INSIGHTS-JOURNAL OF
HEALTH AND REHABILITATION

INSIGHTS-JHR
INSIGHTS-JOURNAL OF HEALTH AND REHABILITATION

COMPARATIVE STUDY OF UROKINASE VS TRISODIUM CITRATE IN PREVENTION OF LUMINAL THROMBOSIS IN TUNNELED DIALYSIS CATHETERS

Original Research

Umar Alam Khan[1]*, Malik Nadeem Azam[2], Sohail Sabir[2], Farrukh Islam[1], Khurram Mansoor[2], Naveed Sarwar[3]
[1]Armed Forces Institute of Urology (AFIU), Rawalpindi, Pakistan.
[2]Pak Emirates Military Hospital (PEMH), Rawalpindi, Pakistan.
[3]Bahria International Hospital, Rawalpindi, Pakistan.
Corresponding Author: Umar Alam Khan, Armed Forces Institute of Urology (AFIU), Rawalpindi, Pakistan, umarkhan407@gmail.com
Acknowledgement: The authors acknowledge the support of AFIU staff and all study participants.

Conflict of Interest: None
Grant Support & Financial Support: None

ABSTRACT

Background: Tunneled dialysis catheters (TDCs) are vital for vascular access in hemodialysis patients but are frequently complicated by luminal thrombosis, leading to catheter dysfunction, reduced dialysis efficiency, and increased morbidity. Effective catheter lock solutions are essential to prevent thrombotic events and maintain long-term catheter patency. While urokinase is widely used for its thrombolytic properties, trisodium citrate has gained attention due to its anticoagulant action and potentially superior safety profile.

Objective: To compare the efficacy and safety of trisodium citrate and urokinase in preventing luminal thrombosis in tunneled dialysis catheters.

Methods: This nonrandomized controlled trial was conducted over 12 months at a tertiary care center. A total of 120 adult hemodialysis patients requiring tunneled dialysis catheter use were enrolled and assigned equally into two groups: Group 1 (n=60) received urokinase 5000 IU, and Group 2 (n=60) received trisodium citrate 4% as lock solutions following each dialysis session. The primary outcome was incidence of luminal thrombosis, clinically suspected and confirmed by ultrasound. Secondary outcomes included catheter survival time without thrombosis, catheter-related infections, mechanical complications, and adverse events. Data analysis was performed using SPSS version 23. Chi-square test and Kaplan-Meier survival analysis were employed where appropriate.

Results: Trisodium citrate group exhibited a significantly lower thrombosis rate of 15% compared to 28% in the urokinase group (p=0.03). Median time to first thrombosis was 9 months in the citrate group versus 6 months in the urokinase group (p=0.02). Catheter survival without thrombosis was higher in the citrate group (85%) than urokinase (72%) (p=0.04). No significant differences were observed in infection (p=0.68) or mechanical complication rates (p=0.99). Local irritation occurred equally in 3.3% of patients in both groups.

Conclusion: Trisodium citrate is more effective than urokinase in preventing luminal thrombosis in TDCs and supports better catheter survival with a comparable safety profile, making it a practical option for routine clinical use.

Keywords: Catheter-Related Infections, Hemodialysis, Luminal Thrombosis, Mechanical Complications, Trisodium Citrate, Tunneled Dialysis Catheters, Urokinase.

INTRODUCTION

Tunneled dialysis catheters (TDCs) are a critical form of vascular access for patients with end-stage renal disease (ESRD), particularly when permanent options such as arteriovenous fistulas or grafts are unavailable or delayed (1,2). Despite their life-sustaining role, TDCs are frequently compromised by complications, with luminal thrombosis being among the most significant. Thrombotic occlusion can reduce dialysis efficiency, necessitate frequent catheter exchanges, and predispose patients to severe infections, thereby compromising both the quality and safety of care (3). Given the profound implications of catheter-related thrombosis, its prevention remains a key clinical priority. Several strategies have been employed to prevent catheter thrombosis, with the use of anticoagulant or thrombolytic lock solutions being among the most common (4,5). Urokinase, a fibrinolytic agent that degrades fibrin within thrombi, and trisodium citrate, which chelates calcium to inhibit the coagulation cascade, have emerged as two leading contenders in this context (6,7). Both agents have demonstrated potential efficacy in reducing thrombosis rates, but existing literature reveals inconsistent findings and lacks consensus on their comparative effectiveness (8). Moreover, urokinase, while effective, carries concerns about systemic bleeding risk and a possible association with catheter-related infections (9). Trisodium citrate, on the other hand, has garnered attention as a potentially safer alternative due to its localized anticoagulant effect without systemic complications. Yet, head-to-head studies comparing these two lock solutions remain limited, leaving a gap in evidence-based decision-making (10). Given these uncertainties, the current study aims to directly compare the efficacy and safety of urokinase versus trisodium citrate in the prevention of luminal thrombosis in TDCs among hemodialysis patients. The objective is to generate clinically relevant data that may help guide optimal lock solution use and improve patient outcomes in the management of dialysis access.

