

# Economic and Health Implications of Risk Factors in Chronic Kidney Disease

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**Abstract:** *Chronic Kidney Disease (CKD) represents a substantial global health and economic challenge, affecting millions of individuals and placing a heavy burden on healthcare systems. This review delves into the major risk factors contributing to CKD, with a focus on diabetes, hypertension, cardiovascular diseases, age, gender, genetic factors, family history, socioeconomic status, chronic use of certain medications, high protein diet, auto-immune diseases, urinary tract obstruction, recurrent kidney infections, and some additional factors. It critically examines how these factors not only accelerate CKD progression but also compound the financial strain on patients. Diabetes, characterized by persistent hyperglycaemia, leads to kidney damage and necessitates extensive medical management, while hypertension exacerbates kidney deterioration through increased vascular pressure. Socioeconomic status further complicates CKD management, as lower income and limited access to healthcare services hinder effective treatment and exacerbate health disparities. This review provides a comprehensive analysis of the impact of these risk factors on both healthcare costs and patient out-of-pocket expenses, highlighting the direct and indirect financial burdens associated with CKD. This article offers insights into potential interventions and policy measures designed to mitigate the economic impact on affected individuals, emphasizing the need for integrated strategies to address both the health and financial aspects of CKD.*

**Keywords:** Chronic Kidney Disease, Risk Factors, Financial Burden, Healthcare Costs, Economic Implications

## 1. Introduction

The economic and health implications of risk factors in chronic kidney disease (CKD) are significant, affecting both patients and healthcare systems worldwide. CKD often progresses to end-stage renal disease (ESRD), which necessitates expensive interventions.<sup>1</sup> Diabetes and hypertension being the primary risk factors of CKD, hasten the decline in kidney function and lead to significantly higher healthcare expenses, driven by increased hospital admissions, medication requirements, and ongoing management<sup>2</sup>. The financial burden on healthcare systems is considerable, and it directly affects patients' quality of life and financial stability. Therefore, effective management of these risk factors is essential to slow CKD progression and reduce the associated economic impact. Emphasizing early detection, preventive measures, and targeted interventions can help alleviate the dual burden of health complications and economic costs posed by CKD and its risk factors.<sup>3</sup>

### Risk Factors Contributing to CKD

Chronic Kidney Disease (CKD) is influenced by a range of risk factors that collectively contribute to its onset and progression. Diabetes, particularly Type 2, and hypertension are major contributors, leading to kidney damage through high blood glucose levels and increased blood pressure<sup>4</sup>. Cardiovascular disease further exacerbates CKD through hypertension and systemic inflammation. Age and gender also play significant roles, with older individuals and men generally facing higher risks. Genetic factors and family history can predispose individuals to CKD through inherited conditions and shared environmental factors. Socioeconomic status impacts CKD management due to limited access to healthcare and resources<sup>5</sup>. Chronic use of certain medications, high-protein diets, and autoimmune diseases can worsen kidney function, while urinary tract obstruction and recurrent infections add additional strain. Understanding

these diverse risk factors is crucial for effective CKD management and improving patient outcomes.<sup>6</sup>

### Diabetes

Diabetes is one of the most significant risk factors for chronic kidney disease (CKD), with profound economic and health implications. Diabetic nephropathy, a common complication of diabetes, accelerates kidney function decline, increasing the likelihood of progressing to end-stage renal disease (ESRD).<sup>7</sup> This progression requires costly interventions such as dialysis or kidney transplantation, placing a substantial financial burden on healthcare systems.<sup>8</sup> The management of diabetes in CKD patients also involves frequent hospital visits, specialized treatments, and expensive medications, contributing to escalating healthcare costs. Diabetes-related CKD complications can severely impact patients' quality of life.<sup>9</sup>

A cost of illness study of type 2 diabetes mellitus was conducted in 2010 in the general medicine department of a tertiary care teaching hospital revealing that the direct cost and indirect cost for managing type 2 diabetes mellitus was 7943.19 (± 3688.92) and 1377.63 (±769.56) respectively. Hence all persons with diabetes require easily accessible and affordable healthcare services. The availability and affordability of services and drugs can help these people to manage their diabetes and diabetic kidney disease.

