Chapter 7

Infective Endocarditis in End-Stage Renal Disease Patients in Developing Countries: What is the Real Problem?

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Additional information is available at the end of the chapter

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Abstract

The epidemiology of infective endocarditis (IE) has changed over the last decades, due to various factors. This chapter focuses on IE in patients with end-stage renal disease. Then it reviews the most relevant reports published in the last decade worldwide; the different scenarios in developing countries versus developed countries; different microorganisms, treatment times, and outcomes; and also our own experience in these patients. Finally, it mentions the recommendations that have helped some developed countries to reduce more than 50% of bacteremia in catheter patients and how to make them possible in developing countries.

Keywords: end-stage renal disease (ESRD), developing countries, hemodialysis (HD), infective endocarditis (IE), catheter-related bacteremia (CRB), rheumatic heart disease (RHD)

1. Introduction

The epidemiology of infectious endocarditis (IE) has changed over the past five decades, with many contributing factors for the increasing incidence. The survival rate of chronically ill patients with nephropathy and cardiac patients has increased by transplanting or immunosuppressing, which is a consequence of medical advances. All risk factors in certain subgroups of patients are associated with the use of intracardiac or intravascular devices, prosthetic implants or catheters, and immunosuppressive drugs, causing increased health care-related infections. Despite advances in medicine, in-hospital mortality rate of IE remains high with no significant decrease observed since the 1960s [1].

Despite many scientific efforts that have been made to realize the magnitude of this problem in different regions of the world, assessing its incidence is difficult because of the few epidemiological studies that currently exist globally; the incidence of endocarditis may vary from one country to another, between 1.5 and 11.6 per 100,000 inhabitants. Apart from its incidence, it is recognizing that this is a condition that involves high morbidity and mortality [2].

Infective endocarditis (IE) in patients with end-stage renal disease (ESRD) is a problem that continues *in crescendo* worldwide, with high morbidity and mortality, but in developing countries, the problem is more alarming due to various factors such as underdevelopment, economic inequality, and limitations in health care systems. The treatment has not changed in recent decades and instead epidemiological characteristics show very specific changes that vary from the developed countries to developing countries [3, 4].

Some authors have proposed modifications in the IE classification to address hemodialysis (HD) patients in a different category, because they represent a crescent population of IE patients and diagnostic and treatment challenge for clinicians and surgeons [5].

This chapter highlights some identified differences as well as some regional differences between developed and developing countries, and provides strategies to reduce IE in HD patients, which can be performed in any health care facility.

2. Epidemiology

The precise incidence of IE is difficult to ascertain because case definition has varied over time between authors and clinical centers [6].

IE varies according to the region. Limited data suggest that the characteristics of IE in low-income countries differ from those in industrialized countries. It is estimated that over 33,700 rheumatic heart disease (RHD)-related IE cases arise each year in developing countries and that this leads to over 8400 deaths [7].

Many literature reports and a few retrospective series have been presented on infective endocarditis in the hemodialysis population. The true incidence of IE in HD patients is, at best, an underestimate in retrospective studies. It is reported that it occurs in 6% of HD patients.

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The incidence of IE in HD patients is estimated to be 308/100,000 patient-years, which is 50- to 180-fold higher than 1.7–6.2 cases per 100,000 patient-years reported for the general population [8].

In a recent retrospective cohort study in Taiwan undertaken to determine IE and the mortality risk factors among HD patients, the prevalence of IE of 6.9% was reported. The overall mortality in HD patients with IE was 60.0% [9]. The mortality rate is also higher (30–77.8%) in HD patients than in IE patients in the general population (17%) [4]. There is a high postoperative mortality 11–80% in HD patients which requires surgical intervention for IE [10].

3. The ESRD patients in dialysis

The main risk factors for HD patients to get IE are recurrent bacteremia, uremia, immune-system damage, and premature degeneration of the heart valves caused by abnormalities in calcium and phosphorus homeostasis and chronic inflammation [8].

In 2006 the National Kidney Foundation established their guideline recommendations to select and place the access of HD being first choice arteriovenous fistula followed by fistula with synthetic graft leaving tunneled catheters and nontunneled as an alternative only when you do not have any of the first two options. Despite the goal since these guidelines were made in 2006 to have 50% of HD in AVF, this percentage has been achieved only in some European countries, but in North America, it has less percentage than what the guidelines suggest [11].

Mechanical and infectious complications most frequently limit the use of a central venous catheter (CVC). Infection is the most common cause of morbidity and the second cause of death after cardiovascular disease in HD patients. The incidence of catheter-related bacteremia (CRB) in HD patients depends on the type and location of the CVC, the characteristics of the population, insertion techniques and safety measures, and manipulation of HD catheters in each center. The CRB rate in nontunneled CVC is between 3.8 and 6.6 episodes/1000 days of the use of CVC and between 1.6 and 5.5 episodes/1000 days of the use of tunneled CVC. The use of a tunneled CVC carries an increased risk of bacteremia 7 to 20 times compared to the arteriovenous fistulas (AVF) [12].