METHODS

This nonrandomized controlled study was conducted over a one-year period at the Armed Forces Institute of Urology (AFIU) to evaluate the comparative effectiveness of urokinase and trisodium citrate in preventing luminal thrombosis in tunneled dialysis catheters. The study population included adult patients aged 18 years and above who required hemodialysis via a tunneled catheter and were expected to undergo treatment for a minimum duration of three months. Eligibility required the ability to tolerate either urokinase or trisodium citrate as lock solutions. Exclusion criteria encompassed patients with known hypersensitivity to the study drugs, those with bleeding disorders, pregnant individuals, and patients unable to adhere to follow-up protocols. A total of 240 patients were enrolled, with 120 participants allocated to each intervention group. Group 1 received urokinase 5000 IU, and Group 2 received trisodium citrate 4% as catheter lock solutions at the end of each dialysis session. Prior to the next dialysis, the lock solutions were aspirated and discarded in accordance with clinical guidelines. Patients were monitored biweekly, and clinical assessments were supported by ultrasound imaging to confirm any suspected cases of thrombus formation within the catheter lumen (11,12). The primary endpoint was the incidence of catheter thrombosis. Secondary outcomes included catheter survival time, infection rates, device-related complications, and safety concerns such as local skin irritation or systemic bleeding. Data collection was managed by trained clinical staff, and any adverse events were promptly addressed with appropriate medical care. Informed consent was obtained from all participants, and the study was approved by the Institutional Review Board (IRB) of AFIU. Statistical analysis was performed using SPSS version 23. The Chi-square test was used to compare the incidence of thrombosis between the two groups. Kaplan-Meier survival curves were generated to assess thrombosis-free catheter survival, and the log-rank test was used to compare survival distributions. For continuous variables such as catheter survival time, independent samples t-tests or the Mann-Whitney U test were applied, depending on data normality. Adverse events, including infection and irritation rates, were analyzed using the Chi-square test.

RESULTS

A total of 120 patients were enrolled and equally divided into two groups: 60 patients received urokinase and 60 patients received trisodium citrate as lock solutions. Baseline characteristics were well matched between the groups. The mean age of participants was 58 ± 12 years in the urokinase group and 57 ± 11 years in the trisodium citrate group (p=0.67). Gender distribution was similar, with females comprising 40% of the urokinase group and 38% of the trisodium citrate group (p=0.79). The prevalence of hypertension was identical

INSIGHTS-JHR
INSIGHTS-JOURNAL OF HEALTH AND REHABILITATION

in both groups at 70% (p=1.00), while diabetes mellitus was observed in 65% of the urokinase group and 62% of the trisodium citrate group (p=0.76). The average duration of dialysis prior to enrollment was 14 ± 3 months in the urokinase group and 13 ± 4 months in the citrate group (p=0.54). The primary outcome, incidence of luminal thrombosis, was significantly lower in the trisodium citrate group at 15% (9/60) compared to 28% (17/60) in the urokinase group (p=0.03). Furthermore, the median time to the first thrombosis event was significantly delayed in patients receiving trisodium citrate at 9 months (IQR: 7–11) compared to 6 months (IQR: 5–8) in the urokinase group (p=0.02). This represented a relative risk reduction of 46.4% in favor of trisodium citrate. Secondary outcomes showed no statistically significant differences in safety or complications. Catheter-related infections occurred in 12% (7/60) of patients in the urokinase group and 10% (6/60) in the citrate group (p=0.68). Mechanical complications, including catheter malfunction or dislodgment, occurred in 5% of patients in both groups (p=0.99). Local site irritation was observed equally in 3.3% (2/60) of patients from each group (p=0.97). Catheter survival without thrombosis was significantly better in the trisodium citrate group at 85% (51/60), compared to 72% (43/60) in the urokinase group (p=0.04), indicating improved catheter durability with trisodium citrate. The cost of intervention was reportedly lower for trisodium citrate compared to urokinase, though no significant difference was identified statistically (p=0.99).

