



ORIGINAL ARTICLE

## Effect of High-Flux versus Low-Flux Dialysis on the Rate of Bacteremia in Hemodialysis Patients: A Single Center Study

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### Abstract

Bacteremia in dialysis patients is a major risk factor of mortality. The aim of this study was to assess the effectiveness of dialysis with high-flux versus low-flux dialyzer regarding risk of bacteremia in dialysis patients. This was a retrospective cohort study that included dialysis patients who underwent dialysis therapy at old dialysis center where old low-flux dialyzers were used and the new dialysis center where high-flux dialyzers were used. The rate of positive culture was more in high-flux group (37.0%) compared to low-flux group (24.5%), although the difference was not statistically significant ( $P = 0.13$ ). The vascular access was mostly permanent catheter in high-flux group compared to low-flux group (48.9% vs. 28.6%, respectively;  $P = 0.06$ ), while arteriovenous (AV) fistula was more prominent in low-flux group compared to high-flux group (65.3% vs. 47.8%, respectively;  $P = 0.06$ ). This was reflected in the type of bacteria, which was mostly from Gram-positive family (*Staphylococcus*). The results showed higher risk of bacteremia in high-flux group as compared to low-flux group; however, permanent catheters were more prominent in high-flux group.

**Keywords:** bacteremia; dialyzer; high flux; low flux

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### Introduction

Since the beginning of dialysis, there has been a significant improvement in the modalities and the machines and filters used due to more understanding and improvement in the principles of dialysis. This has brought down the mortality rates of patients on dialysis (1). In spite of the advances made in the modalities of dialysis, bacteremia has remained as one of the most common complications in dialysis patients (2).

The risk of bacteremia in dialysis differs depending on different factors. It mainly depends on the presence or absence

of dialysis lines such as non-tunneled catheter, permanent catheter, and arteriovenous (AV) graft (2). Until recently, the dialyzers used were considered to have small pores that did not allow the passage of bacteria into blood from dialysate. The average pore size of a dialyzer varies according to flux, ranging from 1.5 nm in low-flux to 5 nm in high-flux dialyzer (3, 4), while the bacterial size is rarely less than 0.1  $\mu\text{m}$  and only fragments of bacteria have small sizes of 5–10 nm in diameter (5). Lately, there has been an increase in the use of high-flux dialyzers because of the increased pore size and

hence the increased clearance of metabolic waste products of middle-size molecules such as beta 2 microglobulin that are associated with the pathogenesis of certain diseases in patients on dialysis (6).

However, in spite of the discrepancy between the pore size of high-flux dialyzer and the bacterial diameter, there are concerns for increasing the flux of dialyzers, since it could raise the risk of exposure to cytokine-inducing bacterial substances in dialysate in this population of patients (7). The relation between pore size of membrane and permeability of bacterial pyrogens is still contentious (7, 8).

In light of the above discussion, the aim of this study was to assess the effectiveness of dialysis with high-flux versus low-flux dialyzers in terms of risk of bacteremia in patients undergoing dialysis.

## Methods

This was a retrospective cohort study comprising hemodialysis patients who were on dialysis at Makassed General Hospital in Beirut between July 2018 and June 2020. Following the approval of the Institutional Review Board, data were collected during the stated period because the dialysis center at Makassed General Hospital was renovated. The new center was opened in July 2019, where new dialysis machines (Fresenius 5004) were installed with the introduction of high-flux dialyzers. Previously, at the old division, machines were used with low-flux dialyzers. Hence, July 2019 was considered as a washout period to separate the use of high-flux from low-flux dialyzers.

Inclusion criteria were all patients who underwent dialysis in the outpatient dialysis center between July 2018 and June 2020 (one year before the start of new dialysis center where low-flux dialyzers were used and one year after the opening of new dialysis center where high-flux dialyzers were used). Only blood culture values (no other cultures such as wound or urine) were recorded. Exclusion criteria for the study included patients who had dialysis outside this time frame, those who did not have blood cultures collected, and hospital inpatients (since dialysis of inpatients was done on low-flux dialyzer machines compared to high-flux dialyzer machines in the new outpatient setting).

Data collected included demographic characteristics, history of bacteremia, type of vascular access in addition to blood culture results and the types of bacteria.

## Statistical analysis

The Statistical Package for Social Sciences (SPSS, version 24) was used for data analysis. Categorical variables were presented as number and percentage values. Continuous variables were presented as mean value and standard deviation. Bivariate analysis was conducted using the Chi square test

for comparing categorical variables. Continuous variables were compared using Student's *t*-test.  $P < 0.05$  indicated statistical significance.