The International Collaboration on Endocarditis Prospective Cohort Study conducted a prospective cohort study with 2781 adults diagnosed with infective endocarditis in 58 hospitals in 25 countries from June 2000 to September 2005, which reported an IE incidence of 21% in chronic HD patients (more than 90 days) and 25% chronic IV access in North America; 8% in chronic HD patients and 5% chronic IV access in South America; and 4% in chronic HD patients and 5% chronic IV access in Europe [13].

The above statistics differ from those reported by other authors from different parts of the world; UK presents a lower incidence of reported cases of endocarditis; and Doulton Timothy et al. reported a series of 28 cases of IE using the Duke criteria, at St. Thomas' Hospital (1980–1995), Guy's (1995–2002), and King's College Hospitals (1996–2002). Of this

28 patients, 27 patients were on chronic HD and 1 in peritoneal dialysis (PD) patient. 40% of the HD patients were treated with AVF's and the AVF was the definite or suspected site of entry for the causative organism in eight cases of IE representing the 26.6% of the total of patients with IE. The presumption that the AVF was the source of bacteremia in these episodes is supported by the fact that the causative organism in seven episodes was commensal skin pathogens *Staphylococcus aureus* (*S. aureus*) in six patients and *Staphylococcus epidermidis* (*S. epidermidis*) in one patient [3]. In contrast, Jones et al. conducted a retrospective study between the years 1998 and 2011. Forty-two patients were identified with developed IE out of a total incident dialysis population of 1500 over 13 years. Ninety-five percent of patients (40/42) were on long-term HD and five percent (2/42) on PD. Mean patient age was 55.2 years (IQR: 43–69), and the mean duration of HD prior to IE was 57.4 months. Primary HD access at the time of diagnosis was an AVF in 35% (14/40), a dual-lumen tunneled catheter (DLTC) in 55% (22/40), and a dual-lumen nontunneled catheter (DLNTC) in 10% (4/40). *S. aureus*, including methicillin-resistant *S. aureus* (MRSA), was present in 57.1% (24/42) [14, 15].

4. IE risk factors in dialysis patients

Dialysis is a well-established risk factor for IE. Mylonakis et al. reported that end-stage renal disease in HD patients has a higher rate of morbidity and mortality compared to general population. Infections are the major cause of morbidity and mortality and are the second leading cause of death in HD patients surpassed only by cardiovascular disease. And these occur in about 12–22% of ESRD patients [15–17].

The mortality rate in patients with IE ranges from 30 to 56% in one year and in-hospital mortality is twice more frequent than the general population with IE.

4.1. HD-related bacteremia

One of the factors that increase the risk of developing IE in HD patients is bacteremia, which are exposed to repetitive vascular access through an arteriovenous fistula (AVF), polytetrafluoroethylene (PTFE) grafts or percutaneous catheters for HD, or cuffed or noncuffed dual lumen catheter.

The incidence of bacteremia is related to vascular access type, ranging from 1.6 to 7.7 per 1000 days with percutaneous catheters and 0.2 to 0.5 per 1000 days with AVF, according to the reference.

The use of catheters during HD is the leading cause of bacteremia in HD patients [4, 8, 15, 18].

A hierarchy of bacteremia risk exists among various types of HD vascular access; it is less common in patients with native arteriovenous fistulae, while synthetic grafts, cuffed catheters, and uncuffed catheters yield a progressively increasing risk.

These episodes of bacteremia during HD are relatively common. They can be endogenous or exogenous: through the microorganism flora found in the patient (endogenous) or through

the pathogen from another source such as might occur through hands or contaminated instruments (exogenous) [5].

There are three points where the pathogens can enter the bloodstream (BS):

(a) Product contamination of the infusion.

Contamination of parenteral fluids is exceptional at the present time due to the rigorous control sterility and subject to quick degradation once the expiration date is reached. In these cases, bacteremia usually caused by Gram-negative bacteria (Enterobacteriaceae or nonfermenting Gram-negative bacilli) particularly serious and epidemic type may occur.

(b) Contamination of connection and intraluminal space.

Contamination of the connection point of vascular catheters is the second most common cause of arrival of microorganisms to the bloodstream (after related to the place of insertion) and the most common involved in intravascular devices longer than 2 weeks. It is, therefore, the usual way of colonization of CVC, whether or not tunneled, when it occurs after 2 weeks from implantation. In this way, microorganism colonizations progress through the intraluminal surface of catheters, forming biofilm colonization all the way from the outside end to the intravascular end.

(c) Contamination adjacent to the site of insertion and extraluminal surface skin.

Access to microorganisms from the skin adjacent the insertion site of the catheter is the most common for colonization and subsequent infection-related pathogenic mechanism. This is the only way for a microorganism to get into the bloodstream in the first 8 days (in the absence of product contamination infusion). Microorganisms on the skin through the insertion point enter the extraluminal surface of catheters and form the biofilm at that level to the intravascular end.

Another option of extraluminal contamination of a vascular catheter colonization can be by hematogenous spread of a microorganism originated in a distant focus, which is very rare, observed mainly in critically ill patients with long-term catheters or in patients with intestinal diseases [19].

4.2. Degenerative heart valve disease (DHVD)

Patients with ESRD have increased incidence of degenerative disease of the heart valves, which is one of the major risks of IE. The calcific aortic stenosis and mitral annular calcification with consequent failure are the most common diseases. It has been found that this condition occurs prematurely in this group of patients 10–20 years prior to the general population. Degenerative heart valve disease is caused due to disorders of calcium and phosphorus homeostasis, in the setting of secondary hyperparathyroidism, and due to the chronic micro-inflammatory milieu of uremia associated with ESRD [5].

