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INVESTIGATION OF THE MEDICAL IMPORTANCE OF HYPERTENSION NEPHROPATHY IN INDIVIDUALS WITH NON-DIABETIC CHRONIC KIDNEY DISEASE

[1]Dr Hina Akram Nagyal, [2]Dr Minahil Pervaiz, [3]Dr Tayyab Mehmood, [4]Dr Habiba Jan Qureshi, [5]Majid Ayaz, [6]Junaid Hussain, [7]Hafsa Anwar, 8Latif ullah Khattak, [9]Kashif Lodhi

[1] Medical Officer, Mohi Ud Din Teaching Hospital (MOTH), Mirpur
[2]Azad Jammu and Kashmir medical college muzaffarbad
[3]Gomal medical college
[4]Ajk medical college muzaffarbad
[5]Department of Medical Laboratory Science and Biotechnology, Asia University, Taichung, Taiwan
[6]Department of Medical laboratory science and biotechnology, Asia University Taiwan
[7]Department of Medical Laboratory Science and Biotechnology, Asia University, Taichung, Taiwan
[8]MD, FRSPH, MSPH, MS community health and nutrition scholar, Department of nutrition and environmental design AIOU Islamabad.
[9]Department of Agricultural, Food and Environmental Sciences. Università Politécnica delle Marche Via Brecce Bianche 10, 60131 Ancona (AN) Italy

ABSTRACT:

Aim: A research was done to understand importance of high blood pressure kidney disease in people who have long-term kidney problems but don't have diabetes. The study involved 2750 patients with kidney disease who were chosen from 15 clinics where kidney problems are treated on an outpatient basis.

Methods: This means that the study involved a total of 1320 patients who had a main problem with their kidneys, 470 patients with a condition called HN, 290 individuals having kidney disease caused by diabetes (DN), and 653 patients with different types of kidney diseases (ONs). All of these patients had chronic kidney disease (CKD), which means their kidneys were not working well. They either had a consistently low level of a substance called estimated glomerular filtration rate (eGFR), that measures kidney function, or they had protein in their urine, as detected by a simple test using a dipstick.

Results: The research looked at factors that increase the risk of heart disease, such as problems with the heart and stroke, as well as the risk of dying from any cause and kidney failure that requires dialysis. They used a statistical model to analyze these risks for each group of patients. Over an average period of 23.7 months, some patients could not be followed up, and some had to start dialysis. A total of 118 heart disease events (including 39 strokes) and 46 deaths occurred. The researchers found significant differences in the risk of heart disease events and death among the different groups of patients with

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different kidney diseases, even after considering other factors that could affect the results. The risk ratios were as follows: PRD, 1.0 (used as a reference); HN, 4.34 (with a 96% confidence interval of 1.83–6.07); DN, 5.94 (with a 3.81–13.53 confidence interval); and ON, 2.23 (with a 1.24–4.06 confidence interval). However, there were no differences in the risk of needing dialysis among the groups with different kidney diseases.

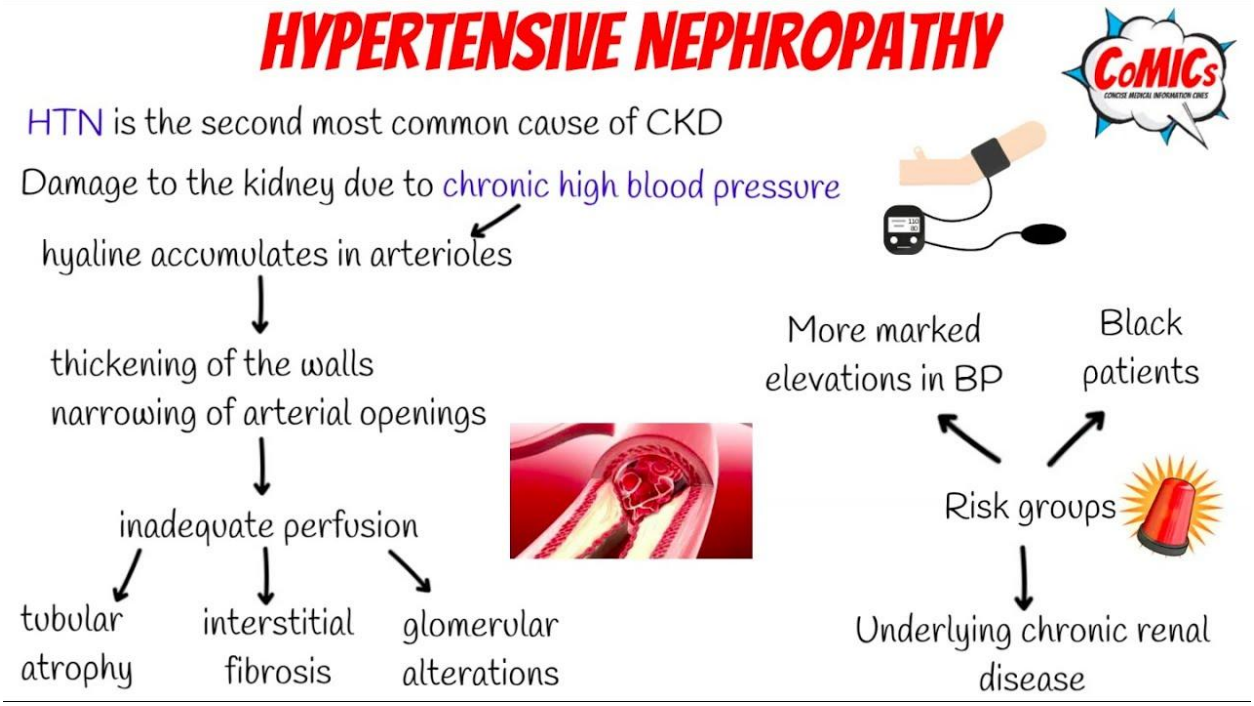
Conclusion: The research shows that people with high blood pressure kidney disease (HN) have a higher chance of experiencing heart and blood vessel problems and dying, especially if they don't have diabetes. This emphasizes the importance of recognizing and treating HN in medical practice.

