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Infective Endocarditis in Hemodialysis: Descriptive Study

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Abstract

Introduction: Infective endocarditis (IE) is a complication associated with high mortality in chronic hemodialysis patients. The aim of our study is to describe the clinical, radiological, microbiological characteristics, and risk factors of mortality in hemodialysis patients with infective endocarditis. ***Methods***: A retrospective study from November 2019 to November 2021 including hemodialysis patients with IE hospitalized in Ibn Sina hospital center in Rabat. ***Results***: Eighteen hemodialysis patients were included. Mean age was 49.5 ± 18 years, sex ratio was 0.8. Catheters were the access sites most commonly used (72.3%). Median duration of hemodialysis was 12 [6; 24] months. *Staphylococcus species* is major causative bacteria in 60%. The mitral valve was the most commonly affected (44%). Frequent complications including valve insufficiency (50%), septic embolism (66.7%). Four patients underwent surgery and eight died during hospitalization (44.5%). Mitral localization of vegetation was the only factor significantly associated with mortality in our study ($P < 0.05$). ***Conclusion***: The catheter was the most commonly used access site compared to the arteriovenous fistula. This confirms that it's the vascular access of choice for his low rate of infectious complication compared to the catheter.

Keywords

Catheters, Endocarditis, Hemodialysis, Mortality, Septic Emboli

1. Introduction

The first case of infective endocarditis (IE) in hemodialysis dates from 1966, although dialysis was started long before [1]. It's a common complication in dialysis patients. The incidence is 50 to 60 times higher compared to the general pop-

ulation [2] and is associated with higher in-hospital and 1 year mortality [3]. Vascular access in hemodialysis represents the source of bacteremia and consequently of endocarditis. *Staphylococcus aureus* is the most commonly isolated organism.

The diagnosis of IE is based on the combination of clinical symptoms, presence of vegetation on echocardiography, and positive blood cultures [4]. The prognosis has improved with antibiotic therapy and surgical management, however, the mortality rate remains high. The duration in hemodialysis (HD), cardiovascular complications associated to chronic renal failure (CRF), the valves involved, septic embolism and the virulence of the germ are the risk factors for this infection. Identifying these predictors of mortality could facilitate the choice of the most appropriate therapeutic strategy.

The objective of our study is to describe the clinical, radiological, microbiological characteristics, and risk factors of mortality in HD patients with IE.

2. Patients and Methods

This is a retrospective study from November 2019 to November 2021 at Ibn Sina Hospital in Rabat, Morocco. WE included all HD patients admitted to the emergency department for IE. The diagnosis was retained according to the criteria of duke (**Table 1**) [5]. We excluded in our study patients admitted for infective endocarditis complicated by acute renal failure during hospitalization.

Table 1. Definition of terms in modified Duke criteria for the diagnosis of infective endocarditis [5].

Major criteria
1) Blood culture positive for IE
a) Typical microorganisms consistent with IE from 2 separate blood culture ● *Viridans streptococci*, *Streptococcus bovis*, HACEK group, *Stapylococcus aureus*; or ● Community-acquired enterococci, in the absence of a primary focus; or
b) Microorganism consistent with IE from persistently positive blood cultures, defined as follows: ● At least 2 positive cultures of blood samples drawn > 12 h apart; or ● All of 3 or a majority of ≥4 separate cultures of blood (with first and last sample drawn at least 1h apart)
c) Single positive blood culture for *Coxiella burnetii* or antiphase I Ig G antibody titer > 1 > 800
2) Evidence of endocardial involvement
a) Echocardiogram positive for IE (TTE recommended in patient with prosthetic valves; rated at least "possible" IE by clinical criteria or complicated IE (paravalvular abcess); TTE as first test in other patients), defined as follows: ● Oscillating intracardiac mass on valve or supporting structures, in the path of regurgitant jets, or on implanted material in the absence of an alternative anatomic explanation; or ● Abcess; or ● New partial dehiscence of prosthetic valve
b) New valvular regurgitation (worsening or changing of pre-existing murmur not sufficient