4.3. Rheumatic heart disease (RHD)

The RHD, which was the leading cause of IE in the preantibiotics era, is now rare in developed countries. However, it remains a highly prevalent disease in developing countries. More developed areas, such as Hong Kong and Thailand, still have a case of IE in 18 and 12%, respectively.

Chou et al. in their study compared 68,426 adult patients with ESRD in HD with two groups: with IE and without IE. They found that 1.2% without IE and 4.4% with IE, respectively, had the RHD, having a statistical significance $p < 0.001$, relative to RHD and IE in HD patients [16]. The same study shows the differences in incidence among Asian countries and the western countries. However, many western countries, such as in the case of Mexico and parts of South America, are still considered to be endemic for this disease. Simsek-Yavuz et al. in their study in Turkey also noted the difference in incidence among the developed countries and found low incidence of RHD compared with developing countries. They presented their work in 325 patients with IE that 33% had RHD.

Although this study is not specifically for HD patients, it demonstrates a high prevalence of RHD in IE [20].

4.4. Chronic degenerative diseases (CDD)

• *Diabetes*

There is a close relationship between HD patients and diabetes, with the incidence of IE.

There are studies that have an incidence of 33–59.4% of patients having statistical significance compared with HD patients with DM without IE, $p < 0.001$ [15, 16].

• *Systemic hypertension*

This condition is related to ESRD patients with HD and IE having an incidence of up 89.9% [15].

• *Coronary artery disease (CAD)*

Kamalakannan et al. in their study with 69 patients showed an incidence of 24.6% of CAD in HD patients with IE. Chou et al. found $p < 0.001$ between HD patients with IE versus the HD patient without IE. This disease is considered to be a potential cause of death in the short and long term in these patients [8, 15, 16].

• *Congestive heart failure (CHF)*

Kamalakannan et al. in their study with 69 patients showed an incidence of 18.8% of CHF in this group of patients. Chou et al. compared CHF in HD patients with IE versus HD patients without IE and found significant differences $p < 0.001$, being the HD patients with IE, the group with more CHF, which also indicates the direct cause of death in these patients in the short term [8, 15, 16].

4.5. Preexisiting cardiac abnormalities

These account for 13.5–33.3% of the causes associated with IE in HD patients, and include the presence of valve prostheses, previous valvular heart disease, heart transplantation, pericarditis, myocarditis, and intracardiac devices.

The incidence of cardiac device infective endocarditis (CDIE) has been reported between 0.06 and 0.6% per year or 1.14 per 1000 device-years [15, 16, 21].

4.6. Intravenous drug users

Although it is a rare case of IE in HD patients, Kamalakannan et al. reported an incidence of 11.6% representing eight patients of the study [8]. Also in some countries such as Finland they found an increase in IV drug abuse as a risk factor for IE patients being 0% in the 1980s and mid-1990s to 20% in 2000–2004 [22].

4.7. Elderly patients

A relationship has been found between the advanced ages of the patient with ESRD on HD; some authors considered ≥ 65 years and others ≥ 70 years with IE. Nori et al. reported a frequency of IE 27%, the highest among age groups for patients ≥ 70 years. Chou et al. reported 48% of HD patients with IE ≥ 65 years. The ages of the Patients in HD with IE were 62.12 ± 13.09 years versus 60.11 ± 14.06 years in HD patients without IE, resulting in a $p < 0.001$, confirming that the advanced age is a risk factor for IE. Watt et al. presented a comparison of patients treated in Rennes, France, versus patients treated in Khon Kaen, Thailand (from rural areas in Thailand), finding a statistical difference in the age with an average of 70 versus 47 years, respectively.

Also elderly patients are considered to have a poor prognostic factor in IE in HD patients.

Also older age is a determinant of the clinical features in IE. Fewer patients can go to surgical treatment and mortality is higher than in younger patients [7, 13, 15, 16, 23].

4.8. Methicillin-susceptible *Staphylococcus aureus* (MSSA) and methicillin-resistant *Staphylococcus aureus* (MRSA) infection

Staphylococcus aureus represents the primary pathogen in IE in HD patients causing up to 80% of the IE. This pathogen is much more frequent than in the general population with IE. This can be explained that more than 50% of patients in dialysis are carriers of *S. aureus*; nose as a reservoir has shown an increased risk of subsequent infections. It is also important to consider that this pathogen by the fact is responsible for a high number of septic complications compared with other microorganisms. Finally, recent studies have shown that as much as 50% of *S. aureus* IE is MRSA. These strains in particular are more difficult to eradicate and are associated with a worse prognosis than methicillin-susceptible *S. aureus*. In general, patients with MRSA got it as an in-hospital infection; however, studies have shown the existence of community-acquired strains, which are microbiologically different from those acquired during hospitalization. Those strains are called community-acquired *Staphylococcus aureus* methicillin-

resistant (CA-MRSA). It is a predisposing factor in these patients and a challenge for physicians involved with patients with MRSA IE [1, 5, 24].

