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ORIGINAL ARTICLE

Multi-drug Resistant Catheter-related Infection Is a Common Culture Finding and Infective Endocarditis is associated with Delayed recovery and Mortality

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ABSTRACT

Background: *The second most common cause of mortality in dialysis patients is infection, and using a central venous catheter for haemodialysis is linked to higher infection rates.* ***Objective:*** *This study assessed the bacterial spectrum of hemodialysis catheter-related infection and its relation to patients' outcomes.* ***Methodology:*** *A prospective study included 57 hemodialysis patients with catheter-related infections excluding Patients with evident sepsis by other causes.* ***Results:*** *The most common organisms were multidrug-resistant (MDR) Enterobacteriaceae and Staphylococci at 40.4% (23 patients) while drug-sensitive Staphylococci and Enterobacteriaceae were at 35.1% (20 patients) and 24.6% (14 patients) respectively. The prevalence of Infective endocarditis (IEC), septic emboli, and mortality were 10.5% (6 patients), 7.0% (4 patients), and 8.8% (5 patients) respectively. The duration of more than 55 days of catheter insertion was associated with risk 13 times to get IEC (odds ratio: 13.214). The median time for recovery was 7 (7 – 15) days, and there was a significant difference as regards time for recovery between MDR, Staphylococci, and Enterobacteriaceae P-value (0.020). Post-hoc analysis showed a significantly longer time for recovery in MDR versus Enterobacteriaceae and Staphylococci P-value 0.013 & 0.030 respectively while no significant difference between Enterobacteriaceae and Staphylococci P-value 0.804. The period of recovery in patients with temporary catheters was positively correlated with CRP (r 0.840, p 0.036).* ***Conclusion:*** *Multidrug-resistant Catheter-related infection is a common culture finding. IEC and MDR organisms are associated with delayed recovery, moreover IEC was associated with a high mortality rate.*

INTRODUCTION

A functional vascular access (VA) is essential to carrying out an effective HD operation[1]. The second most common cause of mortality for dialysis patients is infection. When compared to alternative forms of vascular access, the haemodialysis (HD) central venous catheter (CVC) is linked to higher infection rates. According to current standards, it is strongly advised to prioritize AVF and save CVC for last resort. The prevalence of CVC is over 20% in many countries[2].

Exit-site, tunnel, and catheter-related bloodstream infections are the three different categories of CVC-related infections. One of the leading causes of hospitalization and death among haemodialysis patients is CRBSIs[3]. Up to 80% of CRBSIs are caused by gram-positive bacteria, including coagulase-negative staphylococci and Staphylococcus aureus. Gram-negative bacteria, such as Klebsiellapneumoniae, Escherichia coli, and Pseudomonas aeruginosa, are responsible for other illnesses[4].

Antimicrobial resistance exhibited by a type of microbe to at least one antimicrobial treatment in three or more antimicrobial categories is known as multiple drug resistance (MDR)[5]. Infections caused by multi-resistant organisms are associated with substantial morbidity and mortality[6]. Metastatic infections include endocarditis, osteomyelitis, spinal epidural abscess, septic arthritis, brain abscess, and septic pulmonary emboli[7].

The preventive strategies against CRBSIs are crucial and managing modifiable risk factors is highly warranted. Among concerns are low haemoglobin, a history of prior catheter-related bacteremia, low serum albumin levels linked to bloodstream infections, and an extended length of CVC[8]. That's why this study assessed the bacterial spectrum of dialysis catheter-related infection and its relation to patients' outcomes.

METHODOLOGY

A prospective cohort study was done during six months from June 2023 to 1st of January 2024. Patients were selected from Ain Shams University HD units.All patients who participated in this study have given a written informed consent. The ethical approval was obtained from the ethical committee of our Faculty of Medicine Ain Shams University before the study began, and the procedures used in this study adhere to the tenets of the Helsinki Declarations.Ethical committee approval no. FMASU M S 631/2022 on 27/9/2022.

This study examined 5٧ adult hemodialysis patients with catheter-related infections. Inclusion criteria were all Patients aged 18-70 years and patients on hemodialysis through double-way venous catheter. Exclusion criteria were patients with sepsis evident by other causesof infection.