Continued

Minor criteria
● Predisposition, predisposing heart condition or injection drug use ● Fever, temperature > 38˚C ● Vascular phenomena, major arterial emboli, septic pulmonary infarcts, mycotic aneurysm, intracranial hemorrhage, conjunctival hemorrhages and Janeway's lesions ● Immunologic phenomena: glomerulonephritis, Osler's nodes, Roth's spots and rheumatoid factor ● Microbiological evidence: positive blood culture but does not meet a major criterion as noted above * or serological evidence of active infection with organism consistent with IE
Interpretation
Definite infective endocarditis: Pathological criteria ● Microorganism: demonstrated by culture or histology in a vegetation or in a vegetation that has embolized, or in a intracardiac abscess or ● Pathologic lesions: vegetation or intracardiac abscess present confirmed by histology showing active endocarditis Clinical criteria: ● 2 major criteria, or ● 1 major and 3 minor, ● or 5 minor **Possible infective endocarditis** ● 1 major and 1 minor, or ● 3 minor ● Rejected **Diagnosis of infective endocarditis is rejected** ● Firm alternate diagnosis explaining evidence of infective endocarditis, or ● Resolution of infective endocarditis syndrome, with antibiotic therapy for 4 days or less, or ● No pathologic evidence of infective endocarditis at surgery or autopsy, with antibiotic therapy for 4 days or less

The data studied were collected from patient's records, and included the following demographical parameters: such as age, sex, duration of hemodialysis, vascular access and the time interval between its placement and the diagnosis of IE. Clinical parameters included general status at admission, fever, and presence of heart murmur, dyspnea, and hemodynamic status. Bacteriological diagnosis was based on blood culture results or catheter culture. Other biological elements were collected including hemoglobin, leukocytes and platelet count, albumin and C-reactive protein (CRP) on admission.

The radiological diagnosis by transthoracic echocardiography was used to locate the vegetation and the presence of other associated cardiac lesions. The type and duration of antibiotic treatment has been specified. We have defined two types of groups (non-survivors and survivors) and we compared the characteristics to identify the risk factors associated with mortality during hospitalization.

Data is presented as means and standard derivation when the distribution is

normal or median and interquartile if the distribution is not homogeneous. The difference was considered significant from a P value less than 0.05. The statistical software used was SPSS, IBM, version 20.

3. Results

There were 18 HD patients with IE with a mean age of 49.5 ± 18 years and a sex ratio of 0.8. The duration of dialysis is 12 [6; 24] months. The duration of vascular access was 2 years [1; 7.5] for AVF and 15.07 weeks ± 9.68 for catheter (Table 2).

The symptoms were dominated by fever and altered general condition found in all HD patients, a heart murmur in two patients (11.2%) and dyspnea in 09 patients (50%). The mean systolic blood pressure (BP) is 114 ± 18 mmHg and the diastolic BP is 64 ± 8.5 with an average pulse rate of 104 ± 16.5 beats per minute.

Septic pulmonary embolism was observed in 9 patients and cerebral embolism in 3 patients. Transthoracic echography (TTE) was used to identify vegetation in all patients. The mitral valve (44%) was the most frequently involved (Figure 1), followed by tricuspid (33%) and aortic (6%). The valve insufficiency was identified in 09 cases (50%).

Microbiologically, Blood and catheter cultures were positive in 14 patients and *staphylococcus* [including *methicillin resistant Staphylococcus aureus* (MRSA)] was the most common germ found in patients (60%). The biological result and causative organisms are respectively listed in Table 3 and Table 4.

The catheter was removed in 12 patients before any antibiotic therapy. In one patient, catheter removal was discussed due to the vascular capital exhaustion but patient died 24 hours after admission from septic shock.

Patients were treated with intravenously antibiotics, administered after dialysis

Table 2. Demographic and clinical characteristics of the study patients.