Keywords: Hypertensive Nephropathy (HN), chronic kidney disease (CKD), Non-Diabetic.

INTRODUCTION:

Chronic kidney disease (CKD) is very well-known condition that increases the risk of heart and blood vessel problems, like stroke, kidney failure, and death for everyone [1]. In simpler terms, research has found a link between heart problems and reduced kidney function in people who have diabetes, heart disease, high BP, high cholesterol, or are older. People with kidney diseases have certain factors that increase their chances of experiencing heart problems. These factors include high cholesterol and blood clotting issues due to kidney problems, inflammation-related blood vessel diseases, other diseases like collagen or infections, and the use of certain medications like steroids [3]. While it is believed that people through hypertensive nephropathy (HN) are at high risk for kidney failure, it is not clear how HN compares to other kidney diseases (ONs) when it comes to the frequency of heart problems [4-6]. Therefore, this is very important to understand results of CKD based on the underlying kidney disease, particularly for cases not caused by diabetes. Only a few studies, including our early research, have looked into this issue [7]. This study aims to address this question by examining a group of patients from kidney clinics [8].

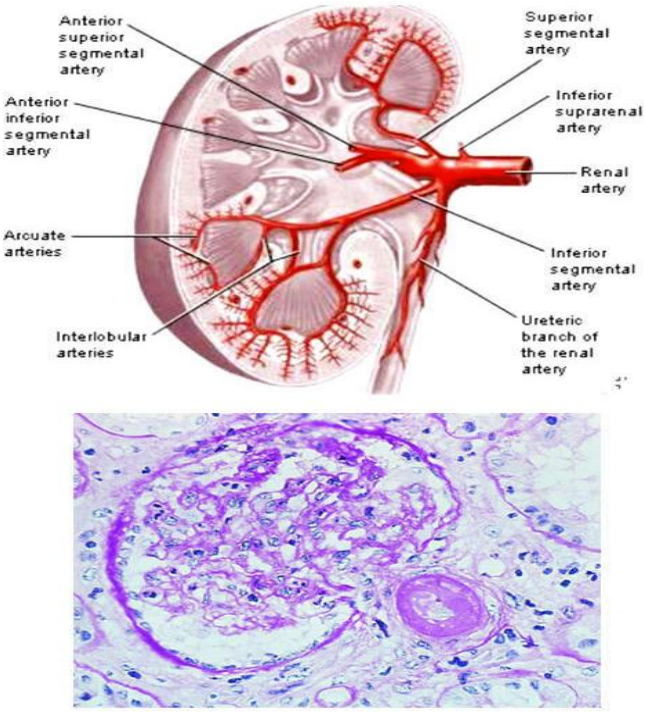
Image 1:



