Evaluation of risk factors for catheter-related infections with gram-negative bacteria in Tehran, Iran

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ABSTRACT

Introduction: Catheter infection is due to gram-negative, gram-positive bacteria, and fungi. Gram-positive bacteria are the most prevalent cause of catheter infection, although gram-negative bacteria seem to have escalated in recent years, which may have numerous risk factors. In this report, we intended to study these risk factors.

Objectives: This study aimed to investigate the risk factors for catheter-related infections caused by gram-negative bacteria in hemodialysis patients, to prevent catheter-related infections, which are unfortunately abundant.

Patients and Methods: This cross-sectional study was conducted on128 hemodialysis patients known cases Hasheminejad hospital in Tehran, Iran in 2019. Patients were assigned into two groups as the case group (catheter-related infection caused by gram-negative bacteria) (n = 64) and the control group (catheter-related infection caused by gram-positive bacteria) (n = 64). Risk factors for catheter-related infection, including hemoglobin, phosphorus, albumin, erythrocyte sedimentation rate (ESR), C-reactive protein (CRP), total iron-binding capacity (TIBC), catheter insertion site, urinary tract infection (UTI), urinary tract manipulation, and urinary tract anomalies were obtained and analyzed via SPSS version 26.

Results: Two groups were significantly different in serum albumin level (3.7 ± 0.5 g/dL in gram-negative group and 3.9 ± 0.5 g/dL in gram-positive group; $P = 0.009$) and in UTI (23.4 % in gram-negative group and 7.8 % in gram-positive group; $P = 0.015$). Additionally, no significant differences were observed in serum ferritin, phosphorus, ESR, CRP, TIBC, duration, and site of catheter insertion. Regression analysis shows that, for every unit increase in albumin, the chance of developing a gram-negative catheter infection is 0.356, or about one-third. In other words, with decreasing each unit of albumin, the chance of a gram-negative catheter infection is 2.8 times (reverse 0.356).

Conclusion: Serum albumin levels were significantly low in gram-negative group. Moreover, UTIs were significantly higher in this group. It is also important to consider hypoalbuminemia and UTI as risk factors for catheter infection with gram-negative bacteria.

Implication for health policy/practice/research/medical education:
In a cross-sectional study on 128 hemodialysis patients, we found a significant relationship between low-albumin level and gram-negative bacterial catheter infection. We found, alongside decreasing each unit of albumin, the chance of a gram-negative catheter infection was 2.8 times increased.

Introduction

Catheters are often used as access for dialysis; however, the infectious complications resulting from it remain a major clinical problem. Despite many advances in the design of catheters used, catheter-related infections are a prominent cause of death in dialysis patients. In particular, the mortality rate and the cost of general care for catheter-induced bloodstream infections and hospitalization are among the issues that highlight the importance of further studies in this area (1-3).

The relative risk of catheter infections in dialysis patients is ten times greater than that caused by venous arterial fistulas (4,5). Catheter-induced bacteremia is 0.5 to 5.5 episodes per 1000 catheters per day and the bacteremia

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episode is 2-9 catheter-years (6). Depending on where the catheter is inserted, the type of device (tunnel and non-tunnel catheters), and the duration of catheter use, the risk of developing bacteremia varies. The most important risk factor for catheter infection is the duration of catheter use (7-9).

Gram-positive organisms are responsible for most catheter infections. Coagulase-negative staphylococci and Staphylococcus aureus infections are responsible for the cause of 40% to 81% of infections. Other infections are enterococci and gram-negative bacteria (10-12). However, it seems that in the last years, the prevalence of catheter infections has shifted from gram-positive bacteria to negative bacteria, which may be due to urinary tract infections (UTIs) and urinary tract abnormalities (13-15).

Objectives

This study aimed to investigate the risk factors for catheter-related infections caused by gram-negative bacteria in hemodialysis patients, to prevent catheter-related infections, which are unfortunately abundant.

Patients and Methods
Study design

This cross-sectional study was performed on 128 patients, aged more than 18 years, with the aim of investigating the risk factors for catheter-related infections caused by gram-negative bacteria in hemodialysis patients, to prevent catheter-related infections, which are unfortunately abundant. Cases of end-stage renal disease on maintenance hemodialysis three times per week for 4 hours through a double-lumen tunnel cuffed catheter at Hasheminejad hospital in Tehran, Iran in 2019.

Patients were allocated to two groups as a case group (catheter-related infection caused by gram-negative bacteria) (n = 64) and the control group (catheter-related infection caused by gram-positive bacteria) (n = 64).

