A Case Report and Literature Review: Chlorhexidine-induced anaphylaxis in a hemodialysis patient

Case reports

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ABSTRACT

Chlorhexidine is a widely used antiseptic in healthcare settings, particularly for catheter site preparation in hemodialysis patients. While generally considered safe, chlorhexidine can rarely cause severe IgE-mediated anaphylactic reactions. Here we report the case of a 47-year-old man on maintenance hemodialysis who experienced two episodes of severe allergic reactions during dialysis sessions. During the first episode the patient presented with dyspnea, hypotension, and pruritus, which we initially attributed to the dialyzer membrane reaction. After changing the dialyzer membrane, the patient remained asymptomatic for 19 sessions. However, a second, more severe episode occurred with urticaria, profound hypotension, and respiratory distress requiring intravenous adrenaline. Retrospective analysis revealed chlorhexidine antisepsis at the tunneled catheter site as the causative agent, confirmed by elevated serum IgE (285 IU/mL), with complete resolution after switching to povidone-iodine as an antiseptic instead. This case demonstrates a concept called “sensitization window” where compromised skin integrity at the catheter exit site facilitated chlorhexidine penetration despite three years of uneventful exposure of the same during fistula use. This case highlights the importance of considering chlorhexidine hypersensitivity in such unexplained dialysis-related allergic reactions. Early recognition and prompt antiseptic substitution are thereby crucial to prevent potentially fatal anaphylactic episodes in this vulnerable population.

KEYWORDS: Chlorhexidine, anaphylaxis, hemodialysis, hypersensitivity, catheter-related complications, IgE-mediated reaction, dialysis safety, antiseptic allergy

Introduction

Chlorhexidine gluconate, a bisbiguanide antiseptic, has been widely used in healthcare since the 1950s [1]. Due to its broad-spectrum antimicrobial activity, prolonged efficacy, and low toxicity, this agent is the preferred antiseptic for skin preparation prior to invasive procedures, including central venous catheter insertion and also for maintenance [2]. The Centers for Disease Control and Prevention (CDC) recommend chlorhexidine-based solutions (ideally >0.5% concentration) for catheter site antisepsis in hemodialysis patients because they are more effective than povidone-iodine at lowering catheter-related bloodstream infections [3].

Though it has extensive use and usually good safety profile, chlorhexidine can occasionally cause hypersensitivity reactions which can range from mild contact dermatitis to life-threatening anaphylaxis [4, 5]. The reported incidence of chlorhexidine-induced anaphylaxis varies considerably, with substantial underreporting [4]. The immunological process involves IgE-mediated type I hypersensitivity reactions, wherein chlorhexidine functions as a possible hapten that associates with carrier proteins, resulting in the formation of immunogenic complexes [6].

Krautheim et al. [7] recognized chlorhexidine hypersensitivity reactions. Tan et al. [8] reported cases in the dialysis population, with repeated chlorhexidine exposures through vascular access. While these studies have established chlorhexidine anaphylaxis as a recognized clinical entity, diagnostic challenges still persist in dialysis patients.

Hemodialysis patients represent a particularly vulnerable population for developing chlorhexidine hypersensitivity for several reasons. First, repeated exposure through catheter site preparation leads to sensitization [8, 9]. Second, compromised skin integrity at catheter insertion sites facilitates deeper penetration of chlorhexidine, increasing the likelihood of systemic absorption and immune response [10]. Third, uremic patients demonstrate altered immune function with paradoxical hypersensitivity to certain antigens [11]. Finally, the closed circuit of the hemodialysis system may result in recirculation and also amplification of the allergic response once it is initiated.

Considering symptoms frequently appear during dialysis sessions and might be falsely attributed to more prevalent causes such as dialyzer membrane responses, dialysate contamination, or hemolysis, diagnosing chlorhexidine-induced anaphylaxis can be very difficult . Furthermore, the timing of reactions can be variable, occurring immediately upon exposure or after multiple uneventful sessions following sensitization [12]. Skin prick testing and measurement of chlorhexidine-specific IgE antibodies can aid in diagnosis, though these tests are not universally available and have variable sensitivity [13].

We describe a case of recurrent anaphylactic reactions in a chronic hemodialysis patient, ultimately attributed to chlorhexidine antisepsis at the tunneled dialysis catheter site. This case exhibits a unique “sensitization window” phenomenon, in which the same patient tolerated chlorhexidine for nearly three years while using an arteriovenous fistula, but developed severe responses after switching to a tunnelled catheter with a damaged skin barrier. This case underscores the importance of maintaining a high index of suspicion for chlorhexidine hypersensitivity in patients presenting unexplained allergic reactions during dialysis and highlights the need for vigilance when such reactions occur.