4.9. Other microorganisms

Streptococcus viridans is currently considered to be the second cause of IE after *S. aureus*. Other pathogens such as *Enterococci* occupy the third place. The relevance of the latter is that its incidence has been increasing, plus it is more associated with nosocomial infection compared with *Streptococcus*. These pathogens if presented in prosthetic valves are more likely to cause intracardiac abscesses and less likely to have detectable vegetations on echocardiography than those presented in IE in native valves [1].

4.10. Immunosuppression

In patients with ESRD, there is a malfunction in polymorphonuclear and mobility of granulocytes, which reduce defense of the patient's cells, thus failing to remove bacteria from the bloodstream properly [5].

5. Heart valves with IE in HD

As mentioned earlier the incidence of IE in HD patients is higher than in general population and it is caused by multiple factors. But it is closely related to frequent episodes of bacteremia related to dialysis access and the predisposition of these patients to present premature degeneration of the heart valves eventually causing bacterial implantation in the valves. This is an issue of major public health presenting a very poor prognosis in short and long term, with 23.5% in-hospital mortality and 61.6% mortality in 1 year.

Despite the high rates of IE and poor prognosis for these patients, there has not been a substantial change in mortality over the past two decades. This can be the result of not having important changes in the therapeutic armamentarium [25]. Reports of multiple studies have shown that left valves with IE in HD patients are affected twice the time compared to the right valves; as well as the mitral valve is affected in more patients than the aortic valve. It is theorized that the thickening of these valves, which is common in this group of patients, can lead to increased susceptibility to acquire IE because of alterations in the laminar flow. Mitral annular calcification, which is also common in ESRD, has also shown increased susceptibility to IE [8].

5.1. Transthoracic echocardiogram (TTE) versus transesophageal echocardiogram (TEE)

TTE as a first-line diagnostic tool can work, but Kamalakannan et al. reported only 55.3% positive for vegetations in IE in HD and after using TEE 92.5% were positive for vegetations [8].

5.2. Medical treatment

Medical treatment for IE in HD patients, if considering the current guidelines for IE in general population, must have some important considerations in this group of patients.

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Vancomycin should not be used in IE with MSSA, because of two reasons: (1) its low bactericidal activity when compared with oxacillin or cefazolin and (2) its main role in strains of *S. aureus* with reduced glycopeptides and vancomycin-resistant *Enterococci* sensitivity. Conversely, when dealing with a patient with IE with MRSA, vancomycin (possibly in combination with rifampicin) remains the drug of choice, if it is possible to obtain and maintain plasma levels between 15 and 20 mg/L without toxicity [5].

5.3. Surgical treatment

You can repair a valve anytime with a TEE confirmation of good valve function, which is better than replacement.

Valve replacement is a key part of therapy in patients with IE [25]. A large retrospective study by Rankin et al. used the Society of Thoracic Surgeons national database to analyze 1862 valve surgery operations in dialysis patients with endocarditis from 1994 to 2003 and reported an operative mortality of 24.4%. In this study, several risk factors for hospital mortality were proposed in HD patients with IE, including (salvage surgery/shock, surgery on both valves, elderly, affected mitral valve, high BMI, arrhythmias, active endocarditis, and female gender) [26]. A more recent study of Leither et al. found lower mortality in patients who underwent surgery of left-sided surgery compared to those reported by Ranki et al.

Current indications for surgery in a patient with IE (general population) according to the guidelines are valve disease causing CHF, recurrent emboli, persistent despite appropriate antibiotic treatment infection, and mobile and large vegetation formation of myocardial abscesses. However, these recommendations are made for IE general population; currently, there are no specific guidelines for IE in HD patients, taking into account that this indication may be debatable for these patients. Dialysis patients have a higher risk for mortality in the context of IE, lower life expectancy, high surgical risk, and often other associated morbidities [25]. In this context, there are some studies with very different results: Spies et al. reported 73% mortality and Kamalakannan et al. reported 80% survival in patients undergoing surgery, in in-hospital survival and only 43% survival with medical treatment. However, in the study of Kamalakannan et al. 12 of the 15 patients (80%) survived, but 24 of the 69 patients had indication for surgery according to the guidelines of IE for the general population, indicating that selection bias likely strongly influenced the outcomes reported in these studies [8, 25, 27].

About surgical treatment in this group of patients, there has always been controversy over what type of prosthesis to be used: biological or mechanical. These controversies started from two studies from the 1970s that were case series (n = 4 patients) in dialysis, where accelerated calcification of biological valves was documented. Now there are enough studies that compare the use of mechanical versus. bioprosthesis with no significant differences. Thourani et al., in 2011, demonstrated a in HD patients with IE patients undergoing valve replacement of 18.1%, with no difference between mechanical and bioprosthetic after 10 years [28]. Other studies have shown a higher incidence of bleeding and cerebrovascular events in patients with mechanical valves compared with bioprosthesis. In addition to oral anticoagulants, which are problematic in ESRD patients, most patients are prone to bleeding.

Since no significant differences are found between the types of valve prosthesis to be placed in HD patients with IE, it is recommended to individualize each case. But as a general rule, bioprosthesis is placed in most HD patients with IE, especially in patients with increased risk of bleeding associated with anticoagulation, leaving mechanical prostheses for young patients without other morbidity in whom life expectancy is longer than the bioprosthesis and also, for young patients who are candidates for renal transplantation in the future [25].