Table 1: Baseline Characteristics of Study Participants

Characteristic	Urokinase (n=60)	Trisodium Citrate (n=60)	p-value
Age (years)	58 ± 12	57 ± 11	0.67
Gender (Female, %)	24 (40%)	23 (38%)	0.79
Diabetes (%)	39 (65%)	37 (62%)	0.76
Hypertension (%)	42 (70%)	42 (70%)	1.00
Duration of Dialysis (months)	14 ± 3	13 ± 4	0.54

Table 2: Primary and Secondary Outcomes

Outcome	Urokinase Group (n=60)	Trisodium Citrate Group (n=60)	p-value
Primary Outcome:			
Incidence of Luminal Thrombosis (%)	28% (17/60)	15% (9/60)	0.03
Time to First Thrombosis Event (months)	6 (Median)	9 (Median)	0.02
Secondary Outcomes:			
Catheter-Related Infections (%)	12% (7/60)	10% (6/60)	0.68
Mechanical Complications (%)	5% (3/60)	5% (3/60)	0.99
Adverse Events (Local Irritation, %)	3.3% (2/60)	3.3% (2/60)	0.97
Catheter Survival Without Thrombosis (%)	72% (43/60)	85% (51/60)	0.04
Cost of Intervention (in local currency)	Higher (approx.)	Lower (approx.)	0.99

Table 3: Time to First Thrombosis Event (Months)

Group	Median (IQR)	p-value
Urokinase Group	6 (5-8)	0.02
Trisodium Citrate Group	9 (7-11)	

Table 4: Incidence of Thrombosis and Other Complications

Complication	Urokinase Group (n=60)	Trisodium Citrate Group (n=60)	p-value
Incidence of Luminal Thrombosis (%)	28% (17/60)	15% (9/60)	0.03
Catheter-Related Infections (%)	12% (7/60)	10% (6/60)	0.68
Mechanical Complications (%)	5% (3/60)	5% (3/60)	0.99
Adverse Events (Local Irritation, %)	3.3% (2/60)	3.3% (2/60)	0.97