Parameters	N (%)
Age of patients	49.5 ± 18
Female/male	08/10
Duration of HD (month)	12 [6; 24]
The duration of access:	
AVF (years)	2 [1; 7.5]
Catheter (weeks)	15.07 ± 9.68
The type of vascular access:	
Arteriovenous fistula (AVF)	05 (27.7%)
Single jugular catheter	01 (5.6%)
Single femoral catheter	03 (16.7%)
Jugular tunnel catheter	09 (50%)
Clinical symptoms:	
Fever	18 (100%)
Heart murmur	02(11.2%)
Dyspnea	09 (50%)

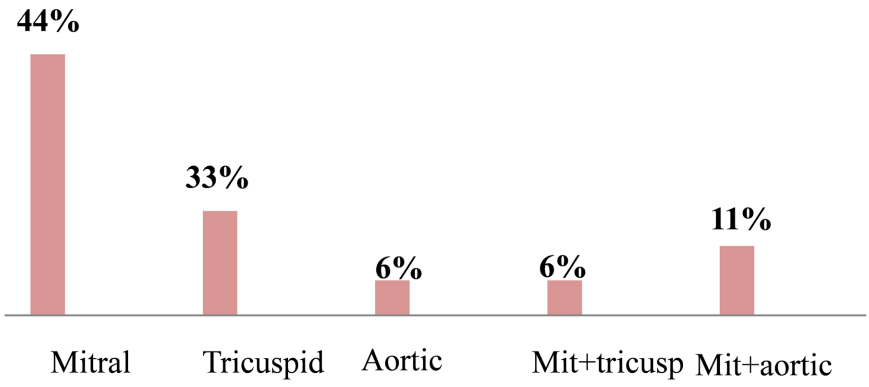

Figure 1. Localization of vegetation on TTE in the study patients.

Table 3. Biological aspect of the study patients.

Parameters	Mean	N (%)
CRP (mg/l ± SD)	116 ± 72	
Albumin (mg ± SD)	28.85 ± 5.57	
Hemoglobin (g/dl ± SD)	8.43 ± 1.97	
Thrombocytopenia (n)		4 (22.2%)
Hyperleucocytosis (n)		9 (50%)

Table 4. Bacteriological aspects of the study patients.

Pathogens causal	N (%)
Staphylococcus aureus	7 (38%)
Staphylococcus coagulase negative	4 (22%)
Acinetobacter baumannii	1 (6%)
Enterobacter cloacae	1 (6%)
Enterococcus faecalis	1 (6%)
Not identified	4 (22%)

sessions. Probabilistic treatment includes vancomycin or teicoplanin (depending on availability in the hospital) associated with gentamicin for at least 6 weeks.

The treatment was adapted according to the antibiogram's results. Valve replacement was performed after 2 weeks of beginning treatment in four patients, motivated by congestive heart failure in two cases and uncontrolled infection in the two others case. Eight patients died during hospitalization (44.5%). The characteristics such male gender, age > 60 years, duration of HD, hypoalbuminemia, anemia, and presence of MRSA in blood culture did not differ significantly between the groups of survivor and not survivors (Table 5). Mitral vegetation was significantly associated with risk of mortality during hospitalization in our study (Table 5).

4. Discussion

Infectious disease is the second cause of death in hemodialysis patients [6] [7] [8] [9]. Compared to the general population, hemodialysis patients have higher

Table 5. Characteristics of survivors and non survivors in our study.

Characteristics	Non survivors (n = 8)	Survivors (n = 10)	P value
Male gender	06 (75%)	04 (40%)	0.138
Age (years ± SD)	45.62 ± 18.81	52.6 ± 17.77	0.639
Age (>60 years)	02 (25%)	04 (40%)	0.502
Albumin (mg/L ± SD)	29.4 ± 6.76	28.55 ± 5.22	0.452
Hemoglobin (g/dL ± SD)	8.61 ± 1.77	8.29 ± 2.2	0.254
CRP level (mg/L ± SD)	117.37 ± 76	114.8 ± 81	0.522
Catheters	06 (75%)	07 (70%)	0.814
Duration of catheterism (weeks)	12.5 ± 11.4	17.28 ± 8.11	0.184
Vegetation Mitral	07 (87.5%)	01 (10%)	**0.001**
Ejection fraction < 50%	03 (37.5%)	03 (30%)	0.558
Staph MetiR	02 (25%)	00 (0%)	0.094
Secondary septic locations	06 (75%)	06 (60%)	0.502
Valve replacement	0 (0%)	04 (40%)	**0.040**