Case Presentation

Patient Background

A 47-year-old male with end-stage renal disease (ESRD) secondary to chronic glomerulonephritis

presented with recurrent severe allergic reactions during hemodialysis sessions. His past medical history was significant for hypertension (well-controlled on amlodipine 5 mg daily and metoprolol 25 mg twice daily) and secondary hyperparathyroidism (managed with calcium carbonate and calcitriol). He had no known drug allergies prior to these events and no personal or family history of atopy, asthma, or allergic disorders. Latex allergy was specifically excluded by the patient's history of tolerating latex glove exposure during routine medical examinations without any adverse reactions.

The patient had been on maintenance hemodialysis for nearly three years, initially dialyzing three times weekly (Monday-Wednesday-Friday schedule) via a left brachiocephalic arteriovenous fistula. Prior to his arteriovenous fistula creation, the patient required temporary hemodialysis access via a right internal jugular vein (IJV) non-tunneled catheter for three months (December 2021 till February 2022). During this period, dialysis was performed using povidone-iodine for catheter insertion and 2% chlorhexidine gluconate for routine catheter site antisepsis during dialysis sessions, with no adverse reactions noted. During the three years of arteriovenous fistula use, the rope-ladder technique was used for venipuncture. His dialysis prescription consisted of 4-hour sessions using a Fresenius Polysulfone F8 dialyzer (surface area 1.8 m^2), bicarbonate dialysate, blood flow rate of 300 mL/min, and dialysate flow rate of 500 mL/min. Anticoagulation was achieved with unfractionated heparin (loading dose 2000 IU, maintenance 1000 IU/hour). Dialysis adequacy was consistently satisfactory with Kt/V values of 1.4-1.6.

Approximately six months before the index event, the patient experienced fistula thrombosis following a hypotensive episode during a particularly challenging dialysis session with significant ultrafiltration requirements (3.5 kg interdialytic weight gain). Despite attempts at thrombectomy, the fistula could not be salvaged. The decision was then made to place a tunneled catheter based on several factors. The patient had a history of previous access failures, with two prior fistula attempts that had failed to mature adequately before the successful left brachiocephalic fistula. The patient also presented very late and it was an organized older thrombus with probable underlying significant stenosis; immediate surgical revision was hence unsuccessful. The patient also required urgent dialysis, and a tunneled catheter hence was necessary while planning for creation of a new arteriovenous fistula or graft if feasible in an alternative site. Detailed physical examination revealed limited suitable vessels in the right upper extremity for fistula creation. The catheter was hence planned as a bridge to new permanent access. A right femoral vein tunneled cuffed catheter (14.5 French × 28 cm, cuff-to-tip length, Palindrome catheter, Covidien) was inserted under ultrasound guidance as a bridge before creation of a new vascular access. Initial attempts at right and left internal jugular vein catheterization was unsuccessful due to stenosis / fibrosis from prior IJV catheter use. Given these difficulties and the urgent need for dialysis access, the decision was made to proceed with femoral vein catheterization. Catheter insertion was uneventful, performed under sterile conditions with 2% chlorhexidine skin preparation, and the patient resumed regular hemodialysis sessions without immediate complications.

First Allergic Episode

On March 1, 2025, during his routine Monday dialysis session, the patient developed acute symptoms within 5 minutes of dialysis initiation. He complained of sudden onset shortness of breath, chest tightness, and generalized pruritus without visible rash. Vital signs revealed tachycardia (heart rate 118 beats per minute), hypotension (blood pressure 82/54 mmHg, baseline 140/85 mmHg), and tachypnea (respiratory rate 26 breaths per minute). Oxygen saturation was found to be 91% on room air. On auscultation there was bilateral wheeze throughout both lung fields. Body temperature was 37.1°C (98.8°F). There was no fever, and the patient remained conscious and oriented throughout the episode.

The dialysis session was immediately discontinued, blood lines were clamped, and the patient was placed in Trendelenburg position. Emergency management included intravenous hydrocortisone 200 mg, chlorpheniramine 10 mg, and rapid infusion of 500 mL normal saline. Within 20 minutes, symptoms improved significantly with blood pressure recovering to 110/70 mmHg, heart rate decreasing to 92 beats per minute, oxygen saturation improving to 97% on room air, and complete resolution of respiratory distress and pruritus. The patient was monitored for an additional 2 hours in the dialysis unit and discharged home in stable condition with instructions to report any delayed symptoms.

Initial Diagnostic Approach and Intervention

Given the timing of symptom onset shortly after dialysis initiation and the patient's recent transition from fistula to catheter, we initially suspected a dialyzer membrane reaction. Although the patient had previously tolerated the Fresenius F8 polysulfone membrane without any issues, hypersensitivity reactions can develop after years of uneventful exposure due to progressive sensitization [14]. Alternative considerations included first-use syndrome (despite reprocessing protocols), air embolism (though no radiographic evidence), hemolysis (normal plasma hemoglobin and no red-tinged plasma observed), or dialysate contamination (quality control checks were negative).