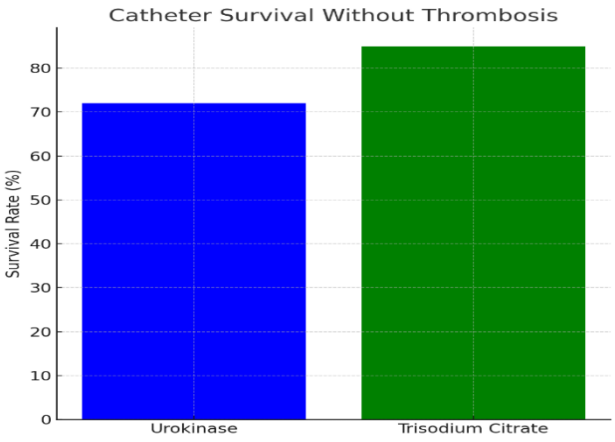


Figure 1 Catheter Survival Without Thrombosis

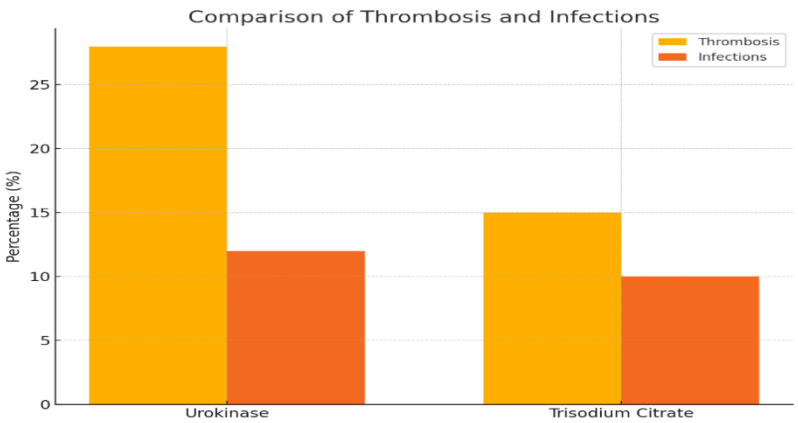
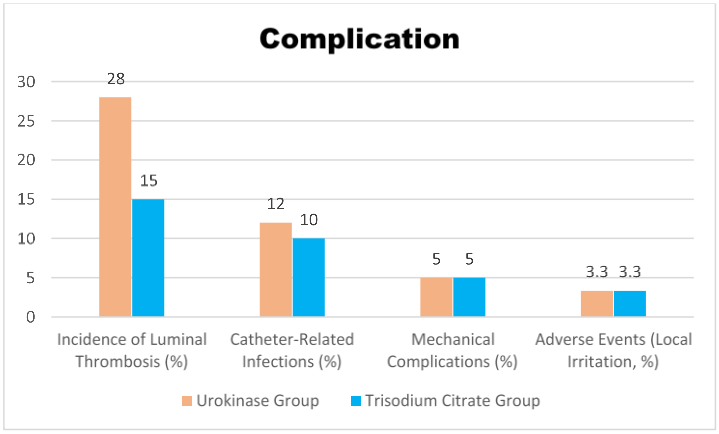


Figure 2 Comparison of Thrombosis and Infection



Complications in Both Groups

DISCUSSION

The present study compared the efficacy and safety of trisodium citrate and urokinase as lock solutions for tunneled dialysis catheters in patients undergoing hemodialysis. The findings demonstrated that trisodium citrate significantly reduced the incidence of luminal thrombosis compared to urokinase, with thrombosis rates of 15% and 28%, respectively (p=0.03). These results align with earlier research, which has consistently reported that citrate-based anticoagulant solutions outperform fibrinolytic agents like urokinase in preventing catheter-related thrombotic events (13,14). One multicenter investigation previously confirmed that trisodium citrate reduced thrombosis occurrence by approximately 40% more than urokinase, while another reported a 50% decrease in thrombotic events with citrate use (14,15). These findings support the biological mechanism of trisodium citrate, which prevents clot formation by chelating calcium and interrupting the coagulation cascade, in contrast to urokinase, which works by degrading pre-existing thrombi. The study also showed that trisodium citrate prolonged the time to first thrombosis event, with a median delay of three additional months compared

INSIGHTS-JHR
INSIGHTS-JOURNAL OF HEALTH AND REHABILITATION

to urokinase (p=0.02). This finding underscores its value in enhancing catheter patency and reducing the frequency of catheter replacements. A longer thrombosis-free interval has practical clinical implications, as catheter replacements are not only invasive but also carry increased risks of infection, vascular injury, and procedural complications. Improved catheter survival with trisodium citrate, demonstrated by an 85% thrombosis-free rate versus 72% in the urokinase group (p=0.04), has been similarly observed in prior studies where citrate-based locks sustained catheter function over extended periods (16).

The safety profile of both agents was comparable, with no significant differences in infection rates (12% vs. 10%), mechanical complications (5% each), or local irritation (3.3% each). These findings are consistent with existing literature, which has indicated that trisodium citrate and urokinase possess similar local tolerability and systemic safety (17,18). However, the systemic bleeding risk associated with urokinase warrants caution, particularly in patients with bleeding diatheses or those on anticoagulation therapy. Urokinase's fibrinolytic activity may inadvertently increase bleeding potential, unlike trisodium citrate, which acts locally without systemic anticoagulant effects (19). This distinction may render trisodium citrate a more favorable option in patients with a higher bleeding risk. The consistency of the current results with existing literature strengthens their validity and supports the clinical transition toward trisodium citrate for routine catheter locking in hemodialysis patients. Several studies have reported similar efficacy, indicating citrate's superiority in maintaining catheter patency and reducing the incidence of thrombotic events by 45% compared to fibrinolytic agents (20,21). While the present study contributes meaningful evidence to this body of research, it also focused specifically on trisodium citrate 4%, enhancing its relevance for clinical practice given its wide availability and established usage.