rates of bacteremia and mortality [10] [11]. Of these bacteremic patients, the incidence of infective endocarditis is been reported to develop in 300 cases per 100,000 people in hemodialysis, compared to 3 to 9 cases per 100,000 in the general population [3].

The mortality rate from IE in hemodialysis patients varies between 16.7% and 28.8% in the literature [12] [13] [14] [15]. In our series, a higher mortality rate was observed (44.5%).

The incidence of bacteremia linked to vascular access in hierarchical order is as follows: temporary catheter, permanent catheter, arteriovenous grafts, and native AVF. Which is consistent with our results: permanent or temporary catheter (72.3%), AVF (27.7%). Therefore, an AV fistula should not be overlooked as a source of bacteremia, even if the site does not appear to be infected.

Clinical symptoms of IE are not typical, particularly in HD patients. Therefore, diagnosis and initial management are difficult. In our study, the symptoms were dominated by the association of fever and dyspnea. The presence of peripheral septic embols is not pathognomonic of IE but their presence directs the diagnosis towards IE.

In our study, the mean age is 49.5 ± 18 years. The age is relatively young in chronic hemodialysis patients who have presented with infective endocarditis compared to the general population. This is explained by the epidemiology of the end renal failure disease in our context (mean age is 38 years in Morocco) [2].

Endocardial lesions require the use of a combination of two intravenous bactericidal antibiotics with synergistic action. The antibiotic of choice is decided according to the bacteriological results and must be administered for a period of six weeks in our patients. This antibiotic alone was not sufficient in 22% of patients and surgery was required. Valve replacement has a positive impact on the survival of our patients ($P < 0.05$). The surgery should be performed as early as

possible to avoid embolic complications and therefore improve the prognosis [16]. There is insufficient data in the literature on the success of valve surgery after IE. A retrospective study has shown that the mortality rate in 30 days after cardiac surgery is 8.5% and the cumulative late mortality is 25.6% [17].

The occurrence of infective endocarditis is an indication for the immediate removal of the catheter. The hemodialysis must therefore be continued using a temporary catheter inserted at another site [18].

Comparing our results with other studies [19] [20] [21] [22] [23], mitral localization was the most frequent in our population. In addition to being the most valve most affected, it was significantly associated with in-hospital mortality and had a negative impact on the overall survival of patients. *Staphylococcus* was the most common pathogen in our series and in other series in the literature [20] [21] [22] [23] but contrary to previous observations [24], MRSA did not influence death in hospital. A high C reactive protein, septic embolism and hypoalbuminemia were also a risk factor to predict mortality in patients with infective endocarditis [25] [26] [27], but which not considered being a risk factor for mortality in our series.

This study has limitations. First, this a retrospective study carried out in our dialysis center which recruits all hemodialysis patients hospitalized for IE. Second, only hemodialysis patients were included and could not be compared to patients without dialysis.

5. Conclusion

Our study identified the mitral valve involvement as a risk factor for mortality in hospital and patients who underwent cardiac surgery had better in-hospital outcomes. The results of our study for chronic hemodialysis patients were unsatisfactory. Only 55.5% of these patients survived during hospitalization. Septic shock and valve failure during hospitalization were causes of in-hospital mortality. The catheter was the most commonly used access site compared to the AVF, which confirms that AVF remains the best access for longevity and for the lowest risk of morbidity and mortality.

Conflicts of Interest

The authors declare no conflicts of interest regarding the publication of this paper.

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