Laboratory investigations performed immediately after the episode revealed: hemoglobin 9.1 g/dL (unchanged from baseline), we ruled out significant hemolysis, and negative bacterial cultures of dialysate samples.

As a precautionary measure, the dialysis membrane was changed to a Fresenius F6 polysulfone dialyzer (surface area 1.3 m^2, smaller pore size, different manufacturing lot) for subsequent sessions. Pre-dialysis premedication with intravenous hydrocortisone 100 mg and chlorpheniramine 4 mg was initiated 30 minutes before each session. All other dialysis parameters remained unchanged, including blood flow rate, dialysate composition, heparin dosing, and importantly, continued use of 2% chlorhexidine gluconate for catheter site antisepsis.

Asymptomatic Interval

Following the membrane change and premedication regimen, the patient successfully completed 19 consecutive hemodialysis sessions over a 6-week period (March 3, 2025 to April 14, 2025) without any further allergic symptoms. Dialysis adequacy also remained satisfactory with Kt/V which was consistently >1.4, ultrafiltration volumes were satisfactorily achieved (2.0-3.2 kg per session), and the patient reported good overall well-being. Vital signs remained stable throughout all sessions, with no episodes of hypotension, respiratory symptoms, or any cutaneous reactions. The absence of reactions during this prolonged period reinforced the initial hypothesis we had of dialyzer membrane-related hypersensitivity, and we considered gradually tapering and discontinuing the premedication regimen.

Second Allergic Episode

On April 17, 2025, the patient arrived for his scheduled Friday dialysis session in his usual state of health. Notably, and also critically for establishing the causation, the second severe reaction occurred during catheter exit site preparation, which was before connection to the dialysis circuit. Within 2-3 minutes of applying 2% chlorhexidine gluconate solution to the catheter exit site and allowing it to dry, the patient developed rapidly progressive symptoms.

He first noted perioral and periauricular tingling sensation, followed immediately (within 30-60 seconds) by generalized urticaria with raised, erythematous, intensely pruritic wheals covering his trunk, arms, neck, and face. Within one minute, he developed severe respiratory distress with

inspiratory stridor, persistent dry cough, and sensation of throat tightness and tongue swelling suggestive of laryngeal and lingual angioedema. Blood pressure dropped to 68/40 mmHg and his heart rate was 134 beats per minute (sinus tachycardia on monitor). Oxygen saturation fell to 86% on room air despite increased respiratory effort. The patient became increasingly anxious and diaphoretic, reporting an overwhelming sensation of "impending doom", a classic and ominous symptom of severe anaphylaxis. No chest pain or loss of consciousness occurred.

This presentation met the diagnostic criteria for anaphylaxis as defined by the World Allergy Organization: acute onset of illness (minutes) with involvement of skin/mucosal tissue (urticaria, angioedema) plus respiratory compromise (dyspnea, wheeze, stridor, hypoxemia) plus cardiovascular involvement (hypotension, tachycardia) [15]. The Brighton Collaboration Criteria level 1 diagnostic certainty for anaphylaxis was found to be fulfilled.

Emergency Management of Second Episode

Given the severity, rapid progression, and clear diagnosis of anaphylaxis, the patient received the following interventions according to standard anaphylaxis treatment guidelines:

- Intramuscular adrenaline (epinephrine) 0.5 mg (1:1000 dilution) was injected into the anterolateral aspect of the right thigh, which was administered within 2 minutes of symptom onset. A second dose of 0.5 mg was administered 5 minutes later due to persistent hypotension and respiratory distress. High-flow oxygen via non-rebreather mask at 15 liters per minute was given. Intravenous hydrocortisone 200 mg bolus, intravenous chlorpheniramine 10 mg, intravenous ranitidine 50 mg, rapid infusion of 1000 mL normal saline and nebulized salbutamol 5 mg (two doses) was given.

The patient showed gradual improvement over 15-20 minutes following the second dose of adrenaline. Blood pressure stabilized at 95/60 mmHg by 10 minutes and improved to 108/68 mmHg by 20 minutes. Heart rate decreased to 105 beats per minute. Oxygen saturation improved to 97% by 30 minutes. The urticarial rash began to fade though pruritus persisted for approximately 2 hours. Respiratory distress markedly improved with resolution of stridor.

Given the severity of the reaction, requirement for two doses of adrenaline, and risk of biphasic reaction (occurring in 1-20% of cases, typically 4-12 hours after initial episode), the patient was transferred to the intensive care unit for 24-hour monitoring. He received 100 mg of intravenous hydrocortisone every 6 hours, continuous intravenous fluids, and antihistamines. No biphasic reaction occurred.

