Research Article

Hemodialysis catheter-related bloodstream infections during 10 years and factors associated

Irene Galindo Marin[1*], Carmen Mon Mon[1], Milagros Ortiz Librero[1], Sara El Fellah[1], María Sánchez Sánchez[1], Rosa Elena Camacho Juarez[1], Carolina Lentisco Ramírez[1], Santiago Andrés Cedeño Mora[1], Juan Carlos Herrero Berrón[1], Esther Galvez[2], Jose María Abadal[2]

[1]Department of Medicine of UAX, Nephrology, Severo Ochoa University Hospital, Madrid, Spain.
[2]Department of Medicine of UAX, Interventional Radiology, Severo Ochoa University Hospital, Madrid, Spain.

Catheter-associated Blood Stream Infection (CVC-BSI) is a significant cause of morbidity and mortality among hemodialysis patients. In our center was a notable increase in CVC associated with patient age and morbidity. This 10-year retrospective study investigated catheter-associated blood stream infection (CVC-BSI) in hemodialysis patients. We recorded a total of 67 bacteremia episodes in 52 patients, predominantly linked to gram-positive microorganisms, particularly *Staphylococcus aureus*, the study found a mean age of 68 years, 74.6% males, and 88% with tun-neled jugular catheters. Notably, catheter removal occurred in 65.7% of cases, more frequently in Gram-positive instances. Two episodes of endocarditis and five ICU admissions were reported. The study identified a higher incidence in the summer and a significant decrease in bacteremia from 2017, coinciding with the introduction of Tauro-Lock™. Despite enhanced preventive measures during the COVID-19 pandemic, there was no significant impact on catheter infection rates. This research emphasizes the importance of early catheter removal, highlights seasonal variations in incidence, and suggests a potential positive influence of Tauro-Lock™ on decreasing CVC-BSI rates in hemodialysis units.

Keywords: Blood stream infection, Catheter, Hemodialysis, SARS-CoV-2

INTRODUCTION

Central Venous Catheter (CVC)-associated bacteriemia is a significant cause of morbidity and mortality among our hemodialysis patients. The incidence rate ranges between 1.1 and 6.1 episodes per 1000 catheter days according to some large-scale series (Allon, et al., 2004 and Martin, et al., 2020). Both national and international guidelines recommend, whenever possible, the arteriovenous fistula as the preferred vascular access (Ibeas, et al., 2017 and Lok, et al., 2019). However, a substantial percentage of end-stage chronic kidney disease patients initiate hemodialysis using a catheter, and prevalent patients may choose it as their definitive vascular access (Johansen, et al., 2021). In this context, standardizing protocols across different hemodialysis units (Lok, et al., 2019) and having a specialized multidisciplinary vascular access team are crucial to minimize complication rates, mortality, and

consequently, associated costs (Mokrzycki, et al., 2006). During the SARS-CoV-2 coronavirus pandemic, certain preventive measures for air-borne transmission were implemented, which seem to have had a collateral benefit in reducing episodes of catheter-associated bacteremia in hemodialysis patients (Heidempergher, et al., 2021 and Johansen, et al., 2022).

The objective of our study was to characterize the episodes of bacteremia in our hospital based hemodialysis unit. Additionally, we analyzed the seasonal distribution and assessed possible variations in incidence during the peripandemic years.

MATERIALS AND METHODS

Population and study design

We conducted a single-center, observational, and retrospective study in the hospital-based hemodialysis unit

*Corresponding author. Irene Galindo Marin,
E-mail: irenegalindo95@hotmail.com

at Severo Ochoa University Hospital (Leganés, Madrid). The study included all prevalent hemodialysis patients with tunneled central venous catheters who were admitted for catheter-associated bacteremia from January 2013 to December 2022. Catheter insertion was performed by the interventional vascular radiology service under local anesthesia and standard sterile measures. Nasal carriage screening for *Staphylococcus aureus* was not conducted, reserving it for patients with confirmed bacteremia caused by this microorganism and treating those with positive results with nasal mupirocin. Catheter sealing was standardized using Tauro-Lock™ heparin (taurolidine and heparin) during the initial days to prevent biofilm formation. Subsequently, only heparin was used, and the continuation of taurolidine was individualized based on infectious risk. Before 2018, only heparin was used for the initial sealing due to the unavailability of Tauro-Lock™ heparin. Hygiene measures mandated by the units protocol included the use of sterile gloves by nursing staff, surgical masks by both nursing staff and patients, and line disinfection using chlorhexidine. The definition of catheter associated bacteremia was established by the simultaneous growth of the same microorganism in blood extracted from the central line (arterial and venous branches) and peripheral line or only from the peripheral line in catheter carriers, with the absence of other suspicious infection foci. However, episodes with a high suspicion, initiation of antibiotic therapy, and negative microbiological isolation were not excluded from the study.