All patients were subjected to Full history taking and clinical examination including etiology of end-stage renal disease (ESRD), duration of HD and dialysis prescription, other co-morbidities and duration of catheter insertion, duration of infection, symptoms of infection, and complication of infection. Complete blood count, chemistry (BUN, Creatinine, Na, K, Total protein, Albumin, ALT, AST, calcium, and phosphorus), urea reduction ratio, C-reactive protein, and Culture of the tip of the hemodialysis catheter and blood culture from a peripheral vein.

Gram positive and gram negative bacteria were isolated and identified from cultures were tested for drug sensitivity to the following antibiotics: **penicillin** (amoxicillin /clavulanic acid, piperacillin/ tazobactum), **carbepenem** (meropenem), **vancomycin, linzolide, cephalosporin** (cefoxitin, cefotaxime, ceftrixoneceftazidme, cefepime) **fluorinated quinolones** (ciprofloxacin, levofloxacin) **aminoglycosides** (tobramycin, gentamycin, amikacin).

All patients were followed for six weeks either for recovery or developing complications such as septicemia, endocarditis, septic emboli, and death.

Diagnosis catheter-related infections:

Clinical symptoms and at least one positive blood culture from a peripheral source (dialysis circuit or vein) with no other apparent source are required to confirm the diagnosis of CVC infection. This can be either a positive semi-quantitative (>15 CFU/catheter segment, hub or tip) or quantitative (>102 CFU/catheter segment, e.g., hub or tip) culture, in which the same organism (species and antibiogram) is isolated from the catheter segment (e.g. hub or tip) and a peripheral source (dialysis circuit or vein) blood sample (KDOQI guidelines 2019).

Statistic evaluation:

Statistical analysis Data were collected, revised, coded, and entered into the statistical package for the social science, version 20 (SPSS Inc., Chicago, Illinois, USA). While quantitative data were displayed as a mean with standard deviation (SD) for parametric data or a median with interquartile ranges (IQR) for nonparametric data, qualitative data were displayed as numbers and percentages. Comparison between two groups with qualitative data was done by using the $\chi 2$ Test. Comparison between two groups with quantitative data was done by a two-tailed independent t-test when the distribution of the data was found parametric. Mann–Whitney test was used with the nonparametric data andAnova test for 3 variables followed by post-hoc analysis. The Spearman test was used for correlation.

The P value was considered significant as follows:

P>0.05: non-significant.

P<0.05: significant.

P<0.01: highly significant.

RESULTS

The demographic data for patients with CVC-related infection was displayed in (Table 1). The mean age was 48.0±15.1 years, most of the patients were females 52.6% (30 cases) and males 47.4% (27 cases) and the most common comorbidities were hypertension and diabetes with prevalence of 71.9% & 43.9% respectively.The most common prevalent culture finding was multidrug-resistant (MDR) at 40.4% (23 patients) while Staphylococciand Enterobacteriaceae were at 35.1% (20 patients) and 24.6% (14 patients) respectively (Figure 1).

Table (1): Comparison between temporary and permeant catheters as regards demographic data, co-morbidities, and laboratory data