The baseline information, including demographic data (age and gender), medical history (diabetes mellitus, UTI and history of catheter-related infection), catheter-related information (type and location of catheter placement, time from catheter insertion), laboratory data [hemoglobin, ferritin, serum iron, phosphorus, and albumin, erythrocyte sedimentation rate (ESR), C-reactive protein (CRP) and total iron-binding capacity (TIBC)], urinary anomaly such as stenosis of the ureter to the pelvis, stenosis of the ureter to the bladder and urinary manipulation such as nephrostomy, Double J, and Foley catheter were retrieved from the patients' recorded files.

Statistical analysis

SPSS (version 26, SPSS Inc., Chicago, IL, USA) was used for statistical analysis. Qualitative variables were analyzed by chi-square and quantitative ones conducted by t test, respectively. Additionally, P values less than 0.05 were considered statistically significant.

Results

In this study, 64 patients with catheter infection with gram-negative bacteria and 64 patients with catheter infection with gram-positive bacteria were included in the study. The mean of age in the two groups of gram-negative and positive was 55 ± 16 and 58 ± 18 years, respectively), which was not statistically significant ($P = 0.425$). Among these patients, the most of patients in both groups with gram-negative (62.5%) and positive (59.4%) infections were men; however there was no significant difference between the two groups ($P = 0.717$).

In terms of hemoglobin, serum levels of phosphorus, iron, ferritin, CRP, ESR, there was no difference between the two groups ($P > 0.05$).

Although in the gram-positive group diabetes was more common than the gram-negative group, this difference was not statistically significant ($P = 0.273$). There was no relationship between catheter location and gram-negative and positive infection ($P = 0.958$). The mean duration of catheterization in the gram-negative group was 6.9 ± 8.4 months and in the gram-positive group was 7.2 ± 7.8 months, which was not significant between the two groups ($P = 0.811$; Table 1).

Serum albumin was lower in the gram-negative group than in the gram-positive group (3.7 ± 0.5 g/dL in gram-negative group and 3.9 ± 0.5 g/dL in gram-positive group), which was statistically significant ($P = 0.009$; Table 1 and Figure 1).

Regression analysis shows that, for every unit increase in albumin, the chance of developing a gram-negative catheter infection is 0.356, or about one-third. In other words, with decreasing each unit of albumin, the chance of a gram-negative catheter infection is 2.8 times (reverse 0.356).

Table 1. Logistic regression analysis of albumin based on 95% C.I. For EXP (B)

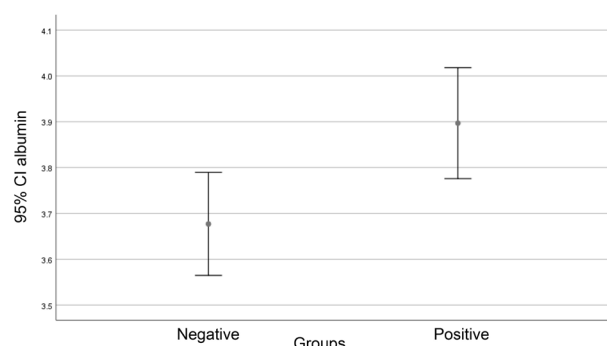|	P value	Exp (B)	95% CI Lower	95% CI Upper
Albumin	0.011	0.356	0.160	0.792

Figure 1. Serum albumin in patients with gram-negative and gram-positive infection of dialysis catheter.

The incidence of UTI was higher in the gram-negative group (23.4 % in the gram-negative group and 7.8 % in the gram-positive group) and this difference was statistically significant ($P=0.015$; Table 2 and Figure 2).

We examined patients for urinary manipulations including Double J, stent, nephrostomy and urinary system abnormalities such as stenosis of the ureter to the pelvis, stenosis of the ureter to the bladder, and the presence of a Foley catheter.

On patient ultrasound, we came across a common incidental finding: simple cortical cysts of the kidney, which were higher in the gram-positive group.

Fourteen (21.9%) gram-positive people had simple renal cortical cysts, while seven (10.9%) gram-negative people had it; however, this difference was not statistically significant ($P=0.095$; Table 1).

Among the four factors of TIBC, albumin, UTI, and urinary tract abnormalities that had a P value less than 0.2, in 2 cases, we found a significant relationship between gram-negative and gram-positive infections (UTI and decreased serum albumin levels) and in both cases, the only albumin was associated with the type of catheter infection (Nagelkerke's $R^2 = 0.071$ and $P=0.008$; logistic regression).