Data collection

Patient demographic data (age, gender) and comorbidities (Charlson index) were extracted from medical records: Collected on paper until 2015 and computerized thereafter through the Selene® health program. Similarly, information related to hospitalization episodes (date and duration of admission, ICU stay, complications, catheter removal, microbiological isolation) as well as previous hospitalizations for bacteremia was extracted this way. Dialysis (start date, cause of end-stage renal disease) and vascular access data (location, insertion date) were extracted from the Neuralink® software.

Objectives

The main objective was the descriptive analysis of hospitalization episodes due to catheter-associated bacteremia in dialysis patients. As a secondary objective, the annual incidence rate (expressed as episodes/1000 catheter days) was analyzed to assess the possible impact of the COVID-19 pandemic.

Statistical analysis

Statistical analysis was performed using IBM SPSS Statistics® version 25.0. Categorical variables were reported as proportions, and continuous variables were presented as means (with 95% confidence intervals) or medians (with interquartile range) based on normal or non-normal distribution. Contingency tables were created for comparisons of categorical variables using the Spearman chi-square test or continuous variables using the Student's t-test or Wilcoxon test depending on their distribution. The odds ratio (or) was used to compare annual incidences. Statistically significant values were considered those with a p-value <0.05.

RESULTS

Patient characteristics

Over the 10-year study period, a total of 466 catheters were inserted in our center for 426 patients. Only 27.5% of patients who initiated hemodialysis during the study years remained catheter free. We recorded 67 episodes of bacteremia in 52 patients, corresponding to an overall incidence rate of 0.52 episodes per 1000 catheter days. Patient characteristics are summarized in Table 1.

Table 1. Evaluation of patient characteristics over a 10-year study period.

Patient characteristics	Statistical analysis
Age (mean, SD)	67 (+11.016)
Male (n,%)	39 (74.6%)
Charlson index (median, IR)	8 (6-9)
Etiology of CKD	
• Diabetes (n,%)	29 (43.3%)
• Nephroangioesclerosis (n,%)	19 (28.4%)
• Glomerular disease (n,%)	11 (16.4%)
• Polycystic disease (n,%)	1 (1.5%)
• Unknown (n,%)	3 (4.5%)
• Others (n,%)	4 (6%)
Months in hemodialysis (median, IR)	24 (4-48)
Kidney transplant (n,%)	6 (9%)
Site of catheter	
• Jugular (n,%)	60 (89.5%)
• Femoral (n,%)	7 (10.5%)
Catheter half-life until infection (median, IR)	240 (28-930)
Immunosuppressive treatment (n,%)	4 (7.7%)
Note: n: mean; %: Standard deviation.	

The mean age was 67 years (range 56-78), with 74.6% being male and 25.4% female. The median Charlson comorbidity index was 8 (range 6-9). Diabetic kidney disease was the primary etiology of chronic kidney disease (43.3%), followed by nephroangiosclerosis (28.4%) and glomerular pathology (16.4%). The median time on hemodialysis was 24 months (range 4-48). The predominant catheter location was the internal jugular vein (89.5%), with only a small portion having tunneled femoral catheters (10.5%). The median catheter lifespan until infection was 240 days (range 28-930). Four patients (7.69%) were receiving some form of immunosuppressive treatment at the time of infection; three were on corticosteroids as monotherapy for various reasons (recent failed kidney transplant, rheumatoid arthritis, and corticosteroid-dependent nonspecific inflammatory syndrome), and the remaining patient was on corticosteroids and azathioprine due to having a heart transplant.