The planned dialysis session was cancelled. However, given 48 hours without dialysis and developing fluid overload (2.8 kg above dry weight), urgent hemodialysis was performed 6 hours post-stabilization with povidone-iodine 10% solution for catheter antisepsis instead of chlorhexidine. No premedication was given. The 3-hour session was completed successfully without any adverse reactions.

Comprehensive Diagnostic Evaluation

Following the second severe anaphylactic episode, a comprehensive evaluation was undertaken to definitively identify the possible causative agent and exclude alternative diagnoses.

Parameter	Value	Reference Range
Hematology		
Hemoglobin	9.2 g/dL	13.5-17.5 g/dL
WBC count	11,800/μL	4,000-11,000/μL
Neutrophils	78%	40-70%
Eosinophils	2%	1-4%
Platelet count	245,000/μL	150,000-400,000/μL
Peripheral smear	Hypochromic microcytic anemia; no schistocytes or tear drop cells	
Immunology		
Serum total IgE (24h post-reaction)	285 IU/mL	<100 IU/mL
Chlorhexidine-specific IgE	Not performed (clinical diagnosis clear)	
Renal Function		
Serum creatinine	8.4 mg/dL	0.6-1.2 mg/dL
Blood urea nitrogen	86 mg/dL	7-20 mg/dL
Hepatic Function		
AST	15 IU/L	10-40 IU/L
ALT	24 IU/L	7-56 IU/L
Alkaline phosphatase	154 IU/L	44-147 IU/L
Total bilirubin	0.55 mg/dL	0.3-1.2 mg/dL
Direct bilirubin	0.30 mg/dL	0-0.3 mg/dL
Serum LDH	165 U/L	140-280 U/L
Proteins		
Total protein	6.2 g/dL	6.4-8.3 g/dL
Serum albumin	3.2 g/dL	3.5-5.5 g/dL
Serum globulin	3.0 g/dL	2.3-3.5 g/dL
Electrolytes		
Sodium	138 mEq/L	136-145 mEq/L
Potassium	5.2 mEq/L	3.5-5.0 mEq/L
Chloride	102 mEq/L	98-107 mEq/L
Bicarbonate	19 mEq/L	22-29 mEq/L
Microbiology		
Blood culture	No growth	
Equipment Testing		
Dialyzer integrity (F6)	No breach; no fiber rupture on pressure testing	

Table 1. Detailed Investigations done on April 17, 2025, during second episode.

Retrospective Analysis and Identification of Causative Agent

A meticulous timeline analysis of both allergic episodes was conducted by our team in consultation with an allergist-immunologist, examining all potential exposures, equipment changes, and procedural variations which could have triggered the event (detailed in Table 1). This systematic approach revealed several critical observations that pointed conclusively to chlorhexidine as the causative agent:

- First, both reactions occurred after the patient's transition from arteriovenous fistula to tunneled catheter, despite nearly three years of uneventful chlorhexidine exposure during fistula use. This suggested that probably the route or site of chlorhexidine application was relevant to sensitization and the reaction.
- Second, the initial reaction which occurred on March 1st occurred 5 minutes into dialysis, which was shortly after catheter connection which followed chlorhexidine antisepsis of the exit site. While the timing initially suggested a dialyzer-related etiology, in retrospect this was consistent with absorption of chlorhexidine through the compromised skin barrier at the catheter exit site.

- Third, and most critically, the patient remained completely asymptomatic for 19 consecutive sessions (which spanned over 6 weeks) after changing the dialyzer membrane from F8 to F6, despite continued use of chlorhexidine for catheter antisepsis. This prolonged asymptomatic period ruled out an allergic reaction to the F6 membrane itself and suggested that the F8 membrane was not the primary culprit.
- Fourth, the final definitive diagnostic clue emerged when the second, more severe anaphylactic episode occurred during catheter exit site preparation with chlorhexidine application, even before the patient was connected to the dialysis machine. This timing conclusively eliminated all dialysis circuit-related factors (dialyzer membrane, dialysate components, blood tubing, heparin) as potential causes, as the reaction occurred without any exposure to the dialysis system.
- Fifth, when urgent dialysis was performed 6 hours later using povidone-iodine instead of chlorhexidine for catheter antisepsis, the session was completed without any adverse reactions despite using the same F6 dialyzer, same dialysate, same heparin, and even the same tunneled catheter.

Further detailed history has revealed additional supportive evidence. During the nearly three years of arteriovenous fistula use, chlorhexidine had been applied to intact skin before needle insertion. The skin barrier remained uninterrupted, which prevented deep dermal penetration of the antiseptic. In contrast, here with the tunneled catheter, chlorhexidine was applied directly to and around the catheter exit site – an area where the normal epidermal barrier is permanently disrupted by the foreign body (catheter) traversing through all skin layers. This compromised barrier likely facilitated deeper penetration of chlorhexidine into the dermis where antigen-presenting cells reside, enabling sensitization that had not occurred during years of superficial application to intact fistula skin.