	Type of catheter		P-value	Sig.
	Permanent	Temporary		
	No. = 18	No. = 39		
	N (%)	N (%)	*	
Female	10 (55.6%)	20 (51.3%)	0.764	NS
Male	8 (44.4%)	19 (48.7%)		
Femoral	7 (38.9%)	1 (2.6%)	0.000	HS
Jugular	11 (61.1%)	38 (97.4%)		
DM	11 (61.1%)	14 (35.9%)	0.075	NS
HTN	14 (77.8%)	27 (69.2%)	0.504	NS
ISHD	9 (50.0%)	6 (15.4%)	0.006	HS
	Mean±SD	Mean±SD	•	
Age (years)	52.00 ± 11.34	46.13 ± 16.32	0.174	NS
HB (g/dl)	8.13 ± 2.42	8.34 ± 4.46	0.856	NS
Urea reduction ratio %	35.04 ± 13.82	32.72 ± 14.85	0.576	NS
Creatinine (mg/dl)	8.59 ± 4.14	8.64 ± 2.18	0.948	NS
Na (mmol/l)	134.22 ± 4.48	132.31 ± 21.08	0.705	NS
Po4 (mg/dl)	4.17 ± 1.86	5.52 ± 1.96	0.017	NS
Albumin (gm/dl)	3.09 ± 0.52	3.03 ± 0.44	0.620	NS
Total protein (g/dl)	6.33 ± 0.62	6.29 ± 0.78	0.848	NS
	Median(IQR)	Median(IQR)	‡	
WBC (*10^3/uL)	12.8 (6.7 – 21.3)	12.2 (7.4 – 19)	0.925	NS
PLT(*10^3/uL)	179 (98 – 254)	177 (150 – 250)	0.525	NS
Crp on admission	184.5 (138 – 238)	144 (90 – 195)	0.183	NS
Crp on discharge	44.5 (25 – 70)	45 (25 – 70)	0.986	NS
K (mmol/l)	5 (4.4 – 5.8)	4.9 (4.5 – 5.3)	0.763	NS
Ca(mg/dl)	8.85 (8 – 9.1)	8.3 (7.7 – 9)	0.141	NS
AST(U/L)	24 (14 – 26)	15 (12 – 24)	0.135	NS
ALT(U/L)	15 (9 – 24)	14 (9 – 19)	0.502	NS
Duration of insertion in days	60 (40 – 90)	45 (30 – 45)	0.001	HS
Frequency of insertion	3 (2 – 4)	2 (1 – 3)	0.005	HS
Recovery period in days	15 (7 – 15)	7 (7 – 7)	0.009	HS

*:Chi-square test ; •: Independent t-test; ‡: Mann Whitney test.

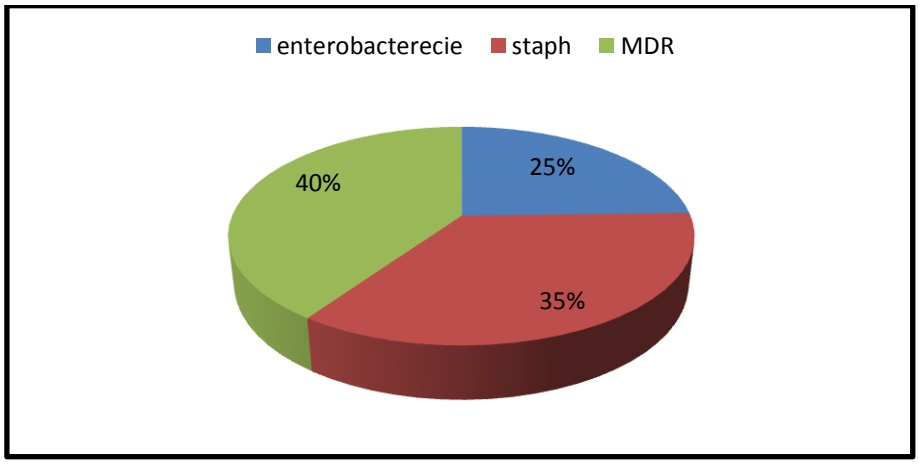

Fig. 1: Bacterial spectrum of catheter-related infection of the studied patients.

The duration of more than 55 days of catheter insertion was associated with risk 13 times to get IEC (odds ratio: 13.214) (Table 2). The prevalence of Infective endocarditis (IEC), septic emboli, and mortality were 10.5% (6 patients), 7.0% (4 patients), and 8.8% (5 patients) respectively (Figure 2).

Table 2: Logistic regression analysis for predictors of IEC

	Uni-variety				Multi-variety			
	P-value	Odds ratio (OR)	95% C.I. for OR		P-value	Odds ratio (OR)	95% C.I. for OR	
			Lower	Upper			Lower	Upper
Duration in days>55	0.023	13.214	1.416	123.307	0.023	13.214	1.416	123.307