6. IE in HD patients in western Mexico

Our group works at a reference center, in the Mexican Institute of Social Security (IMSS for its acronym in Spanish) and takes care of all cardiothoracic surgical patients in the west of Mexico that are affiliated to IMSS. This means that more than 10 states represent more than 8.5 million affiliated people and possible patients. There are other hospitals in western Mexico that deal with endocarditis patients, but a patient who has surgical indication or who is seriously ill is sent to our center.

We retrospectively analyzed the last 5 year cases of IE in our center. There were 173 cases of which 77 (44.5%) were surgically treated. In these 77 patients, 33 (42.85%) patient where in HD. We used the IE in general population guidelines for the decision of medical or surgical treatment in all our patients.

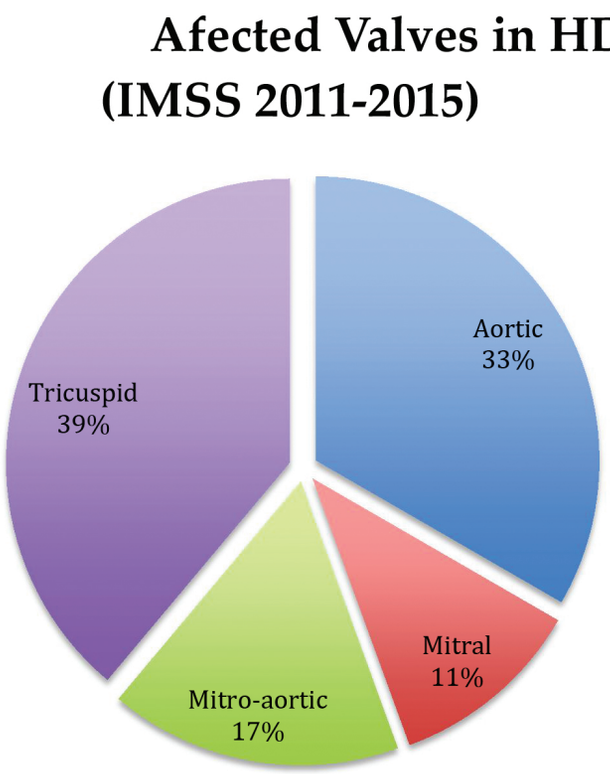

Figure 1. Affected valves in HD patients (IMSS 2011–2015).

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In contrast to what previous publications have described regarding IE in HD patients, the most commonly infected valve in our surgical population was the tricuspid valve (**Figure 1**). Also, having a mean age of 38.5 years ranging between 19 and 76 years, which is significantly lower than previous reports. We consider that this can be related to the long mean time of nontunneled HD catheters observed in our patients and also for not having proper safety protocols for the prevention of bacteremia in the HD facilities. This also could be caused by Mexico's overpopulation in public health services and the long-lasting waiting list for AVFs or kidney transplantation, causing good transplant candidates to end up as chronic dialysis patients and making them more susceptible to bacteremia and infections. Even though our hospital is the leading center for kidney transplantation in all Latin America, the waiting list is affected by the overpopulation commented before.

7. Differences between case series of IE in ESRD patients

The following tables summarizes some of the most representative contemporary case series of IE in ESRD patients published in the last decade. The percentage of HD patients with IE who are undergoing cardiac surgery ranges from 7.8 to 53% in different regions of the world and also the associated pathologies are listed in **Table 1**. *S. aureus* is the microorganism most frequently involved in all series (**Table 1**). The valves involve with IE in previous studies involved most frequently the left side valves (**Table 2**). There are significant differences in the percentage of ESRD patients with AVFs in different regions, the highest being in Europe (**Table 3**). And morbidity and mortality also differ between regions (**Table 4**).

Authors	**Doulton T, Sabharwal N, Cairns H, *et al*.**	**Jones D, McGill L, Rathod K, *et al.***	**Nori U, Manoharan A, Thornby J, *et al*.**	**Kamalakannan D, Manohara R, Johnson L, et al**.	**Chou M, Wang J, Wu W, et al**.	**Chang C, Kuo B, Chen T, et al.**	**Baroudi S, Qazi R, Lentine K, et al**.
Journal	**Kidney International, 2003; 64: 720-727**	**Nephron Clinical Practice, 2013; 123: 151–156**	**Nephrology Dialysis Transplantation 2006; 21: 2184–2190**	**Annals of Thoracic Surgery 2007; 83: 2081–2086**	**International Journal of Cardiology 2015; 179: 465–469**	**Journal of Nephrology 2004; 17:228-235**	**NDT PLUS Nephrology Dialysis Transplantation**
Year	**2003**	**2013**	**2006**	**2007**	**2015**	**2004**	**2008**
Country	UK	UK	USA	USA	Taiwan	Taiwan	USA
Years of the study	**22**	**13**	**5**	**15**	**9**	**15**	**16**