Organisms

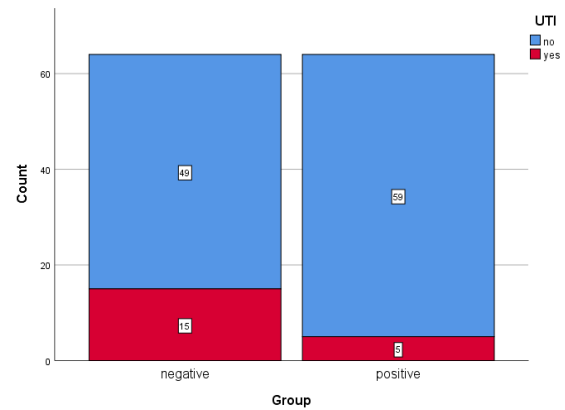Among the gram-positive bacteria, the most common

Figure 2. UTI in patients with gram-negative and gram-positive infection of dialysis.

bacteria were *Staphylococcus epidermidis* (34 cases; 53.1%). The second most common bacteria were *Staphylococcus aureus* (28 cases) (43.8%; Figure 3).

Among patients with a gram-positive infection, there were 34 cases (53.1%) of *S. epidermidis*. Among these patients, 29 (85%) *S. epidermidis* were methicillin-sensitive and five (15%) were methicillin-resistant. There were 28 cases (43.8%) of *S. aureus*. Among these patients, 27 patients (97%) were methicillin-sensitive *S. aureus* and one (3%) methicillin-resistant *S. aureus*.

Table 2. The baseline characteristics and clinical data in groups with gram-negative bacteria catheter infection and gram-positive bacteria catheter infection

Characteristics	Groups with gram-negative catheter infection	Groups with gram-positive catheter infection	P value
Age(year)	55 ± 16	58 ±18	0.425
Male gender, No. (%)	40 (62.5 %)	38 (59.4 %)	0.717
Diabetes, No. (%)	21 (32.8 %)	27 (42.2 %)	0.273
Catheter location, No. (%)			0.958
Jugular	52 (81.3 %)	51 (79.7 %)	
Subclavian	6 (9.4 %)	6 (9.4 %)	
Femoral	6 (9.4 %)	7 (10.9 %)	
Catheter duration (month)	6.9 ± 4.8	7.2 ± 8.7	0.811
History of catheter infection, No. (%)	12 (18.8 %)	10 (15.6 %)	0.639
UTI, No. (%)	15 (23.4 %)	5 (7.8 %)	0.015
History of UTI, No. (%)	6 (9.4 %)	7 (10.9 %)	0.770
Hemoglobin (g/dL)	10.1 ± 2	9.9 ± 2.1	0.608
Iron (mcg/dL)	32 ± 40	43 ± 68	0.276
Ferritin (ng /mL)	447 ± 306	481 ± 623	0.699
TIBC (mcg/dL)	227 ± 58	441 ± 58	0.184
Albumin (g/dL)	3.7 ± 0.5	3.9 ± 0.5	0.009
Phosphorus (mg/dL)	4.1 ± 1.4	4.3 ± 1.8	0.585
ESR (mm/h)	59 ± 35	55 ± 26	0.494
CRP (mg/L)	36.9 ± 29.7	36.8 ± 28.4	0.984
Urinary anomaly, No. (%)	7 (10.9%)	14 (21.9 %)	0.095
Foley catheter, No. (%)	5 (7.8 %)	3 (4.7 %)	0.465
Double J, No. (%)	3 (4.7 %)	1 (1.6 %)	0.310
Renal stone, No. (%)	5 (7.8 %)	5 (7.8 %)	0.999

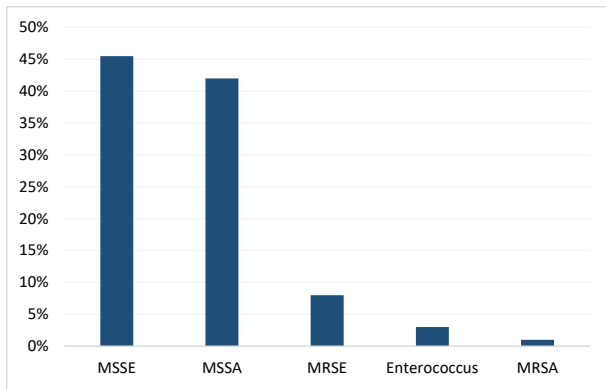UTI, Urinary tract infection, TIBC, total iron-binding capacity.