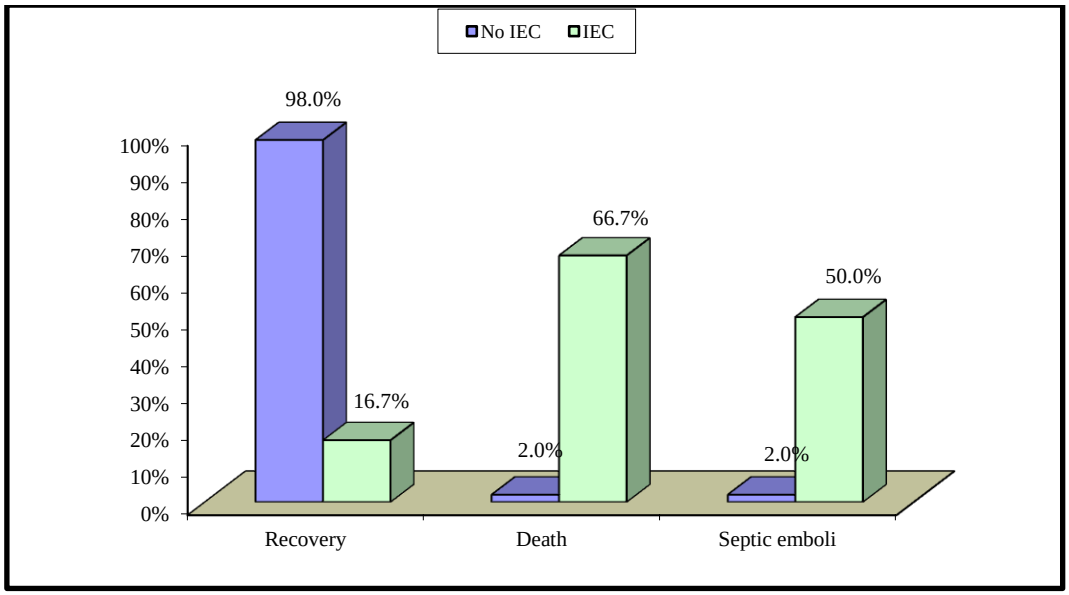

Fig. 2: Effect of IEC on infection outcome

The median time for recovery was 7 (7 – 15) days. The Patients with IEC have a long duration of access insertion compared to a negative P-value of 0.030. There was a significant difference as regards time for recovery between MDR, Staph, and Enterobacteriaceae P value (0.020). Post hoc analysis showed a significantly longer time for recovery in MDR versus Enterobacteriaceae and StaphylococciP-value 0.013 & 0.030 respectively while no significant difference between Enterobacteriaceae and StaphylococciP-value 0.804 (Table 3). Also, patients with permanent catheters had a longer time for recovery compared to temporary catheter P-value (0.009). The period of recovery in the patients with temporary catheters had positive correlation with K, PO4, and CRP (r 0.828 p 0.042) (r 0.840 p 0.036) (r 0.840 p 0.036) respectively.

Table (3): Comparison according to culture findings as regards demographic data, comorbidities and laboratory data, and infection outcome.

	Bacterial Spectrum			P-value	Sig.
	Enterobacteriaceae	MDR	Staph		
	No. = 14	No. = 23	No. = 20		
	N (%)	N (%)	N (%)	*	
Female	5 (35.7%)	12 (52.2%)	13 (65.0%)	0.242	NS
Male	9 (64.3%)	11 (47.8%)	7 (35.0%)		
Permanent	3 (21.4%)	10 (43.5%)	5 (25.0%)	0.276	NS
Temporary	11 (78.6%)	13 (56.5%)	15 (75.0%)		
Femoral	2 (14.3%)	5 (21.7%)	1 (5.0%)	0.289	NS
Jugular	12 (85.7%)	18 (78.3%)	19 (95.0%)		
DM	7 (50.0%)	8 (34.8%)	10 (50.0%)	0.525	NS
HTN	9 (64.3%)	18 (78.3%)	14 (70.0%)	0.638	NS
ISHD	3 (21.4%)	7 (30.4%)	5 (25.0%)	0.822	NS
	Mean±SD	**Mean±SD**	**Mean±SD**	•	
Age (years)	43.71 ± 16.31	49.48 ± 15.28	49.25 ± 14.14	0.483	NS
HB (g/dl)	8.07 ± 1.68	7.40 ± 1.42	9.42 ± 6.20	0.237	NS
URR (%)	30.99 ± 13.28	36.65 ± 16.55	31.50 ± 12.52	0.394	NS
Creatinine (mg/dl)	8.68 ± 2.61	8.48 ± 3.81	8.76 ± 1.84	0.953	NS
Albumin (g/dl)	2.96 ± 0.40	3.08 ± 0.41	3.08 ± 0.56	0.739	NS
	Median(IQR)	**Median(IQR)**	**Median(IQR)**	‡	
Insertion Duration(days)	45 (30 – 50)	45 (30 – 60)	45 (30 – 60)	0.755	NS
Frequency of insertion	2 (2 – 3)	3 (1 – 4)	2 (1.5 – 3)	0.435	NS
WBC(*10^3 /uL)	10.55 (7.9 – 17)	9.8 (5.9 – 21)	15.85 (8.3 – 20)	0.640	NS
Crp on admission (mg/l)	149 (118 – 200)	180 (104 – 238)	145 (78 – 191.5)	0.414	NS
Crp on discharge (mg/l)	50 (36 – 60)	35 (22 – 55)	55.5 (25 – 88.5)	0.252	NS
Outcome of infection					
Recovery	14 (100.0%)	19 (82.6%)	18 (90.0%)	0.246	NS
Death	0 (0.0%)	4 (17.4%)	1 (5.0%)	0.147	NS
IEC	0 (0.0%)	3 (13.0%)	3 (15.0%)	0.328	NS
Septic emboli	0 (0.0%)	2 (8.7%)	2 (10.0%)	0.490	NS
Recovery period (days) Median(IQR) Range	7 (7 – 7) 0 – 15	15 (7 – 15) 0 – 30	7 (7 – 7) 0 – 30	0.020	S
	Post Hoc analysis ofthe Recovery period				
	Enterobacteriaceae Vs MDR	**Enterobacteriaceae Vs staph**		**MDR Vs Staph**	
	0.013	0.804		**0.030**	