Systematic Exclusion of Alternative Diagnoses

- Dialyzer membrane reaction: Excluded by occurrence of second reaction before dialysis connection and successful dialysis with same F6 membrane after chlorhexidine avoidance
- Heparin allergy: Excluded by negative history of prior heparin exposure complications and successful dialysis with identical heparin regimen after chlorhexidine substitution
- Latex allergy: Excluded by patient history of tolerating latex glove exposure and absence of reactions to latex-containing medical devices
- Ethylene oxide residue (sterilant): Excluded by proper dialyzer rinsing protocols, negative quality control testing, and persistence of reactions across multiple dialyzer lots
- Dialysate contamination: Excluded by negative endotoxin testing, negative cultures, and reactions occurring with different dialysate batches
- Catheter material hypersensitivity: Excluded by successful continued use of the same catheter after chlorhexidine substitution
- Other medications: no new medications introduced; all chronic medications continued unchanged through both reaction periods and recovery period

Retrospective Analysis

- We also investigated whether prior surgical procedures could have contributed to initial sensitization. Detailed review of procedural records revealed that povidone-iodine 10% solution was used as the standard antiseptic for skin preparation during both the original arteriovenous fistula creation surgery, but chlorhexidine was used during the tunneled catheter insertion. Additionally, the patient denied any history of urinary catheterization or other procedures where chlorhexidine gel might have been used. This information hence further supports our hypothesis that sensitization occurred specifically through tunneled catheter exit site rather than through prior surgical interventions.
- The increasing number of reported chlorhexidine hypersensitivity cases in recent years requires particular attention. Several factors may contribute to this trend such as the widespread adoption of chlorhexidine as the preferred antiseptic following the CDC guidelines has increased exposure across healthcare settings, particularly in dialysis populations with frequent, repeated applications. Improved recognition and reporting of chlorhexidine allergy by clinicians has led to more case identification that may have previously been missed. In addition, the increasing use of chlorhexidine-coated medical devices (such as urinary catheters, central lines, wound dressings) has created additional sensitization pathways beyond topical antiseptic application. This emerging pattern suggests that healthcare providers, particularly in nephrology and dialysis settings, must maintain heightened vigilance for this increasingly noticed reaction.

Long-term Outcome

Following implementation of the chlorhexidine avoidance strategy in this patient and povidone-iodine substitution, the patient has successfully completed more than 35 consecutive hemodialysis sessions without any allergic symptoms or complications. Dialysis adequacy has been maintained with consistent Kt/V values >1.4. The catheter exit-site has remained clean and infection-free with the alternative antiseptic regimen, with no increase in catheter-related infections compared to the chlorhexidine period. Pre-dialysis premedication with antihistamines was successfully discontinued after the fifth uneventful session with no recurrence of symptoms. He now continues maintenance hemodialysis via the tunneled catheter using povidone-iodine for skin antisepsis before needle cannulation, and remains completely free of allergic reactions through over 35 subsequent sessions. His quality of life has markedly improved with restoration of confidence in dialysis safety and elimination of anxiety related to potential reactions.

The “Sensitization Window” Phenomenon

Our case uniquely demonstrates a “sensitization window” phenomenon that provides us insights into chlorhexidine hypersensitivity development in dialysis patients. The patient tolerated chlorhexidine application to intact skin over his arteriovenous fistula for nearly three years without any adverse reactions. However, after he transitioned to a tunneled catheter, he developed progressive sensitization leading to severe anaphylaxis. This pattern highlights the critical role of skin barrier integrity in determining allergen exposure and immune response.