Years in which the study was conducted	1980–1995, 1995–2002, 1996–2002	1998–2011	1999–2004	1990–2004	1999–2007	1988–2002	1990–2006
Participant centers	St. Thomas H. Guy´s H. King´s College H. (London)	Royal London Hospital. (London)	Columbus, Ohio Detroit, Michigan Houston, Texas	St. John Hospital and Medical Center. Detroit, Michigan.	National	Taipei Veterans General Hospital.	Saint Louis University Hospital.
IE patients (n)	28 pts.	42 pts.	52 pts.	69 pts.	502 (39 surgical)-7.8	20 pts.	59 pts.
Cardiac surgery	53% (15/28 pts.)	21% (9/42 pts.)	24% (13/52 pts.)	34% (24/69 pts.)	7.8% (39 pts.)	*(20 /20 pts.)	12% (7/59 pts.)
Male patients	60.7% (17 pts.)	52.2% (22 pts.)	52%	45% (31 pts.)	35.9% (14 pts.)	(13 pts.)	47% (28 pts.)
Mean age	54.1 (22-81)	55.2 (43-69)	60 (36-82)	56 +-13	52.6 +- 11.7	64.6+-12.9	57.3 +- 13.8
Diabetic%	8	33.3% (14 pts.)	42% (22 pts.)	37.7% (26 pts.)	46.2% (18 pts.)	45% (9 pts.)	59% (35)
Hypertension %	*	66.6% (28 pts.)	79% (41 pts.)	89.9% (62 pts.)	NR	75% (15 pts.)	93% (55)
Immuno suppression %	*	9.5% (4 pts.)	*	(3 pts.)	NR	*	5% (3 pts.)
Staphylococcus aureus	63.3% MRSA	57.1% (24/42 pts.)	20% (11 pts.)	*	*	*	45% (27 pts.)

* For the type of stratification of patients in the publication, the data are present but not reported in this table. NR: not reported.

Table 1. Infective endocarditis publications in ESRD patients in dialysis surgical treatment: demographic information.

Authors	**Doulton T, Sabharwal N, Cairns H, *et al.***	**Jones D, McGill L, Rathod K, *et al.***	**Nori U, Manoharan A, Thornby J, *et al.***	**Kamalakannan D, Manohara R, Johnson L, et al.**	**Chou M, Wang J, Wu W, et al.**	**Chang C, Kuo B, Chen T, et al.**	**Baroudi S, Qazi R, Lentine K, et al.**
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Year	**2003**	**2013**	**2006**	**2007**	**2015**	**2004**	**2008**
Country	UK	UK	USA	USA	Taiwan	Taiwan	USA
Involved heart valve%							
Mitral	41.4%	30.9% (13/42 pts.)	50% (27 pts.)	*	*	64%	63% (37 pts.)
Aortic	37.9%	42.8% (18/42 pts.)	43% (23 pts.)	*	*	18%	17% (10 pts.)
Tricuspid	NR	5 pts.	19% (10 pts.)	*	*	9%	*
Mitral and aortic	17.2%	9.5% (4/42 pts.)	*	*	*	9%	*
Previous valve lesions	13 pts. (51.7%)	33.3% (14 pts.)	*	10.1% (7 pts.)	*	*	*
Previous valvular prosthesis	2 pts	9.5% (4 pts.)	13% (7 pts.)	4.3% (3 pts.)	*	*	*

* For the type of stratification of patients in the publication, the data are present but not reported in this table. NR: not reported.

Table 2. Infective endocarditis publications in ESRD patients in dialysis surgical treatment: involved heart valves.

Authors	**Doulton T, Sabharwal N, Cairns H, et al.**	**Jones D, McGill L, Rathod K, *et al.***	**Nori U, Manoharan A, Thornby J, *et al.***	**Kamalakannan D, Manohara R, Johnson L, et al.**	**Chou M, Wang J, Wu W, et al.**	**Chang C, Kuo B, Chen T, et al.**	**Baroudi S, Qazi R, Lentine K, et al.**
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Year	**2003**	**2013**	**2006**	**2007**	**2015**	**2004**	**2008**
Country	UK	UK	USA	USA	Taiwan	Taiwan	USA
Dialysis access route%							
PTFE graft	10.8%	NR	13% (7 pts.)	21.7% (15 pts.)	*	15% (3 pts.)	44.1% (26 pts.)
AVF	41.3%	35% (14/40 pts.)	4% (2 pts.)	11.6% (8 pts.)	*	25% (5 pts.)	5.1% (3 pts.)
Tunneled catheter DL	37.9%	55% (22/40 pts.)	72% (39 pts.)	66.7% (46 pts.)	*	5% (1 pt.)	26 pts.

Nontunneled catheter	3.4%	10% (4/40 pts.)	2% (1 pt.)	0 (0%)	*	55% (11 pts.)	2 pts.
Peritoneal dialysis	3.4% (1)	5% (2/42 pts.)	NR	0 (0%)	*		
Mean time of HD before IE	46.3 (1.5-180)	57.4 (9.7 -85.5)	*	37+-32	*	12.9+-19.1	52.9 +- 58

* For the type of stratification of patients in the publication, the data are present but not reported in this table. NR: not reported.

Table 3. Infective endocarditis publications in ESRD patients in dialysis surgical treatment: dialysis access route.