*:Chi-square test ; •: Independent t-test; ‡: Mann Whitney test

DISCUSSION

Patients receiving haemodialysis in all centers are susceptible to CRBSIs because of immunological dysfunction and repeated exposure to a medical setting[9]. The primary risk factor for bacteremia in HD is the use of a CVC. In more than 10% of patients, bacteremia can lead to potentially fatal consequences such septic shock, endocarditis, septic arthritis, osteomyelitis, and epidural abscesses. Compared to patients with AVF or vascular grafts, patients utilizing CVC have a 2-3 times higher relative risk of hospitalization for infection and mortality, which results in higher health care costs[10]. To determine whether there are any variations from other dialysis patient populations worldwide, an audit of the causal organisms in CRBSI in haemodialysis patients and their distribution pattern with respect to gender, age, and comorbidities in a particular community is necessary[11]. This study evaluated the bacterial spectrum of hemodialysis catheter-related infection and its relation to patient outcome.

In our study, the patient's mean age was 48.0±15.1 and most of the patients were females 52.6% and males 47.4% and the most common comorbidities were hypertension and diabetes with the prevalence of 71.9% & 43.9% respectively. This is in line with Nanyunja et al.[12] study that showed the mean age was 50±14.9 years and Diabetes mellitus was the most common comorbidity but

most of the patients were males [n=76 (62.8%)]. Patil&Mulay,[13] study, using multivariate analysis, hypertension was found to be independently linked to an elevated risk of infection[13].

Catheter tips were cultured in our study after the catheter was taken out. Similar to blood and swab cultures, many bacterial pathogens that commonly affect this population (such as Staphylococcus aureus, Enterococcus species, and the Enterobacteriaceae, which includes E. coli and Klebsiella species) are showing signs of antibiotic resistance.MDR organisms are the most common spectrum with a prevalence of 40% of the studied cases followed by gram-positive and gram-negative organisms with a prevalence of 35.1%, and 24.6% respectively. In addition, MDR has a delayed time to recovery compared to other spectra with a P value of 0.02. This was in contrast to a research by Pop-Vicas et al.[14] that found that 28% of patients had one or more multidrug-resistant organisms (MDROs) colonized in serial surveillance cultures taken from patients receiving ambulatory haemodialysis. A study conducted in 2017 byMohsin[11]revealed that 38.5% of the cases under investigation were caused by Gram-positive germs, whereas 61.5% were caused by Gram-negative microbes and Parameswaran et al.[15]found that 36% of the bacteria causing CRBSI were Gram-negative, whereas 64% of the pathogens were Gram-positive.

In our study, there was a significant difference as regards time for recovery between MDR, Staph, and Enterobacteriaceae P value (0.020). Post hoc analysis showed a significantly longer time for recovery in MDR versus Enterobacteriaceae and StaphylococciP-value 0.013 &0.030 respectively while no significant difference between Enterobacteriaceae and StaphylococciP-value 0.804. This was in line with a research by Amanati et al.[16]that shown that MDR bacterial infections, especially those caused by MDR Enterobacterales like Enterobacter cloacae, are frequently refractory since there are few antibiotic treatment choices available.