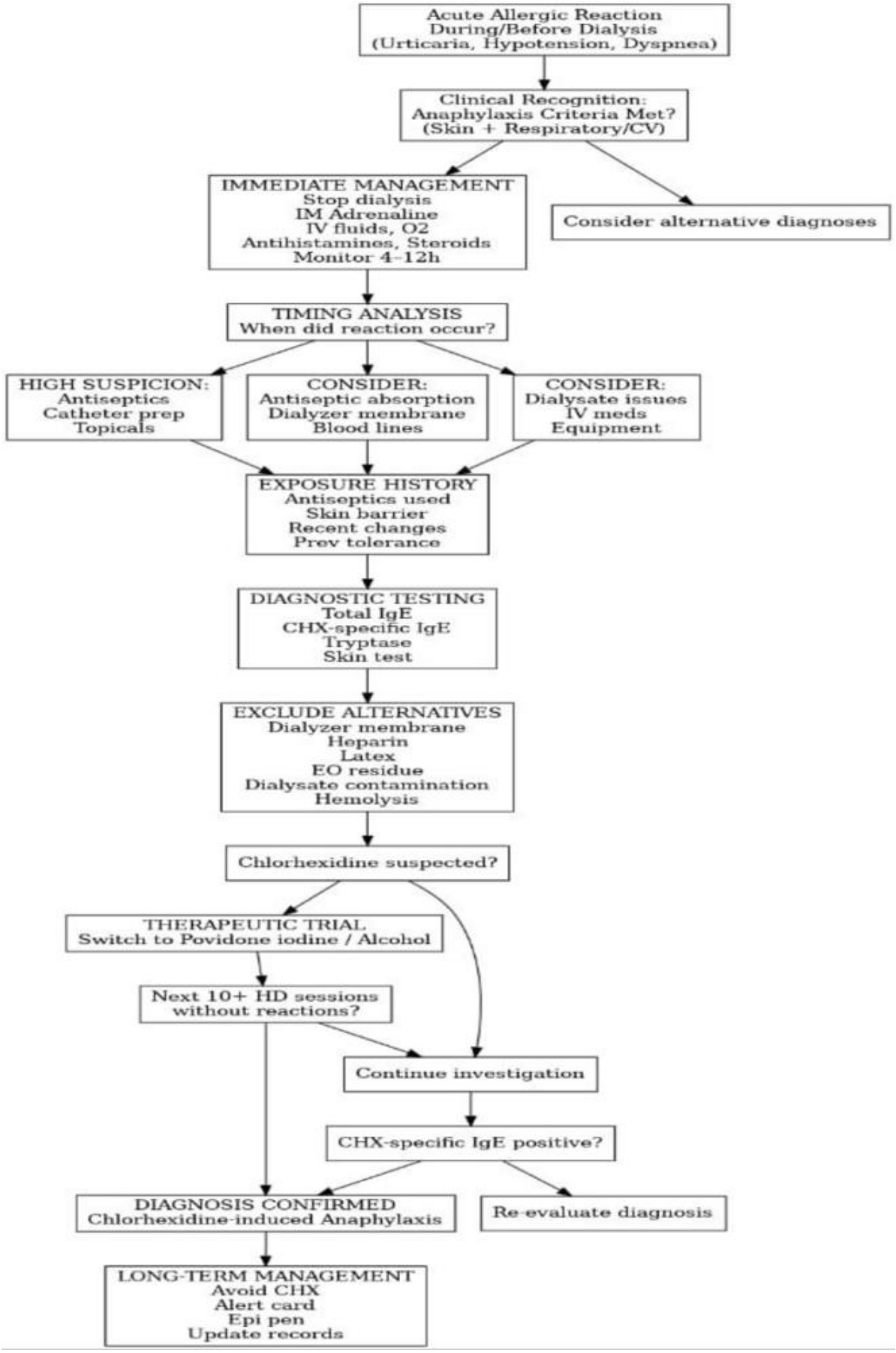

Figure 1. Proposed diagnostic approach for suspected chlorhexidine anaphylaxis in dialysis patients.

Date/Period	Dialyzer	Vascular Access	Antiseptic Agent	Premedication	Clinical Events	Management	Outcome
Dec 2021 (3 Months)	Fresenius F8 (1.8 m2)	Right IJV non tunneled catheter (Povidone Iodine)	Povidone Iodine for insertion and 2% chlorhexidine gluconate during HD	None	None	Routine HD	Asymptomatic throughout entire period
Feb 2022-sept 2024 (2 years)	Fresenius F8 ($1.8m^2$)	Left brachiocephalic AVF	Povidone Iodine 10%used during surgery and 2% chlorhexidine gluconate during HD	None	None	Routine HD	Asymptomatic throughout entire period
Sept 2024	N/A	Right femoral tunneled catheter inserted	2% chlorhexidine for insertion	None	None	Catheter placement	Successful insertion, no immediate reactions
Sept 2024-Feb 2025 (6 months)	Fresenius F8 ($1.8m^2$)	Tunneled catheter	2% chlorhexidine gluconate for HD	None	None	Routine HD	Asymptomatic (sensitization window)
March 1, 2025	Fresenius F8	Tunneled catheter	2% chlorhexidine	None	Onset 5 min after HD initiation: dyspnea, hypotension (82/54 mmHg), pruritus, tachycardia (HR 118), SpO_2 91%, bilateral wheeze	HD stopped; IV hydrocortisone 200mg, chlorpheniramine 10mg, NS 500mL bolus	Resolution in 20 min; discharged stable
March 3, 2025	Fresenius F6 ($1.3m^2$) [CHANGED]	Tunneled catheter	2% chlorhexidine	Hydrocortisone 100mg + chlorpheniramine 4mg pre-HD	None	New membrane + premedication	Session completed successfully
March 3-April 14 (19 sessions)	Fresenius F6	Tunneled catheter	2% chlorhexidine gluconate	Continued premedication	None	Routine HD with premedication	All sessions completely asymptomatic
April 17, 2025 (DIAGNOSTIC)	Fresenius F6 (not connected)	Tunneled catheter	2% chlorhexidine	Premedication given	Onset 2-3 min during catheter prep BEFORE HD connection: perioral tingling, generalized urticaria, stridor, throat tightness, severe hypotension (68/40), HR 134, SpO_2 86%, respiratory distress, "impending doom"	HD CANCELLED; IM epinephrine 0.5mg x2 doses, high-flow O_2 15L/min, IV hydrocortisone 200mg, chlorpheniramine 10mg, ranitidine 50mg, NS 1000mL rapid, nebulized salbutamol	ICU admission 24hrs; stabilized in 20 min; no biphasic reaction
April 17, 2025 (6hrs later)	Fresenius F6	Same tunneled catheter	10% povidone-iodine [SWITCHED]	None	None	Urgent HD in different unit	Completed 3hrs without any complications
April 19- Present	Fresenius F6	Tunneled catheter	10% povidone-iodine	None after 5th session	None	Routine HD	All sessions asymptomatic; premedication discontinued