### Hypertension

Hypertension, commonly known as high blood pressure, is a significant risk factor for the development and progression of chronic kidney disease (CKD).<sup>10</sup> Elevated blood pressure increases the pressure exerted on the glomeruli, the kidney's filtering units, which accelerates damage and contributes to the loss of nephrons and a decline in kidney function. The economic burden associated with hypertension-induced CKD is substantial, encompassing expenses for antihypertensive medications, frequent medical monitoring,

and management of associated cardiovascular complications.<sup>11</sup> Effective hypertension management often necessitates a comprehensive approach that may include multiple medications, lifestyle modifications, and regular healthcare visits.<sup>12</sup> This multifaceted treatment regimen can impose a considerable financial strain on patients, further complicating the economic impact of CKD and underscoring the need for strategies to address both the clinical and financial challenges of managing hypertension and CKD.<sup>13</sup>

**Table 1:** JNC 5 Classification of Blood Pressure for adults 18 years and older

Category	Systolic (mmHg)	Diastolic (mmHg)
Optimal	< 120	< 80
Normal	< 130	< 85
High - Normal	130 - 139	85 - 89
Hypertension Stage 1	140 - 159	90 - 99
Hypertension Stage 2	160 - 179	100 - 109
Hypertension Stage 3	180 - 209	110 - 119
Hypertension Stage 4	≥ 210	≥ 120

### Cardiovascular Diseases

Chronic kidney disease (CKD) and cardiovascular disease (CVD) are closely linked, with each condition influencing the progression of the other. This bidirectional relationship exacerbates both CKD and CVD, leading to worsening health outcomes and increased healthcare costs. Major risk factors, including hypertension, diabetes, obesity, and dyslipidaemia, contribute to endothelial dysfunction, arterial stiffness, and vascular inflammation, damaging both the heart and kidneys. Uremic toxins and CKD - related mineral and bone disorders (CKD - MBD) further accelerate cardiovascular and renal damage. CVD, in turn, worsens CKD progression through mechanisms like fluid overload and systemic inflammation, while CKD promotes cardiovascular risk through increased atherosclerosis, volume overload, and dyslipidaemia. The economic implications of this interrelationship are significant, as patients with both conditions often require more frequent hospitalizations, costly medications, and advanced therapies such as dialysis or cardiac procedures. Effective management requires an integrated healthcare approach that addresses both CKD and CVD. Treatment strategies, such as the use of renin - angiotensin - aldosterone system (RAAS) inhibitors, statins, and lifestyle modifications, aim to slow disease progression and improve patient outcomes. Early detection and comprehensive intervention are critical to mitigating the economic burden and improving the quality of life for patients with coexisting CKD and CVD. Addressing this dual challenge not only helps reduce healthcare costs but also extends patients' lives by minimizing complications and improving long - term health outcomes. An integrated approach is crucial in breaking the cycle of worsening CKD and CVD, offering both economic and medical benefits.

### Age

Chronic kidney disease (CKD) has significant economic and health implications, particularly in older adults. As the population ages, the natural decline in kidney function, compounded by the increased prevalence of risk factors such as hypertension and diabetes, escalates healthcare costs associated with managing CKD. The progression of CKD in older individuals often requires more intensive medical interventions, contributing to rising healthcare expenditures.

From a health perspective, the challenges of managing CKD in the elderly include polypharmacy and altered drug metabolism, both of which increase the complexity of treatment and the risk of adverse drug events. This not only affects patient health but also places a burden on healthcare systems due to the need for more specialized care. Additionally, CKD in older adults leads to a diminished quality of life, increased cardiovascular risks, and frequent hospitalizations, all of which further contribute to both direct healthcare costs and the indirect costs related to lost productivity and caregiver burden. Managing CKD in this population necessitates tailored approaches to reduce these financial strains while addressing the multifaceted health challenges.