Temporary catheters were used more frequently than permanent ones in our study (68.4% versus 31.6%), and the jugular vein was used more frequently than the femoral vein (86% versus 14%, respectively). These findings were in line with a study by Sedhain et al.[17] that found that the right internal jugular vein was the most frequently used site for CVC insertion (77.94%), followed by the femoral vein (19.86%) and the left internal jugular vein (2.2%). The femoral vein (43.9%) was the most common insertion location in the Chin et al.[18] research, followed by the subclavian (33.3%) and jugular (22.0%) veins.

Prolonged CVC catheter use (>30 days), longer insertion times, and longer recovery times for patients with permanent catheters compared to those with temporary catheters were the study's major risk factors for the development of catheter-related infection (P-values 0.001, 0.009).

This was consistent with a research by Iqbal et al.[19] that found that bloodstream infections were the most prevalent kind of infection (68.4%) in people who had used a double lumen catheter (DLC) for more than 14 days. In patients taking DLC for more than 14 days, the incidence of infection was correlated with the length of use (p14 days was 1.92, 95% CI 1.11-33.30), according to the findings of statistical testing. Additionally, this was consistent with a research by Weldentensae et al.[20] that found individuals who had a catheter stay of fewer than 30 days had a lower risk of developing CRBSI than those who stayed for more than 30 days (OR:0.3, CI 95%: 0.18-0.5, P<0.001). This was also in line with a study by Demirci et al.[21]that found that patients with CRBSI had a significantly longer catheter duration than those without (254 days vs. 166, p=0.001), and that a 22-day catheter duration was predictive of CRBSI development with a 78% sensitivity and a 76% specificity (AUC: 0.825, 95% CI: 0.724–0.925, p0.001).

The duration of more than 55 days of catheter insertion was associated with risk 13 times to get IEC (odds ratio: 13.214). The Patients with IEC have a long duration of access insertion compared to a negative P-value of 0.030. The median time for recovery was 7 (7 – 15) days. No available study to compare with.

In patients who had temporary catheters, the recovery time was positively linked with K, PO4, and CRP (r 0.828 p 0.042, r 0.840 p 0.036, and r 0.840 p 0.036, respectively). Delistefani et al.'s[22] study, which found a weak positive association between the length of hospital stay and the first CRP levels (r=0.23, p=0.004), was consistent with findings.

In this research, CRBSI outcomes included Infective endocarditis (IEC), septic emboli, and mortality were 10.5% (6 patients), 7.0% (4 patients), and 8.8% (5 patients) respectively compared to recovered cases 89.9% and there was significant statistical difference as regard outcome (IEC, septic emboli) compared to surviving patients P-value 0.001 and patients with IEC has highly significant difference regarding delayed recovery, septic emboli, mortality compared to patients without IEC, P-value (0.001, 0.001,0.001) respectively and In line with the findings of the Hajji et al.[23]study, in which IEC was the primary infection complication in this study (14 percent), 13 patients were diagnosed with infection complications (26%), which included IEC in 7 cases, septic arthritis in 3 cases, infective myositis in 1 case, cerebral thrombophlebitis in 1 case, and mediastinitis in 1 case. Additionally, consistent with the findings of the Gallacher et al.[24] study, which shown that IE had poor results for ESKD patients on chronic dialysis. These individuals had a three-year death rate of 33% and a survival rate of only 56.9%.

CONCLUSION

Multidrug-resistant Catheter-related infection is a common culture finding. IEC and MDR organisms are associated with delayed recovery moreover IEC was associated with high mortality. The limitation of this study is the small number of patients.

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Conflicts of interest

On behalf of all authors, the corresponding author states that there is no conflict of interest.

Author Contributions:

W.A., C.R., and N.T., formulation, interpretation, reading, manuscript writing, and final manuscript revision.

S.A.'s idea of the research, study design, formulation, interpretation, reading, manuscript writing, and final manuscript revision.

B.I. Data collection, sampling, clinical follow-up of patients, reading, and, manuscript writing. All authors read and approved the final manuscript.

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