Infection characteristics

The characteristics of hospitalization episodes due to bacteremia are summarized in Table 2. Out of all episodes, 17 (25.3%) occurred within the first 30 days of catheter insertion; among these, 16 were caused by Gram-positive microorganisms (12 *Staphylococcus aureus* and 4 *Staphylococcus epidermidis*), while only 1 involved a Gram-negative organism (*Pseudomonas aeruginosa*). Most hospitalizations took place in the summer

(43.3%) and spring (23.9%), with fewer episodes recorded in the fall (16.4%) and winter (16.4%). These differences were statistically significant when comparing the summer period with fall and winter.Microbiological confirmation was obtained in 61 out of the 67 episodes labeled as catheter-associated bacteremia. The majority isolated a Gram-positive microorganism (67.2%). Among them, *Staphylococcus aureus* was the most prevalent (83%), with 14.7% being methicillin-resistant strains. In the remaining cases, *Staphylococcus epidermidis* (14.6%) and *Staphylococcus hominis* (2.4%) were isolated. Among Gram-negative varieties, *Klebsiella pneumoniae* (35%) was the most frequently isolated, followed by *Escherichia coli* (20%) and *Serratia marcescens* (10%), with others such as *Pseudomonas aeruginosa*, *Proteus mirabilis*, *Klebsiella oxytoca*, *Morganella morgagni*, and *Stenotrophomonas* maltophilia found in smaller proportions. There were two cases of polymicrobial infections involving Gram-negative bacteria (3.2% of the total). No fungal infections were recorded during the study period.

Table 2. The infection characteristics of hospitalization episodes due to bacteremia are summarized.

Infection characteristics	Clinical outcomes
Early infection (n,%)	17 (25.3%)
Season of infection	
• Spring (n,%)	16 (23.9%)
• Summer (n,%)	29 (43.3%)
• Autumn (n,%)	11 (16.4%)
• Winter (n,%)	11 (16.4%)
Microbiological isolation	
• *Staphylococcus aureus* (n,%)	34 (50.7%)
• *Staphylococcus epidermis* (n,%)	6 (9%)
• *Staphylococcus hominis* (n,%)	1 (1.5%)
• *Escherichia coli* (n,%)	4 (6%)
• *Klebsiella pneumoniae* (n,%)	7 (10.4%)
• *Serratia marcescens* (n,%)	2 (3%)
• *Pseudomona aeruginosa* (n,%)	1 (1.5%)
• *Proteus mirabillis* (n,%)	1 (1.5%)
• *Klebsiella oxytoca* (n,%)	1 (1.5%)
• *Morganella morgagni* (n,%)	1 (1.5%)
• *Strerotrophomona philia* (n,%)	1 (1.5%)
• *Klebsiella pneumoniae+Proteus mirabillis* (n,%)	1 (1.5%)
• *Klebsiella pneumoniae+Echerichia coli* (n,%)	1 (1.5%)
Days of hospitalization (median, IR)	7 (5-12)
ICU admissions (n,%)	5 (7.4%)
Metastasic complications (n,%)	2 (2.9%)
Catheter removal (n,%)	45 (67.1%)
Patients with recurrence of bacteriemia (n,%)	10 (19.2%)

Note: n: mean; %: Standard deviation.

The median hospital stay was 7 days (range 5-12), with a minimum duration of 2 days and a maximum of 81 days. Five patients (7.4%) required admission to an intensive care unit (three cases due to *Staphylococcus aureus*, one case due to *Klebsiella pneumoniae*, and one polymicrobial case involving *Klebsiella pneumoniae* and *Proteus mirabilis*). Two cases of endocarditis were identified as metastatic complications (2.9%). There were no deaths directly related to the episodes of bacteremia.

The catheter was removed in 67.1% of cases, with a statistically significant difference between Gram-positive (removed in 90.2% of cases) and Gram-negative cases (removed in 30% of cases, with the remaining cases receiving prolonged antibiotic therapy) (p<0.001). Gram-positive cases where the catheter was preserved corresponded to three cases of coagulase negative Staphylococcus and one case with anatomical difficulties hindering alternative vascular access.

Out of the 52 patients, 10 experienced more than one episode of bacteremia during the study period. No statistically significant differences were found in their baseline characteristics or the etiological agent.

