

The Role of Thiazide Diuretics in Hypertension with Chronic Kidney Disease: Benefits and Risks

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Abstract. Hypertension is a common complication of chronic kidney disease (CKD) and contributes to renal disease progression and cardiovascular risk. Although the effectiveness of thiazide diuretics in advanced CKD has been questioned, recent evidence indicates that thiazide and thiazide-like diuretics remain useful for blood pressure control. This literature review aimed to evaluate the role, benefits, and potential risks of thiazide diuretics in managing hypertension among patients with CKD. A narrative literature review was conducted using national and international journals and clinical practice guidelines published between 2021 and 2026. A total of 806 articles were identified, and 11 studies met the predefined inclusion and exclusion criteria for qualitative analysis. The findings demonstrated that thiazide and thiazide-like diuretics effectively reduced blood pressure in patients with CKD, including those with advanced disease and resistant hypertension. Chlorthalidone significantly reduced systolic blood pressure and albuminuria, indicating potential renoprotective benefits. Combination therapy with angiotensin-converting enzyme inhibitors or angiotensin receptor blockers provided better blood pressure control than monotherapy. However, adverse effects included hypokalemia, hyponatremia, hyperuricemia, hypotension, and transient increases in serum creatinine. Thiazide diuretics remain valuable for hypertension management in CKD, but treatment should be individualized and accompanied by regular monitoring of renal function and electrolytes. Lifestyle modification should complement pharmacological therapy to optimize outcomes.

Keywords: Thiazide Diuretics, Hypertension, Chronic Kidney Disease

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INTRODUCTION

Hypertension is a major complication in patients with chronic kidney disease and contributes to the progression of kidney damage and an increased risk of cardiovascular disease (Husaini, F., & Fonna, 2024; Putri, 2026). Sodium and fluid retention due to declining kidney function causes most patients with chronic kidney disease to experience difficult-to-control hypertension (Alsalloum et al., 2025; Ku et al., 2019; Salman, 2015; Polychronopoulou et al., 2021; Carswell & O'Neil, 2024). Therefore, blood pressure control is an important strategy to slow the progression of chronic kidney disease and reduce patient mortality. Thiazide diuretics have long been used as antihypertensive therapy because they increase sodium and water excretion, thereby helping to lower blood pressure (Blebea et al., 2025; Morales-Olivas, 2024; Ernst & Fravel, 2022; Burnier et al., 2019). Although the use of thiazides in advanced stages of chronic kidney disease was previously considered less effective due to decreased glomerular filtration rate, recent research has shown that thiazide-like diuretics, such as chlorthalidone, are still

effective in patients with chronic kidney disease with resistant hypertension (Jo et al., 2023; Minutolo et al., 2023).

Research developments in recent years have shown that thiazide diuretics are not only beneficial in controlling blood pressure but also have protective effects on the kidneys (Trujillo et al., 2021; Palmer & Clegg, 2018; Kramers et al., 2021; Delanaye & Scheen, 2021). The CLICK study reported that chlorthalidone use in patients with advanced chronic kidney disease significantly reduced systolic blood pressure and albuminuria compared to placebo (Agarwal et al., 2021; Georgianos & Agarwal, 2023; Pitt & Auchus, 2024). Furthermore, a recent systematic review and meta-analysis found that thiazide and thiazide-like diuretics remain effective in patients with advanced kidney function decline, especially when combined with other antihypertensives such as ACE inhibitors or angiotensin receptor blockers (ARBs). These findings support the use of thiazide diuretics as part of hypertension therapy in certain patients with chronic kidney disease (Minutolo et al., 2023; Teles et al., 2023).

Despite significant clinical benefits, the use of thiazide diuretics in hypertensive patients with chronic kidney disease also carries several risks that require attention. Side effects such as hypokalemia, hyponatremia, hyperuricemia, hypotension, and transient increases in creatinine levels can occur, particularly in elderly patients and those with advanced chronic kidney disease. Electrolyte disturbances due to diuretic use can worsen the patient's clinical condition if not monitored regularly. Therefore, selecting the right type of diuretic, the right dose, and monitoring kidney function and electrolyte levels are very necessary so that therapy can run effectively and safely.