Table 2. Detailed chronological timeline of dialysis sessions and allergic reactions.
Abbreviations: **HD, hemodialysis; AVF, arteriovenous fistula; IJV, internal jugular vein; HR, heart rate; SpO_2, oxygen saturation; IV, intravenous; IM, intramuscular; NS, normal saline; ICU, intensive care unit; N/A, not applicable.**

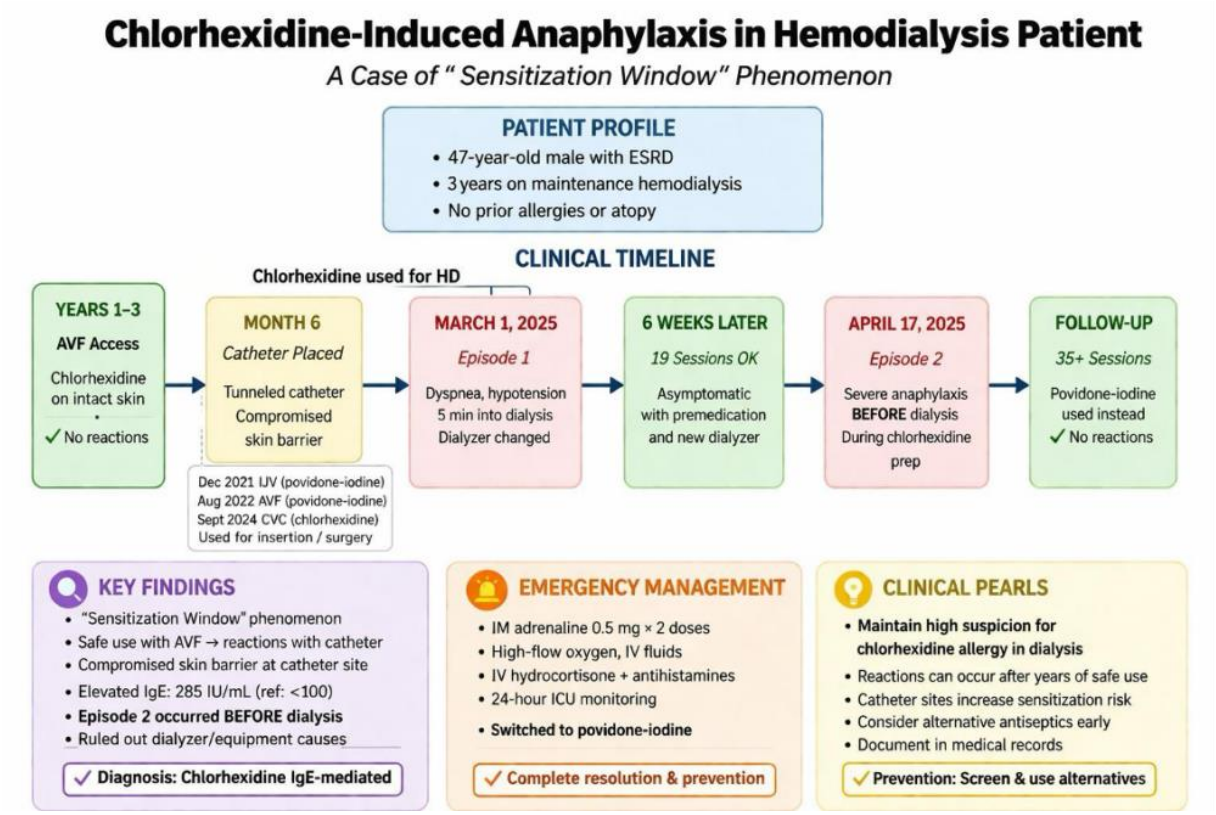

Figure 2. Clinical timeline.