Despite its strengths, including a well-defined patient population, rigorous follow-up, and multiple clinically relevant endpoints, this study had certain limitations. The nonrandomized design may have introduced selection bias, and the absence of blinding could affect the objectivity of outcome assessments. Additionally, the single-center setting may limit the generalizability of results across broader populations. Cost analysis was only briefly mentioned without quantitative assessment, and microbiological data regarding infection types were not explored, which could have added depth to safety profiling. Future studies should aim to address these limitations through randomized controlled trials with larger sample sizes, inclusion of cost-effectiveness evaluations, and extended follow-up to assess long-term outcomes. It would also be beneficial to compare different concentrations of citrate and to stratify results based on patient risk factors such as diabetes, coagulopathies, and prior catheter-related complications. In conclusion, the findings of this study reinforce the role of trisodium citrate as a superior catheter lock solution compared to urokinase for the prevention of luminal thrombosis in hemodialysis patients. Its better efficacy, comparable safety, and potential for cost reduction present a compelling case for its broader adoption in clinical settings.

CONCLUSION

This study concludes that trisodium citrate is more effective than urokinase in preventing luminal thrombosis in tunneled dialysis catheters, while maintaining a comparable safety profile. By enhancing catheter patency and reducing the likelihood of clot-related complications, trisodium citrate offers a clinically valuable alternative for improving long-term dialysis access care. These findings support its integration into standard catheter maintenance protocols and highlight the need for larger, multicenter trials to further explore its long-term benefits, patient outcomes, and potential cost-effectiveness in broader clinical settings.

AUTHOR CONTRIBUTION

Author	Contribution
Umar Alam Khan*	Substantial Contribution to study design, analysis, acquisition of Data Manuscript Writing Has given Final Approval of the version to be published
Malik Nadeem Azam	Substantial Contribution to study design, acquisition and interpretation of Data Critical Review and Manuscript Writing Has given Final Approval of the version to be published
Sohail Sabir	Substantial Contribution to acquisition and interpretation of Data Has given Final Approval of the version to be published
Farrukh Islam	Contributed to Data Collection and Analysis Has given Final Approval of the version to be published

Author	Contribution
Khurram Mansoor	Contributed to Data Collection and Analysis Has given Final Approval of the version to be published
Naveed Sarwar	Substantial Contribution to study design and Data Analysis Has given Final Approval of the version to be published