METHODS

This study employed a narrative literature review approach to examine the role, clinical benefits, and potential risks of thiazide and thiazide-like diuretics in the management of hypertension among patients with chronic kidney disease (CKD). This approach was selected because it enables findings from different types of scientific evidence, including clinical trials, observational studies, systematic reviews, narrative reviews, and clinical practice guidelines, to be integrated into a comprehensive clinical discussion. The review used secondary data obtained from relevant national and international scientific publications.

The literature search focused primarily on studies published between 2021 and 2026. However, several earlier publications were retained when they provided important theoretical explanations, foundational clinical evidence, or established recommendations that remained relevant to hypertension and CKD management. Clinical guidelines and global epidemiological reports, including JNC 8 and other relevant guidance documents, were also considered as supporting references. The inclusion of these earlier sources was intended to strengthen the conceptual and clinical foundation of the review rather than replace the more recent evidence.

The literature was identified through relevant electronic scientific databases and academic search platforms. The search strategy used combinations of terms related to the principal concepts of the review, including “thiazide diuretics,” “thiazide-like diuretics,” “chlorthalidone,” “hydrochlorothiazide,” “hypertension,” “chronic kidney disease,” “advanced chronic kidney disease,” “resistant hypertension,” “blood pressure control,” “albuminuria,” “proteinuria,” “renal protection,” “kidney function,” and “adverse effects.” The keywords were combined according to the functions available on each database or academic search platform to identify publications relevant to the research objective.

Publications were considered eligible when they met the following criteria: (1) discussed thiazide or thiazide-like diuretics in relation to hypertension management; (2) included patients with CKD or presented clinical evidence applicable to the management of hypertension in CKD; (3) evaluated at least one relevant outcome, such as blood pressure reduction, fluid control, albuminuria, proteinuria, renal function, electrolyte disturbances, treatment safety, or adverse effects; (4) presented sufficient information to support the interpretation of the findings; (5) were

available in full text; and (6) were published in English or Indonesian. Clinical practice guidelines and review articles were included when they provided relevant recommendations or synthesized evidence concerning antihypertensive treatment in patients with CKD.

Publications were excluded when they were duplicates, unavailable in full text, unrelated to the research objective, or did not provide relevant information regarding the effectiveness or safety of thiazide diuretics. Studies that focused exclusively on populations without hypertension or CKD were also excluded unless their findings provided relevant supporting evidence regarding diuretic mechanisms, treatment safety, or combination therapy. Publications with insufficient methodological or clinical information were not included in the final synthesis.

The initial search identified 806 potentially relevant publications. The researchers first screened the titles and abstracts to determine their relevance to thiazide diuretic therapy, hypertension, and CKD. Publications that did not meet the eligibility criteria were removed during this stage. The remaining publications were assessed through full-text reading to determine whether they contained adequate information on the study population, intervention, outcomes, therapeutic benefits, and possible risks. Following the screening and eligibility assessment, 11 studies were selected for inclusion in the final review.

Relevant information was extracted from each included publication, including the authors, year of publication, article title, study design, clinical population or context, type of intervention, principal findings, reported adverse effects, and study conclusions. The extracted information was organized in a study-characteristics table to facilitate comparison among the included publications. Because the selected sources differed in their study designs, populations, interventions, and reported outcomes, the findings were synthesized narratively rather than statistically pooled.

The synthesis was organized according to the main themes identified across the included studies. These themes included the effectiveness of thiazide and thiazide-like diuretics in reducing blood pressure, their effects on fluid retention and albuminuria, their potential contribution to renal protection, their use in combination with other antihypertensive agents, and their safety in patients with reduced kidney function. Particular attention was given to clinically important adverse effects, including hypokalemia, hyponatremia, hyperuricemia, hypotension, and transient increases in serum creatinine. Evidence concerning lifestyle modification and regular monitoring of renal function and electrolyte levels was also considered to provide a comprehensive interpretation of hypertension management in patients with CKD.

