas Damasco and colleagues³⁴ reported predominantly HAIE (56%) in two centers in Brazil. In the latter study, an indwelling intravenous catheter was the main source of infection in the entire patient cohort, whereas among HAIE cases, 55% had chronic renal insufficiency as a comorbidity. The authors

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