Evolution of incidence over the study period

The graphical representation in Figure 1 illustrates the trend in both catheter exposure days and bacteremia incidence throughout the study years. As depicted, there is a notable decrease in bacteremia incidence since 2017, coinciding with the introduction of Tauro-Lock™ heparin and the implementation of the taurolidine sealing protocol in 2018. This decline is statistically significant when compared to previous years in Table 3. Simultaneously, there is an observed increase in catheter exposure days over the study period. Despite a slight uptick in bacteremia incidence in 2020, the overall trend indicates a lower incidence rate, and there is no statistically significant reduction in the post-pandemic years (Table 3).
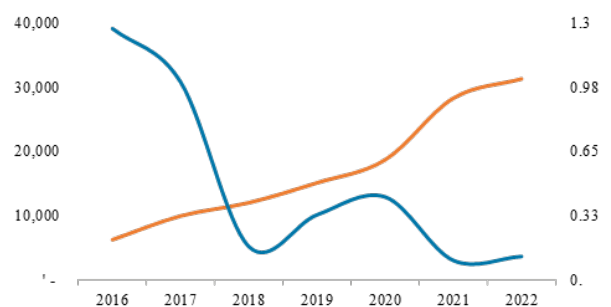

Figure 1. Evolution of catheter exposure days and bacteremia incidence over the study years. **Note:** (—) Days CVC: (—) CRBSI rate.

Table 3. Comparative bacteriemia incidence over years.

Comparative years	OR	CI 95%	p
2016-2017	1.26	0.5-3.21	0.6
2016-2018	7,64	1.62-36.02	0.01
2016-2019	3,84	1.35-11.75	0.01
2016-2020	2.97	1.1-7.92	0.02
2016-2021	11.97	3.17-45.6	<0.001
2016-2022	1.93	2.9-33.01	P<0.001
2017-2018	6.02	1.21-27.49	0.02
2017-2019	3.02	1.03-8.85	0.04
2017-2020	2.34	0.92-5.93	0.07
2017-2021	9.43	2.59-34.29	<0.001
2017-2022	7.82	2.45-24.96	<0.001
2018-2019	0.5	0.97-2.59	0.4
2018-2020	0.38	0.08-1.83	0.4
2018-2021	1.56	0.26-9.37	0.6
2018-2022	1.29	0.23-7.09	0.7
2019-2020	1.29	0.25-2.36	0.6

2019-2021	3.11	0.74-13.04	0.1
2019-2022	2.58	0.69-9.63	0.1
2020-2021	4.02	1.06-15.19	0.03
2020-2022	3.34	1.1-11.1	0.05
2021-2022	0.82	0.18-3.7	0.8

Note: OR: Odds Ratio; P: Significant values; CI: Confidence Intervals.

DISCUSSION

Bacteremia associated with central venous catheters remains a significant cause of morbidity and mortality in our hemodialysis patients. Over the 10-year study period, a total of 466 catheters were implanted in 426 patients in our hospital unit. Among the 588 patients who initiated hemodialysis during this period, only 162 patients (27.5%) were never carriers of a catheter at any point in their treatment. In recent years, especially since the 2020 pandemic, there has been a notable increase in the use of catheters as the definitive vascular access; in 2021, 69.6% of prevalent hemodialysis patients had central venous catheters (CVC). This figure is higher than reported in other registries. In the United States, up to 80% initiate hemodialysis *via* CVC, but only 15% of prevalent patients carry CVC (Johansen, et al., 2021). In Europe, approximately 50% initiate hemodialysis through CVC, and the prevalence varies among different countries (15-38%) (Pisoni, et al., 2015). The increase in catheter use in our center could be attributed to two reasons: The aging population, leading to more lenient criteria for dialysis initiation with older and more comorbid incident patients, and the choice of vascular access depending not only on patient profile but also on the availability of vascular surgery teams. During the pandemic, there was a decrease in surgeries and, consequently, fewer arteriovenous fistulas were created.

Despite the increase in catheter use, the overall incidence rate over the ten-year study period was 0.52 episodes of bacteremia per 1000 catheter days. This rate is lower than reported in some large series (Allon, et al., 2004 and Martin, et al., 2020) and similar to a recent national study where an incidence of 0.4 episodes per 1000 catheter days was recorded over a 14-year observational period (Almenara-Tejederas, et al., 2023). About 26% of these cases were early infections, defined as those occurring in the first thirty days of catheter insertion. The summer season significantly recorded more episodes, a phenomenon also described in other studies. This could be justified by the hypothesis that higher temperature and humidity conditions facilitate microbial adherence and bio-film formation (Johansen, et al., 2022 and Lok et al., 2014). Another explanation could be the seasonality of summer contracts, with less experienced nursing staff.