Authors	**Doulton T, Sabharwal N, Cairns H, *et al.***	**Jones D, McGill L, Rathod K, *et al.***	**Nori U, Manoharan A, Thornby J, *et al.***	**Kamalakannan D, Manohara R, Johnson L, et al.**	**Chou M, Wang J, Wu W, et al.**	**Chang C, Kuo B, Chen T, et al.**	**Baroudi S, Qazi R, Lentine K, et al.**
Journal	**Kidney International, 2003; 64: 720–727**	**Nephron Clinical Practice, 2013; 123:151–156**	**Nephrology Dialysis Transplantation 2006; 21: 2184–2190**	**Annals of Thoracic Surgery 2007; 83: 2081–2086**	**International Journal of Cardiology 2015; 179: 465–469**	**Journal of Nephrology 2004; 17: 228–235**	**NDT PLUS Nephrology Dialysis Transplantation**
Year	**2003**	**2013**	**2006**	**2007**	**2015**	**2004**	**2008**
Country	UK	UK	USA	USA	Taiwan	Taiwan	USA
Survival to discharge after surgery	14 pts (93.3%)	88.8% (8 pts.)	*	*	*	*	*
Survival 3 months after surgery	*	86.9%	*	*	66.5%	*	*
Survival 1 year after surgery	*	77%	*	*	58.4%	*	*
In-hospital mortality% nonsurgical patients	*	14.3%	19 pts. (37%).	*	23.5%	*	*
In-hospital mortality% surgical patients	1 pt. (6.9%)	11.1%	*	*	25.9%	*	*
Subsequent mortality	>50% 1 year survival	29.2% - 1 month	32.7% - 3 months	13 pts. Follow-up	*	*	*

* For the type of stratification of patients in the publication, the data are present but not reported in this table. NR: not reported.

Table 4. Infective endocarditis publications in ESRD patients in dialysis surgical treatment: survival, in-hospital mortality, and overall mortality.

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8. Prevention and future considerations

After analyzing the literature of IE in different regions of the world, we found different pathogens depending on the endemic regions for some pathologies, for example, RHD, usage of antibiotic treatment before having a diagnosis, endemic zones for rare pathogens such as *Brucella* spp. in Turkey or even zoonosis reported by Watt et al. [7, 16, 20].

One of the recommendations for developing countries must be an adequate treatment and follow-up for group A beta-hemolytic streptococcus to prevent rheumatic fever and its cardiac complications, which is one of the most common causes of IE in general population and in HD 19 patients in developing countries [16].

There are many different scenarios between developed and developing countries, but we think that the security measures for prevention of bacteremia in HD can be achieved in any health care unit using HD program regardless of the place. Reducing bacteremia in HD patients will reduce their incidence of IE [16].

Pronovost et al. in their study made in 103 UCIs in Michigan used basic changes in their practice of catheter implantation and management. An evidence-based intervention resulted in a large and sustained reduction (up to 66%) in rates of catheter-related bloodstream infection that was maintained throughout the 18-month study period [29].

8.1. Michigan and bacteremia zero recommendations

1. Wash your hands

Wash your hands before inserting a central venous catheter (CVC). Bottom Line: Proper hand hygiene is required before and after palpating catheter insertion sites, as well as before and after inserting, replacing, accessing, repairing, or dressing an intravascular catheter. In addition, the use of gloves does not obviate the need for hand hygiene. Category IA: Proper hand hygiene procedures can be achieved through the use of either a waterless, alcohol-based product or an antibacterial soap and water with adequate rinsing.

2. Clean the skin with chlorhexidine

Bottom Line: Disinfect clean skin with an appropriate antiseptic before catheter insertion and during dressing changes. A 2% chlorhexidine-based preparation is the preferred solution, Category IA [29].

Chaiyakunapruk et al., in their meta-analysis compared chlorhexidine versus povidone-iodine solution for vascular catheter site care, finding that the use of chlorhexidine reduces the risk for catheter-related bloodstream infection by 49% [30]. The same authors in another study, published one year later, concluded that the use of chlorhexidine, rather than povidone, for central catheter site care resulted in a 1.6% decrease in the incidence of catheter-related bloodstream infection, a 0.23% decrease in the incidence of death, and savings of $113 per catheter used [31].

3. Use of full-barrier precautions during CVC insertion

Bottom Line: Maintain aseptic technique for the insertion of intravascular catheters. Category IA: Maximal sterile barrier precautions (e.g., cap, mask, sterile gown, sterile gloves, and large sterile drape) during the insertion of CVCs substantially reduce the incidence of catheter-related bloodstream infection (CR-BSI) compared with standard precautions (e.g., sterile gloves and small drapes) [29].

4. Avoid the femoral site

Bottom Line: A subclavian site is preferred for infection control purposes, although other factors (e.g., the potential for noninfectious and catheter-operator skill) should be considered for deciding where to place the catheter. Category IA: The site at which a catheter is placed influences the subsequent risk for catheter-related infection and phlebitis. For adults, lower extremity insertion sites are associated with a higher risk of infection than upper extremity sites. As a result, authorities recommend that CVCs be placed in the subclavian site instead of a jugular or femoral site to reduce the risk for infection [29].