### Gender

Gender differences in chronic kidney disease (CKD) have significant economic and health implications. Men tend to develop CKD at earlier ages due to higher rates of risk factors such as hypertension and cardiovascular disease, leading to increased healthcare costs associated with earlier and more frequent medical interventions. However, women often experience a more rapid progression to end - stage renal disease (ESRD), particularly post - menopause, which intensifies the need for advanced treatments such as dialysis or kidney transplantation, further escalating healthcare expenditures. These gender - based disparities in CKD progression contribute to higher long - term treatment costs, particularly for women, who may require more complex care. From a health perspective, the differences in disease progression and treatment responses between men and women complicate CKD management. Women often face faster progression to ESRD, and both genders exhibit distinct responses to medications, as well as different outcomes in dialysis and transplantation. Additionally, socioeconomic factors, such as lower income and limited access to resources, disproportionately affect women, making it harder for them to access timely and adequate care. These challenges not only worsen health outcomes but also increase indirect costs related to reduced productivity and quality of life. Addressing gender - specific factors in CKD management is crucial to improving outcomes and reducing the economic burden on healthcare systems.

### Genetic Factors

Genetic factors have significant economic and health implications for chronic kidney disease (CKD) management. Individuals with genetic predispositions, such as variations in genes affecting kidney function or susceptibility to hypertension, face a higher risk of developing CKD, which can lead to increased healthcare costs due to the need for early screening, diagnosis, and more frequent monitoring. Conditions like polycystic kidney disease and Alport syndrome, directly linked to genetic mutations, often require advanced treatments such as dialysis or kidney transplantation, further elevating healthcare expenditures. The need for specialized care, genetic testing, and personalized treatment strategies adds to the financial burden on both patients and healthcare systems. From a health perspective, genetic factors not only increase the likelihood of developing CKD but also influence its progression and severity. Inherited conditions and genetic mutations may accelerate disease progression, leading to earlier onset of end

- stage renal disease (ESRD) and reducing patients' quality of life. Additionally, the interaction between genetic predispositions and environmental or lifestyle factors complicates disease management, requiring more tailored and targeted therapies to slow progression. Understanding and addressing these genetic influences is essential to improving patient outcomes, enhancing early detection efforts, and reducing long - term healthcare costs associated with CKD.

### Family History

Family history plays a critical role in both the economic and health implications of chronic kidney disease (CKD). Individuals with a family history of CKD or related conditions, such as hypertension or diabetes, are at higher risk, leading to an increased burden on healthcare systems. Early identification of those with genetic predispositions or shared lifestyle factors can reduce long - term healthcare costs by enabling earlier screenings and interventions. Proactive management helps delay the progression of CKD, thus lowering the need for expensive treatments such as dialysis or kidney transplantation. From a health perspective, those with a family history are more likely to develop CKD earlier or experience faster disease progression. This can result in increased healthcare utilization, such as more frequent medical visits, tests, and medications. Additionally, the impact on quality of life is significant, as these individuals face a heightened risk of complications and comorbidities. By promoting early screening and personalized treatment plans, healthcare systems can not only improve patient outcomes but also mitigate the economic burden associated with advanced CKD management.

### Socioeconomic Status

Socioeconomic status (SES) is a pivotal factor influencing both the risk and management of chronic kidney disease (CKD). Individuals with lower SES often face significant barriers to accessing healthcare services, which can lead to delayed diagnosis and inadequate management of CKD. This group is also more likely to experience higher rates of risk factors such as diabetes and hypertension, conditions that exacerbate CKD progression. Financial constraints associated with lower income further impede effective disease management, as limited resources may result in insufficient access to necessary treatments, medications, and regular monitoring. This inadequacy in managing CKD not only accelerates disease progression but also drives up overall healthcare costs, creating a cycle of worsening health outcomes and financial strain. Addressing these socioeconomic disparities is essential for improving CKD management and reducing the associated economic burden on affected individuals.