Gram-positive microorganisms were responsible for approximately 70% of the cases, consistent with literature reports (Allon, et al., 2004, Farrington, et al., 2019, Marr, et al., 1997, Beathard, et al., 1999 and Phillips, et al., 2023). This percentage increased to 94% in cases of early infection. Coagulase-positive *Staphylococcus aureus* accounted for 85% of these cases and half of the total isolates (50.7%). Previous studies have shown a higher number of metastatic complications and mortality in bacteremias caused by Gram-positive bacteria, especially *Staphylococcus aureus* (Farrington, et al., 2019 and Maya, et al., 2007). This is attributed to their greater capacity to create biofilms and adhere to native tissues (Costerton, et al., 1999 and Paharik, et al., 2016). However, it is a controversial issue, as other studies report worse outcomes (septic shock, septic complications, and ICU admissions) in Gram-negative bacteremias due to the tendency to preserve the catheter in these cases (Shahar, et al., 2021 and Abe, et al., 2010). In our study, there was an overall low number of ICU admissions and complications, as well as an absence of mortality directly caused by bacteremia. We believe throughout the study period, there was a decrease in the annual incidence of bacteremias despite a progressive increase in catheter exposure days. This difference became statistically significant from 2017 onwards. In 2018, a new catheter sealing protocol was implemented following the introduction of Tauro-Lock™ heparin. Taurolidine is an antimicrobial that has been shown to significantly reduce the incidence of catheter-related sepsis (González, et al., 2014) Therefore, these findings suggest a potential association between the introduced sealing protocols and the decline in bacteremia incidence. Further analysis may be warranted to explore the specific factors contributing to this trend and assess the long-term effectiveness of the implemented measures.

Recent studies have demonstrated a decrease in catheter-related bacteremias coinciding with the implementation of airborne transmission preventive measures imposed by the COVID-19 pandemic. An observational study conducted in two hospitals in one of the most affected European regions (Lombardy, Italy) showed a 90% reduction in cathe-ter-related bacteremia incidence rates during the peak of the pandemic (February-May 2020) compared to the same period in the previous year (February-March 2019) (Heidempergher, et al., 2021). An-other American study demonstrated a decrease in antibiotic administration in dialysis and specific admissions for catheter-related bacteremia from March 2020 onwards (Johansen, et al., 2022). In our center, despite maintaining a low incidence rate in the years after the pandemic, we cannot conclusively state a significant decrease. This might be because our hygiene measures before the pandemic already included device sterilization, the use of sterile gloves by nursing staff, and the use of surgical masks by both nursing staff and patients.

CONCLUSION

The overall incidence of bacteremias is low compared to other results reported in the literature, despite having a significant number of catheters in our unit. The most frequently isolated microorganism was methicillin-sensitive *Staphylococcus aureus*. Early catheter removal, especially in Gram-positive infections, results in a low number of ICU admissions and septic complications, endorsing the protocol used. The summer period had the highest number of episodes. There seems to be a significant decrease in the annual incidence since 2017, coinciding with the implementation of a catheter sealing protocol with taurolidine. We did not find a clear decrease in the incidence of bacteremia in the years following the pandemic.

REFERENCES

1. Abe R, Oda S, Sadahiro T, Nakamura M, Hirayama Y, Tateishi Y, Shinozaki K, et al. (2010). Gram-negative bacteremia induces greater magnitude of inflammatory response than Gram-positive bacteremia. Crit Care. 14(2):1-7.

2. Allon M (2004). Dialysis catheter-related bacteremia: Treatment and prophylaxis. Am J Kidney Dis. 44 (5):779-791.

3. Almenara-Tejederas M, Rodríguez-Pérez MA, Moyano-Franco MJ, de Cueto-López M, Rodríguez-Baño J, Salgueira-Lazo M (2023). Tunneled catheter-related bacteremia in hemodialysis patients: Incidence, risk factors and outcomes. A 14-year observational study. J Nephrol. 36(1):203-212.

4. Beathard GA (1999). Management of bacteremia associated with tunneled-cuffed hemodialysis catheters. J Am Soc Nephrol. 10(5):1045-1049.