5. Remove unnecessary central venous catheters

Bottom Line: Promptly remove any intravascular catheter that is no longer essential. Category IA: One of the most effective strategies for preventing CR-BSIs is to eliminate, or at least reduce, exposure to central venous catheters. The decision regarding the need for a catheter, however, is complex and therefore difficult to standardize into a practice guideline. Nonetheless, to reduce exposure to central venous catheters, the ICU team should adopt a strategy to systematically evaluate daily whether any catheters or tubes can be removed [29].

6. Hygienic management of catheters

Minimize the manipulation of the connections and clean the injection sites of the catheter with isopropyl alcohol 70° before its use. Category IA: Another characteristic of this study was that the people in charge of the catheters needed to do an auto-test online, assist to safety meetings before they can be part of the study [32]. This study was performed in 68% of all ICUs in Spain, with a reduction of 50% in the bacteremia related to catheter in a two-year period [19].

In addition to the intervention to reduce the rate of catheter-related bloodstream infection, the ICUs implemented the use of a daily goal to improve clinician-to-clinician communication within the ICU, an intervention to reduce the incidence of ventilator-associated pneumonia, and a comprehensive unit-based safety program to improve the safety culture. The period necessary for the implementation of each intervention was estimated to be 3 months [29].

8.2. Our recommendations for developing countries

After analyzing the literature and the results in the different countries and our own experience, we made some recommendations that could help any HD program in developing countries for reducing their bacteremia incidence, and thus reducing the risk of IE.

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1. Form a HD team

They should be the only people involved in the HD process. This can be achieved by online auto-test of the use of catheters and the safety recommendations for it. This team must have a leader, who has to be in constant training through conferences and workshops. This must be transmitted to the whole group, also by training and evaluations. Having a checklist for every procedure could also help reduce errors or omissions in the process. The personnel involved in this HD team must be able to teach all the safety measures for the patient and their family members to avoid infection of any HD access. They must provide standardized knowledge about topics such as vascular access care, hand hygiene, risks related to catheter use, recognizing signs of infection, and instructions for access management when away from the dialysis unit.

2. Cardiac screening for all ESRD patients

An ESRD patient who is going to start HD treatment should have a cardiac screening to rule out previous cardiac pathology. A patient with a heart disease should be considered for closer monitoring.

3. Respect hierarchy in vascular access for HD

Before HD, always consider that the hierarchy of bacteremia risk exists among various types of HD vascular access; it is less common in patients with native arteriovenous fistulae, while synthetic grafts, cuffed catheters, and uncuffed catheters yield a progressively increasing risk.

4. Respect hierarchy in vascular access when using catheters for HD

In the case of using catheters, the hierarchy of bacteremia risk is less common in subclavian catheters, jugular catheters, and femoral catheters, progressively increasing risk.

5. Use the Michigan and bacteremia zero recommendations when using catheters

When using a catheter for HD, always take the six recommendations given above from Pronovost et al. made in ICUs in Michigan and Bacteremia Zero from Spain, which reduce more than 50% of catheter-related bacteremia.

6. Nasal cultures for all ESRD patients

Nasal cultures for *S. aureus* for new patients and serial cultures for chronic patients and use of nasal mupirocin are recommended.

7. Inspect and clean catheter exit sites

Exit sites should be routinely inspected for infection at every dialysis session, and subjected to swabbing and bacterial culture whenever infection is suspected.

8. Suspicion of IE in HD patients? Always use TEE

TTE if not conclusive TEE to rule out or confirm the diagnosis; if TTE conclusive, use TEE to rule out other cardiac lesions or unidentified vegetations in other valves.

9. Vancomycin not as prophylactic

Confirm IE in HD patients; do not use prophylactic vancomycin if you suspect any pathogen different from MRSA.

10. Mechanical prosthesis not the only option for IE in HD patients

Biological prosthesis is a good option for these patients; the heart team must individualize each case; and consider the benefits or disadvantages of mechanical or biological prosthesis.

9. Conclusion

Here we have addressed the different protocols and outcomes among developed countries due to ESRD patients' population, economy and health care differences in each country. This means that the recommendations of different associations and foundations have not been completely followed up by all HD systems even in developed countries.

So to answer the question: what is the problem in developing countries? There are many answers.

Late ESRD diagnosis or any risk factors can end in ESRD, due to not having a routine checkup in primary health care service.

Incomplete protocols, as already stated, are common in developing countries, making changes to these protocols based on "saving" money only or to provide more medical care to a large number of patients, giving them suboptimal care due to inadequate time for each patient. Because health care providers in developing countries have too many patients, it is not possible to offer optimal service quality.

Unavailability of the adequate equipment.

Not having the right timing between dialysis treatments, and especially between diagnosis and definitive treatment with kidney transplant.

Long waiting lists due to fewer transplant centers for kidney transplantation.

In developing countries, most of the patients are uneducated, or they do not have accurate information about their diseases or their HD route.

In the recommendations given in this chapter, after analyzing the literature and the guidelines for preventing IE in ESRD patients, we summarized the prevention strategies and sought to apply them in any developing country for having less incidence of IE in ESRD patients.

Being part of a health care institution in a developing country, you have to learn how to manage this and other related difficulties. The only method to give a solution to this problem is by analyzing the procedure of other hospitals, either from your region or from other countries, which will give you good arguments for requesting anything missing in your program to provide quality care to their patients. In other words, you have to demonstrate that is cost-effective and it will benefit the patient and the hospital.

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