Figure 3. Prevalence of various organisms in people with catheter infection with gram-positive bacteria. MSSE, methicillin sensitive *Staphylococcus epidermidis*; MSSA, methicillin sensitive *Staphylococcus aureus*; MRSE, methicillin-resistant *Staphylococcus epidermidis*; MRSA, methicillin-resistant *Staphylococcus aureus*.

Among gram-negative bacteria, the most common bacteria were *Klebsiella* (28 cases) (43.8 %). The second most common bacteria were *Pseudomonas aeruginosa* (18 cases) (28.1 %; (Figure 4).

Discussion

Catheters are often used as access for dialysis; however, the infectious complications resulting from it remain a major clinical problem. In particular, the mortality rate and the cost of general care for catheter-induced bloodstream infections and hospitalization are among the issues that highlight the importance of further studies in this area (1).

Gram-positive organisms are responsible for most catheter infections. Staph coagulase-negative and *S. aureus* infections are reported to be the cause of 40% to 81% of infections. Other infections are attributed to enterococci and gram-negative categories (10-12). However, it seems that in the last years, the prevalence of catheter infections has shifted from gram-positive bacteria to negative bacteria, which may be due to UTIs and urinary tract abnormalities (13-15).

This study aimed to investigate the risk factors for catheter-related infections caused by gram-negative bacteria in hemodialysis patients so that if their risk factors are identified, we can prevent catheter infections, which are unfortunately abundant.

Among the possible risk factors, we examined the following:

Age, gender, serum hemoglobin, serum iron, ferritin, albumin, phosphorus, CRP, ESR, TIBC, presence of diabetes, UTI, history of UTI, location of the catheter, duration of the catheter, urinary manipulations including Double J, stent, nephrostomy urinary system abnormalities such as stenosis of the ureter to the pelvis, stenosis of the ureter to the bladder and the presence of a Foley catheter.

Around 64 patients with catheter infection with gram-negative bacteria and 64 patients with catheter infection with gram-positive bacteria were included in the study.

The mean (standard deviation) of age in the two groups of gram-negative and positive was 55 ± 16 and 58 ± 18 years, respectively, which was not significant ($P = 0.425$; Table 1).

Among these patients, the most of patients in both groups with gram-negative (62.5%) and positive (59.4%) infections were men; however, there was no significant difference between the two groups. ($P = 0.717$; Table 1)

Regarding hemoglobin, serum levels of phosphorus, iron, ferritin, CRP, ESR, there was no difference between the two groups (Table 1).

In some studies, lower hemoglobin levels and higher phosphorus levels were associated with catheter infection. In our study, the hemoglobin level was lower in the gram-positive group; however, there was no statistically significant relationship between the two groups ($P = 0.608$; Tables 1).

Although the serum level of phosphorus was higher in the gram-positive group, in this case, there was no
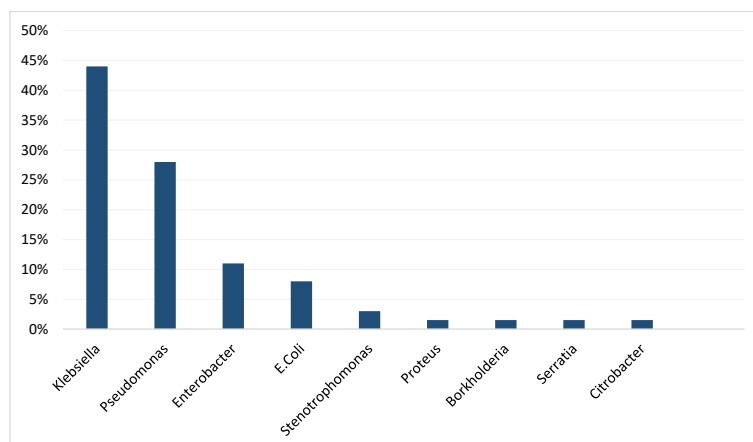

Figure 4. Prevalence of various organisms in people with catheter infection with gram-negative bacteria.

significant relationship ($P=0.585$; Table 1).

In some studies, diabetes was more common in people with catheter infections. In our study, gram-positive had more diabetes than gram-negatives, but this difference was not statistically significant ($P=0.273$; Table 1).