5. Costerton JW, Stewart PS, Greenberg EP (1999). Bacterial biofilms: A common cause of persistent infections. Science. 284(5418):1318-1322.

6. Farrington CA, Allon M (2019). Complications of hemodialysis catheter bloodstream infections: Impact of infecting organism. Am J Nephrol. 50(2):126-132.

7. González Martínez M, Ojeda Ramírez M, García Pérez AM, Redondo Simón M, Caro Rodríguez I, Huerga García M, Gómez Cambronero M, et al. (2014). Estudio de la eficacia del sellado con taurolidina y citrato 4% del catéter para hemodiálisis en la prevención de infección trombosis. Enfermeria Nefrol. 17(1):22-27.

8. Heidempergher M, Sabiu G, Orani MA, Tripepi G, Gallieni M (2021). Targeting COVID-19 prevention in hemodialysis facilities is associated with a drastic reduction in central venous catheter-related infections. J Nephrol. 34:345-353.

9. Ibeas J, Roca-Tey R, Vallespín J, Moreno T, Monux G, Martí-Monrós A, del Pozo JL, et al.(2017) Guía clínica española del acceso vascular para hemodiálisis. Nefrologia. 37:1-91.

10. Johansen KL, Chertow GM, Foley RN, Gilbertson DT, Herzog CA, Ishani A, Israni AK, et al. (2021). US renal data system 2020 annual data report: Epidemiology of kidney disease in the United States. Am J Kidney Dis.77 (4):A7-A8.

11. Johansen KL, Gilbertson DT, Wetmore JB, Peng Y, Liu J, Weinhandl ED (2022). Catheter-Associated bloodstream infections among patients on hemodialysis: Progress before and during the COVID-19 pandemic. Clin J Am Soc Nephrol. 17(3):429-433.

12. Lok CE, Huber TS, Lee T, Shenoy S, Yevzlin AS, Abreo K, Allon M, et al. (2019). Clinical practice guideline for vascular access: Update. Am J Kidney Dis. 75(4):S1-S64.

13. Lok CE, Thumma JR, Mccllough KP, Gillespie BW, Fluck RJ, Marshall MR, Kawanishi H, et al. (2014). Catheter-related Infection and Septicemia: Impact of seasonality and modifiable practices from the DOPPS. Semin Dial. 27 (1):72-77.

14. Marr KA, Sexton DJ, Conlon PJ, Corey GR, Schwab SJ, Kirkland KB (1997). Catheter-related bacteremia and outcome of attempted catheter salvage in patients undergoing hemodialysis. Ann Intern Med. 127(4):275-280.

15. Martin K, Lorenzo YS, Leung PY, Chung S, O'Flaherty E, Barker N, Ierino F, et al. (2020). Clinical outcomes and risk factors for tunneled hemodialysis catheter-related bloodstream infections. Open Forum Infect Dis. 7 (6):117. US: Oxford University Press.

16. Maya ID, Carlton D, Estrada E, Allon M (2007). Treatment of dialysis catheter-related *Staphylococcus aureus* bacteremia with an antibiotic lock: A quality improvement report. Am J Kidney Dis.50 (2):289-295

17. Mokrzycki MH, Zhang M, Golestaneh L, Laut J, Rosenberg SO (2006). An interventional controlled trial comparing 2 management models for the treatment of tunneled cuffed catheter bacteremia: A collaborative team model versus usual physician-managed care. Am J Kidney Dis. 48(4):587-595

18. Paharik AE, Horswill AR (2016). The staphylococcal biofilm: Adhesins, regulation, and host response. Microbiol Spectr. 529-566.

19. Phillips J, Chan DT, Chakera A, Swaminathan R, Patankar K, Boudville N, Lim WH, et al. (2023). Haemodialysis vascular catheter-related blood stream infection: Organism types and clinical outcomes. Nephrology. 28(4):249-253.

20. Pisoni RL, Zepel L, Port FK, Robinson BM (2015). Trends in US vascular access use, patient preferences, and related practices: An update from the US DOPPS practice monitor with international comparisons. Am J Kidney Dis. 65(6):905-915

21. Shahar S, Mustafar R, Kamaruzaman L, Periyasamy P, Pau KB, Ramli R (2021). Catheter-related bloodstream infections and catheter colonization among haemodialysis patients: Prevalence, risk factors, and outcomes. Int J Nephrol. 2021.