### Chronic Use of Certain Medications

The chronic use of certain medications has substantial economic and health implications for individuals with chronic kidney disease (CKD). Medications like nonsteroidal anti - inflammatory drugs (NSAIDs), certain antibiotics, and proton pump inhibitors (PPIs) can worsen kidney function, leading to faster disease progression and increased healthcare costs. As these medications contribute to kidney damage, patients may require more frequent monitoring, additional medications, and, in severe cases, costly interventions such as dialysis or hospitalization due to acute kidney injury. These

escalating healthcare needs drive up direct medical expenses, burdening both patients and healthcare systems. From a health perspective, long - term use of nephrotoxic medications can lead to complications such as electrolyte imbalances and acute kidney injuries, further deteriorating kidney function. For CKD patients, these side effects exacerbate their existing condition, leading to a higher risk of complications and reduced quality of life. Careful monitoring of kidney function and medication management is essential to prevent further kidney damage, improve patient outcomes, and minimize the financial strain on both individuals and the healthcare system.

### High Protein Diet

Excessive protein intake increases the workload on the kidneys, leading to faster disease progression, which in turn drives up healthcare costs due to the need for more frequent monitoring, medications, and eventually, costly interventions like dialysis or kidney transplantation. Poorly managed protein consumption can also result in additional hospitalizations due to metabolic imbalances and complications, adding further financial strain on both individuals and healthcare systems. A high - protein diet exacerbates kidney damage by increasing glomerular pressure and filtration rates, accelerating the decline in kidney function. This dietary factor also contributes to the buildup of uremic toxins, worsening symptoms and reducing the quality of life for CKD patients. Proper management of protein intake is essential not only to slow disease progression but also to mitigate symptoms and improve long - term health outcomes. Tailored dietary interventions can significantly reduce the health risks associated with CKD and lower the overall burden on healthcare resources.

### Auto - Immune Diseases

Conditions such as lupus nephritis, rheumatoid arthritis, and vasculitis can lead to immune - mediated kidney damage, increasing the risk of CKD progression. The frequent need for long - term immunosuppressive therapy to manage these autoimmune conditions adds to healthcare costs, as these treatments require ongoing medical supervision and monitoring, and potentially lead to additional complications. The nephrotoxic effects of certain immunosuppressants can worsen kidney function, contributing to increased medical expenses from more intensive treatments, hospitalizations, or the need for dialysis or transplantation. The inflammation and scarring caused by autoimmune diseases can significantly accelerate CKD progression, resulting in more severe renal impairment. Managing CKD in the context of autoimmune diseases requires a delicate balance of controlling immune responses while preventing further kidney damage. This complex care strategy can lead to a higher risk of complications, reduced quality of life, and a greater reliance on healthcare services. Effective management strategies that integrate both CKD and autoimmune disease treatments are critical for improving patient outcomes and reducing the long - term economic burden on healthcare systems.

### Urinary Tract Obstruction

Conditions such as kidney stones, tumors, or an enlarged prostate can cause blockages that lead to increased pressure on the kidneys, resulting in tissue damage and accelerating CKD progression. From an economic perspective, the costs

associated with diagnosing and managing urinary obstructions, including imaging, surgeries, and potential hospitalizations, can be substantial. If left untreated, prolonged obstruction may result in severe complications like hydronephrosis, which can further escalate healthcare costs by requiring more advanced treatments such as dialysis or kidney transplantation. Health-wise, urinary obstructions can lead to rapid deterioration of kidney function and cause irreversible damage if not addressed promptly. The backpressure created by blocked urine flow impairs kidney filtration, which exacerbates CKD progression and significantly reduces quality of life. Early diagnosis and prompt intervention to relieve obstructions are essential to preserve kidney function and prevent further health complications. Effectively managing urinary tract issues in CKD patients can improve outcomes and help reduce the long-term economic burden on both individuals and healthcare systems.