The conclusions were developed by comparing the consistency and clinical relevance of findings across the 11 included studies. Greater interpretive emphasis was placed on evidence that directly evaluated thiazide or thiazide-like diuretics in patients with CKD, particularly studies involving advanced CKD or resistant hypertension. Nevertheless, the findings were interpreted cautiously because the included publications represented different types of evidence and were not subjected to statistical meta-analysis.

RESULT AND DISCUSSION

Based on the search results, 806 articles were obtained from the keyword search "The Role of Thiazide Diuretics in Hypertension with Chronic Kidney Disease: Benefits and Risks." All journals were included in the search and screening. Then, the researchers screened the titles and abstracts of the articles. At this screening stage, 757 articles were excluded because they contained research that did not meet the inclusion criteria or were published within the last 5 years. Finally, 11 remaining articles were obtained that met the inclusion criteria and will be used for this literature review.

Table 1. Characteristics and Synthesis of Studies Included in the Literature Review on the Role of Thiazide Diuretics in Hypertension Among Patients with Chronic Kidney Disease

No	Year	Title and Author	Research methods	Key Results	Conclusion	Category
1	2023	Therapeutic Roles of Thiazides and Loop Diuretics in Blood Pressure Control and Renal Protection Against Chronic Kidney Disease – W. Jo, E.S. Koh, S. Chung	Narrative review	Thiazide and loop diuretics remain effective in lowering blood pressure in patients with CKD, including those in advanced stages. Chlorthalidone has demonstrated high efficacy in resistant hypertension.	Thiazide diuretics again have an important role in the management of hypertension with CKD but require monitoring of renal function and electrolytes..	Article Review
2	2023	Thiazides in Chronic Kidney Disease: “Back to the Future” – De La Espriella, dkk	Narrative review	The old paradigm that thiazides are ineffective at low eGFR is starting to change after several recent studies showed the effectiveness of chlorthalidone in advanced CKD.	Thiazides can still be used in advanced CKD, especially resistant hypertension, with close monitoring.	Article Review
3	2023	Effectiveness of Thiazide and Thiazide-like Diuretics in Advanced Chronic Kidney Disease: A Systematic Review and Meta-analysis – F. Teles et al.	Systematic review dan meta-analysis	Thiazide diuretics remain effective in lowering blood pressure in patients with advanced CKD and help reduce fluid overload.	Thiazide and thiazide-like diuretics are still useful in advanced CKD even though kidney function is declining.	Systematic Review & Meta-analysis

4	2025	Executive Summary of the KDIGO 2021 Clinical Practice Guideline for the Management of Blood Pressure in Chronic Kidney Disease – Iatridi et al.	Clinical practice guideline	A systolic blood pressure target of <120 mmHg is recommended in most CKD patients with standard measurements.	Optimal blood pressure control can slow the progression of CKD and reduce cardiovascular complications.	Guideline
5	2023	Use of Metolazone as an Adjunct Therapy to Loop Diuretics in Diuretic Resistant Acute Decompensation of Heart Failure: A Systematic Review and Meta-analysis – Shrestha D, et al.	Systematic review dan meta-analysis	The combination of metolazone with loop diuretics increases diuresis and helps overcome diuretic resistance in acute heart failure.	Metolazone is effective as an adjunct therapy for fluid overload but increases the risk of electrolyte disturbances.	Systematic Review & Meta-analysis
6	2021	Chlorthalidone for Hypertension in Advanced Chronic Kidney Disease – R. Agarwal et al.	Randomized Controlled Trial (CLICK Trial)	Chlorthalidone significantly reduces systolic blood pressure and albuminuria in stage 4 CKD with resistant hypertension.	Chlorthalidone is effective in advanced CKD hypertension but carries a risk of hypokalemia and transient increases in creatinine.	Randomized Controlled Trial
7	2024	Thiazide Discontinuation in Chronic Kidney Disease Hypertension Management: A Retrospective Chart Review – Dalangin Veja, et al.	Retrospective chart review	Most thiazide discontinuations are due to electrolyte disturbances, hypotension, and decreased renal function.	The use of thiazides in CKD requires close monitoring to prevent side effects of therapy.	Retrospective Study