Although in previous studies, catheter implantation in the internal jugular was less associated with infection; however, recent studies have shown that there is no difference in the risk of infection in the three jugular, subclavian and femoral sites (16). In our study, there was no significant relationship between catheter location and infection with gram-negative and gram-positive bacteria ($P=0.958$; Table 1)

The most important risk factor for catheter infection is the duration of catheter use (8) the mean duration of the catheter in the gram-negative group was 6.9 ± 4.8 months and in the gram-positive group was 7.2 ± 7.8 months. There was no significant difference between gram-negative bacteria and gram-positive bacteria ($P=0.811$; Table 1).

Some studies have linked decreased serum albumin level to catheter infection. In our study, serum albumin was lower in the gram-negative group than in the gram-positive group (3.7 ± 0.5 g/dL in the gram-negative group and 3.9 ± 0.5 g/dL in the gram-positive group), which was statistically significant ($P=0.009$; Table 1 and Figure 1).

Regression analysis shows that for every unit increase in albumin, the chance of developing a gram-negative catheter infection is 0.356, or about one-third. In other words, with decreasing each unit of albumin, the chance of a gram-negative catheter infection is 2.8 times (reverse 0.356). Although a significant relationship was found between low albumin levels and gram-negative bacterial catheter infection, whether hypoalbuminemia treatment reduces the chances of catheter infection requires an interventional study.

We also examined the presence of concomitant UTI and its association with catheter infection. Our initial guess was that one of the possible causes of catheter infection with gram-negative bacteria was the coexistence of UTI, which was confirmed in the final study because the incidence of UTI was significantly higher in the gram-negative group (23.4 % in gram-negative group and 7.8 % in gram-positive group) and this difference was statistically significant ($P=0.015$; Table 1 and Figure 2). We examined patients for urinary manipulations including Double J, stent, nephrostomy and urinary system abnormalities such as stenosis of the ureter to the pelvis, stenosis of the ureter to the bladder, and the presence of a Foley catheter.

On patient ultrasound, we came across a common incidental finding: simple cortical cysts of the kidney, which were higher in the gram-positive group.

Fourteen (21.9%) gram-positive people had simple renal cortical cysts, while seven (10.9%) gram-negative people had it, but this difference was not statistically significant ($P=0.095$; Table 1).

Since no significant difference in issues such as catheter location or duration of catheter and tests such as serum levels of phosphorus, iron, ferritin, or inflammatory markers (ESR and CRP) between the positive and gram-negative groups was detected, we could not use these elements to predict the type of catheter infection, and therefore the above will have no diagnostic or predictive value.

On the other hand, both decreased serum albumin levels and UTIs were associated with the type of catheter infection (gram-negative and gram-positive). This clinically important point can be used to reduce the risk of catheter infection with gram-negative bacteria and to predict the type of catheter infection, and therefore the above will be of diagnostic or predictive value.

Although a significant relationship was found between low-albumin levels and gram-negative bacterial catheter infection, whether hypoalbuminemia treatment reduces the chances of catheter infection requires an interventional study.

Conclusion

Serum albumin levels were significantly lower in the gram-negative group and UTIs were significantly higher in this group. It is, therefore, necessary to consider hypoalbuminemia and UTI as risk factors for catheter infection with gram-negative bacteria.

Limitations of the study

One of the limitations of our study was the small number of samples. To solve this problem, it is recommended to do studies with higher sample size or multicenter studies. In other words, the existence of a coordinated data registration system in similar centers of this center will help to achieve a higher sample size and multi-centralization of similar projects in the future. Another limitation was the limited number of tests. It can also be evaluated other laboratory variables that have not been studied in this study and may be involved in catheter infection can also be considered. Another limitation was the Lack of interventions. Therapeutic interventions can be performed to investigate the role of lowering serum albumin levels.

Authors' contribution

TM, MZ and AK were the principal investigators of the study. TM and MZ were included in preparing the concept and design. MZ and AK revisited the manuscript and critically evaluated the intellectual contents. All authors participated in preparing the final draft of the manuscript, revised the manuscript and critically evaluated the intellectual contents. All authors have read and approved the content of the manuscript and confirmed the accuracy or integrity of any part of the work.

Conflicts of interest

The authors declare that they have no competing interests.

Ethical issues

The research followed the tenets of the Declaration of Helsinki. The Ethics Committee of Iran University of Medical Sciences approved this study. The institutional ethical committee at Iran University of Medical Sciences approved all study protocols (IR.IUMS.FMD. REC.1399.001). Accordingly, written informed consent was taken from all participants before any intervention. This study was extracted from the nephrology fellowship thesis of Mehdi Zahmatkesh at this university (Thesis #17391). In addition, ethical issues (including plagiarism, data fabrication, double publication) have been completely observed by the authors.

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