### Recurrent Kidney Infections

Frequent infections, such as pyelonephritis, can lead to ongoing kidney inflammation and damage, exacerbating CKD progression and increasing healthcare costs associated with diagnosis, treatment, and management of complications. The need for prolonged or repeated antibiotic courses to address these infections can drive up expenses while also raising the risk of antibiotic resistance and additional renal toxicity, which may further complicate treatment and increase the likelihood of more severe health interventions. From a health perspective, the ongoing inflammation and scarring caused by recurrent infections diminish the kidneys' ability to filter blood effectively, leading to accelerated deterioration of kidney function. This not only impacts patients' quality of life but also necessitates more intensive medical care and monitoring. Effective management and prevention of recurrent kidney infections are crucial in safeguarding kidney function, improving long-term health outcomes, and ultimately reducing the financial burden on both patients and healthcare systems. Prioritizing preventive strategies can help mitigate these risks and promote better overall health for individuals with CKD.

### Additional Risk Factors

Obesity is a key risk factor for diabetes and hypertension, which are major contributors to CKD. It complicates CKD management by increasing comorbidities that exacerbate kidney damage, leading to faster disease progression in diabetic patients. This results in higher healthcare costs due to more intensive monitoring and advanced treatments, decreasing productivity and increasing absenteeism, further straining the economy.

Smoking accelerates kidney damage and raises the risk of cardiovascular disease in CKD patients, leading to more complications, frequent medical visits, and potentially invasive treatments. The associated healthcare costs place additional burdens on healthcare systems.

Both obesity and smoking negatively affect quality of life, contributing to psychological stress and social isolation, which complicate disease management. Targeted interventions and public health initiatives to reduce obesity and smoking are essential for improving health outcomes for

CKD patients and alleviating the economic burden on individuals and healthcare systems. By prioritizing prevention and management strategies, healthcare providers can enhance patient care and reduce overall costs.

## 2. Conclusion

Chronic Kidney Disease (CKD) presents a complex challenge with its progressive decline in kidney function, compounded by a variety of risk factors that significantly influence both health outcomes and financial costs. Factors such as diabetes, hypertension, cardiovascular diseases, and socioeconomic status contribute to the onset and progression of CKD, while gender, genetic predispositions, family history, chronic medication use, high-protein diets, autoimmune diseases, urinary tract obstruction, and recurrent infections further exacerbate the disease. The financial implications are profound, encompassing direct costs for medical treatments and indirect costs related to lost productivity and long-term care needs. Addressing these multifaceted risk factors through effective management and preventive strategies is crucial to mitigating the economic burden and improving patient outcomes. Comprehensive approaches that integrate early detection, personalized treatment, and proactive management of risk factors are essential in alleviating both the health and economic impacts of CKD, ultimately enhancing quality of life and reducing the strain on healthcare systems.

## References

- [1] Plantinga LC. Socio-economic impact in CKD. *Néphrologie & thérapeutique*.2013 Feb 1; 9 (1): 1 - 7.
- [2] Hannan M, Ansari S, Meza N, Anderson AH, Srivastava A, Waikar S, Charleston J, Weir MR, Taliencio J, Horwitz E, Saunders MR. Risk factors for CKD progression: overview of findings from the CRIC study. *Clinical Journal of the American Society of Nephrology*.2021 Apr 1; 16 (4): 648 - 59.
- [3] Kazancioğlu R. Risk factors for chronic kidney disease: an update. *Kidney international supplements*.2013 Dec 1; 3 (4): 368 - 71.
- [4] Kurzhagen JT, Dellepiane S, Cantaluppi V, Rabb H. AKI: an increasingly recognized risk factor for CKD development and progression. *Journal of nephrology*.2020 Dec; 33 (6): 1171 - 87.
- [5] Wang F, He K, Wang J, Zhao MH, Li Y, Zhang L, Saran R, Bragg - Gresham JL. Prevalence and risk factors for CKD: a comparison between the adult populations in China and the United States. *Kidney international reports*.2018 Sep 1; 3 (5): 1135 - 43.
- [6] Yang W, Xie D, Anderson AH, Joffe MM, Greene T, Teal V, Hsu CY, Fink JC, He J, Lash JP, Ojo A. Association of kidney disease outcomes with risk factors for CKD: findings from the Chronic Renal Insufficiency Cohort (CRIC) study. *American journal of kidney diseases*.2014 Feb 1; 63 (2): 236 - 43.
- [7] Zhang X, Fang Y, Zou Z, Hong P, Zhuo Y, Xu Y, Wan J. Risk factors for progression of CKD with and without diabetes. *Journal of diabetes research*.2022; 2022 (1): 9613062.
- [8] Lin CY, Hsieh MC, Kor CT, Hsieh YP. Association and risk factors of chronic kidney disease and incident diabetes: a nationwide population - based cohort study. *Diabetologia*.2019 Mar; 62: 438 - 47.