8	2022	Thiazides and Mineralocorticoid Receptor Antagonists in Chronic Kidney Disease – Niculae, et al.	Narrative review	The combination of thiazide and mineralocorticoid receptor antagonists may help resistant hypertension in CKD.	Combination antihypertensive therapy provides additional benefits but increases the risk of hyperkalemia and renal impairment.	Article Review
9	2026	Management of Hypertension in Chronic Kidney Disease – Doulton, et al.	Clinical review	Management of hypertension in CKD requires a combination of lifestyle modification and individual pharmacological therapy.	Blood pressure control is the main strategy to slow the progression of CKD.	Clinical Review
10	2025	Comprehensive Review of Antihypertensive Therapy: Pathophysiology, Diagnosis, and Management – Yuar.	Comprehensive literature review	Various classes of antihypertensives including ACE inhibitors, ARBs, CCBs, beta blockers, and diuretics have an important role in the management of hypertension.	The choice of antihypertensive therapy must be adjusted to the patient's clinical condition and comorbidities.	Literature Review
11	2021	Identifikasi Drug Related Problems (DRPs) Obat Antihipertensi pada Pasien Hipertensi di Puskesmas Dharma Rini Temanggung – Khusna N, Murdiana H.	Retrospective observational descriptive	Various DRPs were found such as inappropriate dosage, drug interactions, and antihypertensive side effects.	Monitoring of antihypertensive therapy is important to increase the effectiveness and safety of treatment for hypertensive patients..	Descriptive Observational

Based on a review of several journals, hypertension in patients with Chronic Kidney Disease (CKD) is a very common condition caused by impaired fluid regulation and sodium retention in the kidneys. The use of diuretics, particularly thiazide and loop diuretics, has been shown to help control blood pressure in CKD patients, including in advanced stages. Research by Wonji Jo et al. (2023) explains that diuretics are effective in lowering blood pressure and helping reduce fluid overload in CKD patients, thereby slowing the progression of kidney disease. Furthermore, research by Rajiv Agarwal et al. (2021) in the CLICK clinical trial showed that

chlorthalidone was able to reduce systolic blood pressure by 11.0 mmHg in patients with advanced CKD. These findings indicate that diuretics still have important clinical benefits in the management of hypertension in CKD (Shrestha et al., 2023).

In addition to helping lower blood pressure, several journals also indicate that diuretics have antiproteinuric effects that have the potential to provide kidney protection. Research by Jo et al. (2023) stated that the use of chlorthalidone and hydrochlorothiazide can reduce albuminuria by 40–52% in CKD patients. This reduction in proteinuria is important because proteinuria is a major risk factor for the progression of kidney damage. Furthermore, research by Niculae et al. (2022) found that combining diuretic therapy with renin-angiotensin system inhibitors can improve blood pressure control while reducing intraglomerular pressure. Therefore, combination antihypertensive therapy is considered more effective than monotherapy in CKD patients with difficult-to-control hypertension (Vea et al., 2024).

Despite its beneficial effects, diuretic use in CKD patients still carries the risk of side effects that require attention. Several studies have shown increased serum creatinine levels, hypokalemia, and other electrolyte disturbances during diuretic therapy. Research by Kirsten Vea et al. (2024) found that the primary reason for discontinuing thiazide therapy in CKD patients was increased serum creatinine. A similar finding was found in the study by Agarwal et al. (2021), where patients using chlorthalidone experienced a reversible increase in creatinine after therapy was discontinued. This condition suggests that regular monitoring of kidney function and electrolyte levels is crucial to prevent complications during diuretic use (Masella et al., 2019; Kennelly et al., 2022).