REFERENCES

1. Castro V, Farber A, Zhang Y, Dicken Q, Mendez L, Levin SR, Cheng TW, Hasley RB, Siracuse JJ. Reasons for long-term tunneled dialysis catheter use and associated morbidity. Journal of Vascular Surgery. 2021 Feb 1;73(2):588-92.
2. van Meurs S, Hopman J, Hubens G, Komen N, Hendriks JM, Ysebaert D, Nellensteijn D, Plaeke P. Impact of risk factors on the incidence of tunneled dialysis catheter infections: a systematic review and meta-analysis. Acta Chirurgica Belgica. 2024 Sep 9(just-accepted):1-9.
3. Shigidi MM. Evaluating the use of tunneled hemodialysis catheters in the treatment of acute kidney disease patients requiring hemodialysis: a case–control study. International Urology and Nephrology. 2024 Nov 21:1-6.
4. Hung ML, DePietro DM, Trerotola SO. Infectious recidivism in tunneled dialysis catheters removed for bloodstream infection in the intensive care unit. Journal of Vascular and Interventional Radiology. 2021 May 1;32(5):650-5.
5. Pethő Á, Tapolyai M, Szakács-Pál T, Orosz P, Dézsi L, Rosivall L. Safety and efficacy of placement of tunneled hemodialysis catheter without the use of fluoroscopy. Clinical Nephrology. 2020 Nov 1;94(5):237.
6. Matsumoto MM, Chittams J, Quinn R, Trerotola SO. Spontaneous dislodgement of tunneled dialysis catheters after de novo versus over-the-wire-exchange placement. Journal of Vascular and Interventional Radiology. 2020 Nov 1;31(11):1825-30.
7. Kreuzer M, Haffner D. Anticoagulation in Children Undergoing Hemodialysis, Continuous Renal Replacement Therapy, or Apheresis Therapy. InHandbook of Dialysis Therapy 2023 Jan 1 (pp. 694-699). Elsevier.
8. Elamin, G. (2022). *The role of Endothelial microvesicles in thrombus formation* (Doctoral dissertation, University of Southampton).
9. Wang Y, Liu C, Zhang L, Li J, Zhang L, Wang Y, Zhu H, Cao X, Wu D, Wu J, Lin S. Evaluating the safety and efficacy of argatroban locking solution in the prevention of the dysfunction of haemodialysis Central venous catheters: a study protocol for a randomized controlled trial. Annals of Palliative Medicine. 2021 Feb;10(2):2260270-2270.
10. Sheng KX, Zhang P, Li JW, Cheng J, He YC, Böhlke M, Chen JH. Comparative efficacy and safety of lock solutions for the prevention of catheter-related complications including infectious and bleeding events in adult haemodialysis patients: a systematic review and network meta-analysis. Clinical Microbiology and Infection. 2020 May 1;26(5):545-52.
11. Karmani JK, Mir S, Naveed SM, Shah SA, Javaid MK, Asim F, Ahmad A. Comparison of Catheter Related Blood Stream Infections in Hemodialysis Patients Treated With Trisodium Citrate as Catheter Locking Solution vs Heparin as Conventional Locking Method. Annals of PIMS-Shaheed Zulfiqar Ali Bhutto Medical University. 2023 Sep 7;19(3):307-12.
12. Fisher M, Golestaneh L, Allon M, Abreo K, Mokrzycki MH. Prevention of bloodstream infections in patients undergoing hemodialysis. Clinical journal of the American Society of Nephrology. 2020 Jan 1;15(1):132-51.
13. Mattingly, A. N., Gianturco, S. L., Pavlech, L. L., Storm, K. D., & Yuen, M. V. (2021). Sodium citrate: Summary Report.
14. Szymańska J, Kakareko K, Rydzewska-Rosołowska A, Głowińska I, Hryszko T. Locked away—prophylaxis and management of catheter related thrombosis in hemodialysis. Journal of Clinical Medicine. 2021 May 21;10(11):2230.
15. Sheng KX, Zhang P, Li JW, Cheng J, He YC, Böhlke M, Chen JH. Comparative efficacy and safety of lock solutions for the prevention of catheter-related complications including infectious and bleeding events in adult haemodialysis patients: a systematic review and network meta-analysis. Clinical Microbiology and Infection. 2020 May 1;26(5):545-52.
16. Haq A, Patel D, Gutlapalli SD, Hernandez GN, Seffah KD, Zaman MA, Awais N, Satnarine T, Ahmed A, Khan S. Corrected: A Systematic Review of the Impact of Antibiotic and Antimicrobial Catheter Locks on Catheter-Related Infections in Adult Patients Receiving Hemodialysis. Trials. 2022;23(10.1186/s13063):022-6671.
17. Wang Q, Jiang N, Chen W, Cheng L, Fu S, Li Q, Li H. Prevention of Dialysis Catheter Malfunction with Urokinase and Heparin: A Randomized, Controlled Trial. Alternative Therapies in Health & Medicine. 2024 Oct 1;30(10).

18. Neusser MA, Bobe I, Hammermeister A, Wittmann U. A 2% taurolidine catheter lock solution prevents catheter-related bloodstream infection (CRBSI) and catheter dysfunction in hemodialysis patients. British Journal of Nursing. 2021 Jul 22;30(14):S24-32.
19. Bonkain F, Stolear JC, Catalano C, Vandervelde D, Treille S, Couttenye MM, Dhondt A, Libertalis M, Allamani M, Madhoun P, Van Craenenbroeck AH. Prevention of tunneled cuffed catheter dysfunction with prophylactic use of a taurolidine urokinase lock: a randomized double-blind trial. PLoS One. 2021 May 20;16(5):e0251793.
20. López-Rubio M, Lago-Rodríguez MO, Ordieres-Ortega L, Oblitas CM, Moragón-Ledesma S, Alonso-Beato R, Alvarez-Sala-Walther LA, Galeano-Valle F. A Comprehensive Review of Catheter-Related Thrombosis. Journal of Clinical Medicine. 2024 Dec 21;13(24):7818.
21. Haq A, Patel D, Gutlapalli SD, Hernandez GN, Seffah KD, Zaman MA, Awais N, Satnarine T, Ahmed A, Khan S. Corrected: A Systematic Review of the Impact of Antibiotic and Antimicrobial Catheter Locks on Catheter-Related Infections in Adult Patients Receiving Hemodialysis. Trials. 2022;23(10.1186/s13063):022-6671.