- [9] Levey AS, Bilous R, Shlipak MG. CKD and diabetes: what can we learn from their similarities and differences?. *American Journal of Kidney Diseases*.2016 Mar 1; 67 (3): 360 - 3.
- [10] Lea JP, Nicholas SB. Diabetes mellitus and hypertension: key risk factors for kidney disease. *Journal of the National Medical Association*.2002 Aug; 94 (8 Suppl): 7S.
- [11] Burnier M, Damianaki A. Hypertension as cardiovascular risk factor in chronic kidney disease. *Circulation research*.2023 Apr 14; 132 (8): 1050 - 63.
- [12] Barri YM. Hypertension and kidney disease: a deadly connection. *Current hypertension reports*.2008 Feb; 10 (1): 39 - 45.
- [13] Hamrahian SM, Falkner B. Hypertension in chronic kidney disease. *Hypertension: from basic research to clinical practice*.2017; 307 - 25.
- [14] Yamagata K, Ishida K, Sairenchi T, Takahashi H, Ohba S, Shiigai T, Narita M, Koyama A. Risk factors for chronic kidney disease in a community - based population: a 10 - year follow - up study. *Kidney international*.2007 Jan 2; 71 (2): 159 - 66.
- [15] Zelnick LR, Weiss NS, Kestenbaum BR, Robinson - Cohen C, Heagerty PJ, Tuttle K, Hall YN, Hirsch IB, De Boer IH. Diabetes and CKD in the United States population, 2009–2014. *Clinical Journal of the American Society of Nephrology*.2017 Dec 1; 12 (12): 1984 - 90.
- [16] Anders HJ, Huber TB, Isermann B, Schiffer M. CKD in diabetes: diabetic kidney disease versus nondiabetic kidney disease. *Nature Reviews Nephrology*.2018 Jun; 14 (6): 361 - 77.
- [17] Perkovic V, Agarwal R, Fioretto P, Hemmelgarn BR, Levin A, Thomas MC, Wanner C, Kasiske BL, Wheeler DC, Groop PH, Bakris GL. Management of patients with diabetes and CKD: áconclusions from a “Kidney Disease: Improving Global Outcomes” (KDIGO) Controversies Conference. *Kidney international*.2016 Dec 1; 90 (6): 1175 - 83.
- [18] McQueen RB, Farahbakhshian S, Bell KF, Nair KV, Saseen JJ. Economic burden of comorbid chronic kidney disease and diabetes. *Journal of medical economics*.2017 Jun 3; 20 (6): 585 - 91.
- [19] Vupputuri S, Kimes TM, Calloway MO, Christian JB, Bruhn D, Martin AA, Nichols GA. The economic burden of progressive chronic kidney disease among patients with type 2 diabetes. *Journal of Diabetes and its Complications*.2014 Jan 1; 28 (1): 10 - 6.
- [20] Horowitz B, Miskulin D, Zager P. Epidemiology of hypertension in CKD. *Advances in chronic kidney disease*.2015 Mar 1; 22 (2): 88 - 95.
- [21] Hamrahian SM, Falkner B. Hypertension in chronic kidney disease. *Hypertension: from basic research to clinical practice*.2017; 307 - 25.
- [22] Muntner P, Judd SE, Gao L, Gutiérrez OM, Rizk DV, McClellan W, Cushman M, Warnock DG. Cardiovascular risk factors in CKD associate with both ESRD and mortality. *Journal of the American Society of Nephrology*.2013 Jul 1; 24 (7): 1159 - 65.
- [23] Doan QV, Gleeson M, Kim J, Borker R, Griffiths R, Dubois RW. Economic burden of cardiovascular events and fractures among patients with end - stage renal disease. *Current medical research and opinion*.2007 Jul 1; 23 (7): 1561 - 9.