## Results

A total of 358 outpatient dialysis patients were enrolled at our center during the study period. Of these, 141 patients had blood culture recorded and hence eligible to be included in the study. Of these 141 patients, 49 were in low-flux group and 92 in high-flux group. Regarding the demographics of patients, age was similar in both the groups ( $72.06 \pm 14.08$  years in low-flux and  $71.83 \pm 11.63$  years in high-flux group). Around 63% of patients in low-flux group were males compared to 53.3% in high-flux group. Diabetes mellitus (DM) was prevalent in both the groups. High-flux patients had double the rate of malignancy at the time of the study, although the difference was not statistically significant (13% vs. 6.1%;  $P = 0.20$ ). Likewise, high-flux patients had more episodes of previous bacteremia at the time of the study (53.3% vs. 44.9%;  $P = 0.34$ ). However, the rate of blood transfusion was comparable between both the groups (52.2% in high-flux vs. 53.1% in low-flux group;  $P = 0.92$ ) (Table 1).

Regarding the primary outcome of this study examining the risk of bacteremia in high-flux versus low-flux patients, it was apparent that patients on high-flux dialysis had higher risk of bacteremia than those on low-flux dialysis, although the difference was not statistically significant (37% vs. 24.5%;  $P = 0.13$ ) (Table 2).

Regarding vascular access, it was found that AV fistula was more prominent in low-flux compared to high-flux patients (65.3% vs. 47.8%;  $P = 0.06$ ). On the other hand, permanent catheter usage was more in high-flux compared to low-flux patients (48.9% vs. 28.6%;  $P = 0.06$ ) (Table 2).

Regarding the type of pathogen that caused bacteremia in blood cultures, coagulase negative *staphylococci* was the most prominent pathogen found in high-flux group (44.1%), which could have been related to catheter placement, followed by equal percentage (8.8%) of *Escherichia coli*, *Staphylococcus aureus*, and *Staphylococcus saprophyticus*. In the low-flux group, *Enterobacter* species were the most common causal pathogen (41.7%), followed by *Staphylococcus aureus* and *Staphylococcus saprophyticus* (16.7% each) (Table 2).

## Discussion

The present study showed that the rate of bacteremia was slightly more in high-flux patients compared to low-flux patients, although the difference was not statistically significant. Moreover, AV fistula was more prominent in low-flux patients whereas usage of permanent catheter was more in high-flux patients.

**Table 1:** Patients' demographic characteristics.

		Low-flux patients (n = 49)	High-flux patients (n = 92)	P-value
Age	Years	72.06 ± 14.08	71.83 ± 11.63	0.92
Gender	Male	31 (63.3%)	49 (53.3%)	0.25
	Female	18 (36.7%)	43 (46.7%)	
Diabetes mellitus		33 (67.3%)	66 (71.7%)	0.59
Malignancy		3 (6.1%)	12 (13.0%)	0.20
Duration of dialysis	Years	4.45 ± 1.26	4.55 ± 1.88	0.69
History of blood transfusion		26 (53.1%)	48 (52.2%)	0.92
History of bacteremia		22 (44.9%)	49 (53.3%)	0.34
Number of previous bacteremia episodes		1.73 ± 0.99	1.73 ± 1.11	0.98

**Table 2:** Primary outcome of the risk of bacteremia in high- and low-flux patients.

		Low-flux patients (n = 49)	High-flux patients (n = 92)	P-value
<b>Vascular access</b>	AV fistula	32 (65.3%)	44 (47.8%)	0.06
	Permanent catheter	14 (28.6%)	45 (48.9%)	
	Non-tunneled catheter	3 (6.1%)	3 (3.3%)	
<b>Positive culture</b>	No	37 (75.5%)	58 (63.0%)	0.13
	Yes	12 (24.5%)	34 (37.0%)	
<b>Bacteria type</b>	Coagulase-negative Staphylococci	2 (16.7%)	15 (44.1%)	0.06
	Enterobacter species	5 (41.7%)	1 (2.9%)	
	E coli	0 (0.0%)	3 (8.8%)	
	Klebsiella pneumonia	1 (8.3%)	1 (2.9%)	
	Staphylococcus aureus	2 (16.7%)	3 (8.8%)	
	Staphylococcus MRSA	0 (0.0%)	2 (5.9%)	
	Staphylococcus saprophyticus	2 (16.7%)	3 (8.8%)	
	Viridans streptococci group	0 (0.0%)	1 (2.9%)	
	Pseudomonas aeruginosa	0 (0.0%)	1 (2.9%)	
	Pseudomonas stutzeri	0 (0.0%)	1 (2.9%)	
	Chryseobacterium	0 (0.0%)	1 (2.9%)	
	Bacillus species	0 (0.0%)	1 (2.9%)	
	Alcaligenes species	0 (0.0%)	1 (2.9%)	