The pathophysiology can be understood through a multi-step model: (1) Initial exposure phase: During fistula use, chlorhexidine applied to intact skin remained largely confined to the stratum corneum, with minimal dermal penetration and limited access to antigen-presenting cells; (2) Sensitization phase: After catheter placement, the catheter exit site represents a permanent breach in the epithelial barrier, allowing deeper penetration of chlorhexidine into the dermis where Langerhans cells and dermal dendritic cells reside [16]; (3) These antigen-presenting cells process chlorhexidine-protein conjugates and initiate a type I hypersensitivity sensitization response, in which T-helper cells stimulate B cells to produce allergen-specific IgE antibodies [4, 17]; (4) Sensitization establishment: Over approximately 6 months (September 2024 to March 2025) of repeated exposure through the compromised catheter site, chlorhexidine-specific IgE antibodies accumulated and bound to mast cells and basophils throughout the body; (5) Effector phase: Subsequent chlorhexidine exposure triggered IgE cross-linking, mast cell degranulation, and the clinical manifestations of anaphylaxis [4, 17].

This sensitization window concept has several important clinical implications. It suggests that patients who have generally tolerated chlorhexidine during fistula use are NOT immune to developing hypersensitivity if at all they subsequently require catheter access. Clinicians should maintain vigilance for chlorhexidine reactions even in patients with long histories of uneventful exposure, particularly after transitioning to catheter-based access.

Our case shares important similarities with previously reported cases while contributing unique features that helps us in understanding of chlorhexidine hypersensitivity in dialysis patients, we provide detailed documentation of a prolonged "sensitization window" with almost three years of safe chlorhexidine exposure during fistula use, followed by reaction which occurred only after catheter placement with compromised skin integrity – a phenomenon not extensively noted in prior reports. The occurrence of the reaction during catheter preparation before dialysis connection provided strong evidence, distinguishing this case from reports where multiple triggers remained

confounded with the dialysis circuit. We also document a 19-session asymptomatic interval between reactions, which highlights the diagnostic challenges clinicians face. Finally, our long-term follow-up (35+ sessions) with successful alternative antiseptic use demonstrates practical management approaches. Together, these features help us in understanding chlorhexidine sensitization mechanisms and aids in diagnostic strategies in dialysis populations.

Table 3 provides a systematic comparison of key published cases.

Study	Age/Sex	Access Type	Exposure Duration	Diagnostic Confirmation	Management	Unique Features
Bahal et al. 2017 [18] (UK)	54/M	Tunneled catheter	Not specified	Skin prick test positive	Switched to povidone-iodine	First UK dialysis case; emphasized diagnostic delays
Tan et al. 2022 [8] (Singapore)	2 patients 52-68 yrs	Tunneled catheters	Variable	Skin prick test positive for both	All switched to alternatives	Case series; highlighted diagnostic protocol need
Current Case 2025 (India)	47/M	Tunneled catheter (prior AVF 3yrs)	6 months on catheter; 3yrs prior fistula exposure	Elevated total IgE (285), Therapeutic response	Switched to povidone-iodine	"sensitization window" with prior safe fistula use; reaction BEFORE dialysis connection (diagnostic); detailed 19-session asymptomatic interval; long-term follow-up

Table 3. Comparison of published chlorhexidine anaphylaxis cases in hemodialysis patients.

Conclusion

This case report provides detailed documentation of chlorhexidine-induced anaphylaxis in a hemodialysis patient, demonstrating critical diagnostic and management principles. The patient's "sensitization window" phenomenon with almost three years of safe chlorhexidine exposure during arteriovenous fistula and subsequent 19 sessions asymptomatic after first episode followed by severe anaphylaxis second episode which all occurred after transition to tunneled catheter with compromised skin barrier integrity needs to be noted. The definitive diagnostic clue – occurrence of the second severe reaction during catheter site preparation before dialysis connection – indicated chlorhexidine as the causative agent and excluded all dialysis circuit-related factors.

Future research should focus on identifying patient-specific risk factors for chlorhexidine sensitization, developing validated screening tools, investigating whether lower chlorhexidine concentrations reduce sensitization risk while maintaining antimicrobial efficacy, and conducting comparative effectiveness studies of alternative antiseptics in dialysis populations. Increased reporting of cases from diverse geographical regions will improve understanding of the true global incidence and inform evidence-based practice guidelines.

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