- [24] Goldberg I, Krause I. The role of gender in chronic kidney disease. *Emj*.2016 Apr 5; 1 (2): 58 - 64.
- [25] Eriksen BO, Ingebretsen OC. The progression of chronic kidney disease: a 10 - year population - based study of the effects of gender and age. *Kidney international*.2006 Jan 2; 69 (2): 375 - 82.
- [26] Roderick PJ, Atkins RJ, Smeeth L, Nitsch DM, Hubbard RB, Flectcher AE, Bulpitt CJ. Detecting chronic kidney disease in older people; what are the implications?. *Age and ageing*.2008 Mar 1; 37 (2): 179 - 86.
- [27] Obrador GT, Schultheiss UT, Kretzler M, Langham RG, Nangaku M, Pecoits - Filho R, Pollock C, Rossert J, Correa - Rotter R, Stenvinkel P, Walker R. Genetic and environmental risk factors for chronic kidney disease. *Kidney international supplements*.2017 Oct 1; 7 (2): 88 - 106.
- [28] Vehaskari VM. Genetics and CKD. *Advances in Chronic Kidney Disease*.2011 Sep 1; 18 (5): 317 - 23.
- [29] Baker M, Perazella MA. NSAIDs in CKD: are they safe?. *American Journal of Kidney Diseases*.2020 Oct 1; 76 (4): 546 - 57.
- [30] Gooch K, Culleton BF, Manns BJ, Zhang J, Alfonso H, Tonelli M, Frank C, Klarenbach S, Hemmelgarn BR. NSAID use and progression of chronic kidney disease. *The American journal of medicine*.2007 Mar 1; 120 (3): 280 - e1.
- [31] Arora P, Gupta A, Golzy M, Patel N, Carter RL, Jalal K, Lohr JW. Proton pump inhibitors are associated with increased risk of development of chronic kidney disease. *BMC nephrology*.2016 Dec; 17: 1 - 8.
- [32] Klatte DC, Gasparini A, Xu H, de Deco P, Trevisan M, Johansson AL, Wettermark B, Ärnlöv J, Janmaat CJ, Lindholm B, Dekker FW. Association between proton pump inhibitor use and risk of progression of chronic kidney disease. *Gastroenterology*.2017 Sep 1; 153 (3): 702 - 10.
- [33] Ko GJ, Rhee CM, Kalantar - Zadeh K, Joshi S. The effects of high - protein diets on kidney health and longevity. *Journal of the American Society of Nephrology*.2020 Aug 1; 31 (8): 1667 - 79.
- [34] Friedman AN. High - protein diets: potential effects on the kidney in renal health and disease. *American Journal of kidney diseases*.2004 Dec 1; 44 (6): 950 - 62.
- [35] Boesen EI, Kakalij RM. Autoimmune - mediated renal disease and hypertension. *Clinical Science*.2021 Sep; 135 (17): 2165 - 96.
- [36] Chevalier RL. Congenital urinary tract obstruction: the long view. *Advances in chronic kidney disease*.2015 Jul 1; 22 (4): 312 - 9.
- [37] Liu KD, Yang J, Tan TC, Glidden DV, Zheng S, Pravoverov L, Hsu CY, Go AS. Risk factors for recurrent acute kidney injury in a large population - based cohort. *American Journal of Kidney Diseases*.2019 Feb 1; 73 (2): 163 - 73.
- [38] Luyckx VA, Tuttle KR, Garcia - Garcia G, Gharbi MB, Heerspink HJ, Johnson DW, Liu ZH, Massy ZA, Moe O, Nelson RG, Sola L. Reducing major risk factors for chronic kidney disease. *Kidney international supplements*.2017 Oct 1; 7 (2): 71 - 87.