Several previous studies had controversial results regarding the effect of high-flux versus low-flux dialyzers on the translocation of bacterial products (7, 8). Gordon et al. conducted a study assessing the incidence of pyrogenic reactions when shifting from conventional dialysis to high-efficiency high-flux dialysis, taking data from three different dialysis centers with a total of 27,087 hemodialysis patients. However, there was no significant difference in the pyrogenic reaction rates (9).

This shows discrepancy in the effect of dialyzer flux on different outcomes. However, few studies have focused on the risk of infection per se when comparing high- and low-flux dialyzers (10). Instead, the main comparisons included patients' overall mortality, hospital admission, and quality of life (11–14). In this regard, Kantartzi et al. compared the quality of life of hemodialysis patients using low- and high-flux dialyzers, and concluded that the quality of life of dialysis patients was significantly better with high-flux dialyzers compared to when they used low-flux dialyzers (12). Results of the Hemodialysis Study (HEMO) indicated that infection-related death or hospitalization did not differ in patients randomized to high- or low-flux membranes (13). Another study conducted by Kavyannejad et al. pointed no significant differences in the incidence and severity of complications (variations in blood pressure, nausea, vomiting, itching, headache, and fever and chills) in patients during hemodialysis with low- or high-flux dialyzers (14).

In the present study, when comparing the demographic characteristics of patients, age was comparable in both groups (mean age of around 72 years). Regarding comorbidities, diabetes mellitus was comparable in both groups (67.3% low flux vs. 71.7% high flux). Malignancy was more in high-flux group than in low-flux group (6.1% vs. 13%, respectively), while history of blood transfusion was comparable in both the groups (53.1% vs. 52.2%).

Regarding the modality of dialysis, it was found that most of patients who underwent high-flux dialysis had permanent catheter access (48.9% vs. 28.6%;  $P = 0.06$ ), while the majority of patients who underwent low-flux dialysis had AV fistula (65.3% vs. 47.8%).

Although it was apparent from the above results that rate of bacteremia was slightly more in high-flux group, there are several factors that might affect the results. First, age was similar in both groups, so it could not play a key role in affecting the outcomes of this study. Also, both groups were comparable for diabetes mellitus. However, the risk of malignancy in high-flux group was double than in low-flux group. Neither the type of malignancy was reported at the time of the study (solid vs. hematologic), nor the time of diagnosis of tumors, whether patients were on chemotherapy, and whether they were neutropenic at the time of the study.

Second, it is a known fact that patients with end-stage renal disease have erythropoietin deficiency as well as a state

of iron resistance and relative iron deficiency, and hence need blood transfusions occasionally (15). However, there was no discrepancy in the rate of blood transfusion in low- and high-flux dialysis patients (53.1% vs. 52.2%, respectively).

Maybe, the most important factor is the mechanism of dialysis used in patients regarding vascular access (AV fistula vs. permanent or non-tunneled catheter). Permanent and non-tunneled catheters are foreign bodies and despite that the permanent catheter carries lower risk of bacteremia and is more sustainable as an access for dialysis due to its quality (tunneled catheter under the skin with subsequent fibrous sealing of the skin over the catheter that carries lower risk of bacteremia) (16). Nonetheless, such access carries greater risk of bacteremia than AV fistula (lower risk due to absence of line insertion into central venous system and absence of foreign bodies) (16). This was a major confounding factor in this study, since AV fistula was more prominent in low-flux than high-flux dialysis (65.3% vs. 47.8%, respectively) as compared to tunneled catheters, which were more prominent in high-flux group (28.6% vs. 48.9%).

A limitation of the present study was that it included a single center with small sample size. Yet, to our knowledge, it is the first study in Lebanon that exclusively assessed the rate of bacteremia in dialysis patients of outpatient department.

## Conclusion

Results of the study showed that there was an increase in risk of bacteremia when shifting from low- to high-flux dialysis; however, the difference was not statistically significant. The prominence of permanent catheters as access for dialysis in high-flux group could be a confounding factor. Supporting this idea was the presence of *Staphylococcal bacteremia* (Gram-positive) as a causal bacterial agent of blood bacteremia in this group. A direct causal relationship between high-flux dialysis and increased risk of bacteremia could not be established partly due to the presence of confounding factors.

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