In addition to pharmacological therapy, several journals also emphasize the importance of lifestyle modifications in managing hypertension in CKD patients (Elendu et al., 2023; Stambolliu et al., 2025; Hamrahian, 2017). Tim Doulton et al. (2026) stated that salt restriction, weight control, physical activity, and medication adherence are essential in achieving a blood pressure target of <130/80 mmHg. Meanwhile, Yuar (2025) explained that hypertension therapy should be individualized based on the patient's cardiovascular risk level and clinical condition. A comprehensive approach combining pharmacological and nonpharmacological therapies can improve treatment success and reduce the risk of cardiovascular complications in hypertensive patients with CKD (Danneel et al., 2025; Shiukashvili, 2026; Caturano et al., 2024; Abramov et al., 2026; Marrone et al., 2024).

Based on all the journals analyzed, it can be concluded that the use of thiazide diuretics in hypertension therapy in CKD patients remains relevant and effective, particularly for controlling blood pressure and reducing proteinuria. However, therapy must be carried out carefully with regular monitoring of kidney function and electrolytes. A combination of antihypertensive therapy, patient education, and lifestyle modifications is an important strategy in improving patient quality of life and slowing the progression of kidney disease. Therefore, managing hypertension in CKD patients requires a multidisciplinary and individualized approach tailored to each patient's condition.

CONCLUSION

Based on a literature review of 11 articles on the role of thiazide diuretics in hypertension in patients with chronic kidney disease, it can be concluded that thiazide and thiazide-like diuretics still play an important role in controlling blood pressure in patients with chronic kidney disease, including in advanced stages. This is explained in articles 1, 2, 3, 4, 6, 9, and 10, which show that thiazide use effectively helps lower blood pressure, reduces fluid retention, and reduces proteinuria or albuminuria associated with progressive kidney damage. The use of chlorthalidone is one of the most widely studied therapies because it has been proven effective in lowering systolic blood pressure in patients with advanced chronic kidney disease. In addition to helping control blood pressure, several articles also demonstrate the renoprotective effects of thiazide diuretic use. Articles 1, 3, and 6 explain that the use of chlorthalidone and hydrochlorothiazide can significantly reduce albuminuria in patients with chronic kidney disease.

Reducing proteinuria is important because proteinuria is a major risk factor for chronic kidney disease progression. Furthermore, combination diuretic therapy with an ACE inhibitor or ARB has been reported to improve blood pressure control and preserve kidney function compared to monotherapy. Despite its benefits, the use of thiazide diuretics in patients with chronic kidney disease still requires attention to potential side effects. Articles 4, 7, and 8 state that thiazide use can cause hypokalemia, increased serum creatinine levels, hypotension, and other electrolyte disturbances, requiring regular monitoring of kidney function and electrolytes. However, most studies indicate that the increase in creatinine is reversible and tolerated if patients are closely monitored during therapy. Furthermore, articles 5 and 8 explain that the combination of thiazides with loop diuretics or mineralocorticoid receptor antagonists can increase fluid excretion and help improve blood pressure control, especially in patients with diuretic resistance or severe fluid overload. Furthermore, article 11 emphasizes the importance of evaluating antihypertensive medication use to prevent Drug-Related Problems (DRPs), such as dosing errors and drug interactions, which can impact the success of hypertension therapy in patients with Chronic Kidney Disease. Overall, all articles demonstrate that thiazide diuretics remain relevant and effective in the treatment of hypertension in patients with Chronic Kidney Disease. The use of thiazide diuretics can help achieve blood pressure targets, reduce proteinuria, and slow the progression of kidney disease when used appropriately. However, therapy must be individualized, taking into account the patient's clinical condition, kidney function, and the risk of potential side effects. Therefore, regular monitoring, appropriate combination therapy, and lifestyle modifications are essential for the successful management of hypertension in patients with Chronic Kidney Disease.

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