Hypertensive nephropathy, also known as hypertensive kidney disease, is a progressive condition characterized by kidney damage caused by chronic high BP. It is one of very main reasons of end-stage renal disease worldwide. Hypertensive nephropathy typically develops over a long period of time as a consequence of uncontrolled hypertension [9]. Prolonged high blood pressure exerts excessive force on the delicate blood vessels within the kidneys, leading to renal injury and impaired kidney function. If left untreated or poorly managed, hypertensive nephropathy can result in irreversible kidney damage and eventually lead to kidney failure [10]. The kidneys play a crucial role in maintaining body's overall health by filtering waste products, balancing fluids and electrolytes, and regulating blood pressure [11-13]. When hypertension persists, it can cause structural and functional changes in the renal system, disrupting these vital processes. Over time, the damaged blood vessels within the kidneys become narrowed, reducing blood flow and impairing the filtration capabilities of the kidneys. The clinical manifestations of hypertensive nephropathy may vary from mild to severe, and individuals affected by the condition may experience symptoms such as fluid retention, decreased urine output, fatigue, hypertension that is difficult to control, and the presence of blood or protein in the urine [14]. However, in its early stages, hypertensive nephropathy may be asymptomatic, making it challenging to detect without routine

screening tests. Diagnosis of hypertensive nephropathy involves a comprehensive evaluation of the patient's medical history, physical examination, blood tests, urine analysis, and imaging studies. Detecting and managing high blood pressure promptly is crucial in preventing or slowing the progression of kidney damage in individuals with hypertensive nephropathy. Treatment for hypertensive nephropathy focuses on blood pressure control and the prevention of further kidney damage. Lifestyle modifications, including adopting a healthy diet, engaging in regular physical activity, and maintaining a healthy weight, are essential in managing hypertension [15].

Image 2:



METHODOLOGY:

The Gonryo CKD project is a study that examines the traits and results of individuals who go to kidney clinics at Mayo Hospital in Lahore. The project involves twelve hospitals affiliated with the University of Punjab, including one university hospital. Patients who agreed to participate in the project were registered and their information was collected. The research received approval from the review board at Mayo

Hospital and the hospitals involved in the study. Registration took place from April 2021 to March 2022, and 4050 patients were registered. Some patients remained excepted from analysis since they didn't have certain data or had unknown kidney diseases. Patients with high blood pressure and good kidney function were also excluded if they didn't have protein in their urine or if they didn't have results from urinary tests. In the end, 2692 patients with complete criteria for chronic kidney disease were selected for analysis.

The doctors at the hospitals sorted patients into different groups based on the kidney diseases they had. There were four main groups: primary renal disease, high blood pressure-related kidney disease, kidney disease related to diabetes, and other kidney diseases. The doctors made these classifications based on the patients' medical history and test results. For example, the primary renal disease group included cases of glomerulonephritis and tubulointerstitial nephritis, and the high blood pressure-related group included cases where patients had a history of hypertension without other disorders. The classification also considered biopsy results for some cases. The patients in the high blood pressure-related group had either a low kidney function or protein in their urine as determined by a dipstick test.

This survey looked at different health problems related to the heart and blood vessels. The main things they studied were heart-related events like chest pain, heart attacks, heart failure, and strokes. They also looked at the number of people who died from any cause before starting a certain type of treatment. The researchers collected information from medical records, death certificates, and interviews with doctors. They focused on what happened to the participants within 18 months after they joined the study. They defined a heart-related event as a problem with the circulatory system. For people with chest pain or heart attacks, they included those who had certain procedures done or had a clear diagnosis of a heart attack. For people with heart failure, they solitary counted these who remained admitted to the hospital for treatment.

We used a method to measure the levels of a substance called serum creatinine in the blood. To assess kidney function, we used a formula specifically for Japanese individuals. We found that 27 people had positive results for protein in their urine when we tested a small sample or used a machine. We considered patients to have a condition called macroalbuminuria if the protein level in their urine was 430mg/dl or higher. We checked the patients' blood pressure at local medical centers during their visits using an automatic blood pressure monitor while they were sitting. We gathered information about the medications the patients were taking and their medical history, with cardiovascular disease, diabetes, high blood pressure, and high levels of uric acid, from their medical records or blood test results. If a person was taking medication to lower cholesterol or had a blood cholesterol level of 220mg/dl or higher, we considered them to have high cholesterol. We defined a person as having diabetes if their fasting blood sugar level was 126mg/dl or higher, or if their non-fasting blood sugar level was 200mg/dl or higher, or if they used insulin or oral medications to control their blood sugar.

We used a statistical method called Cox proportional hazard model analysis to study the connections between the main results and either the initial kidney function or the underlying kidney disease. We made

sure to consider other factors that could affect the results. The information we gathered is presented as averages with a standard deviation. Once P-value remained less than 0.06, it meant that results were statistically substantial. We used a software called STATA version 10.0 to perform all the statistical analyses.

RESULTS:

Over a period of around 23.8±12.8 months, 110 patients stopped participating in the study either because they started receiving medical care from other services or because they decided to stop owing to personal motives. Additionally, follow-up for 196 patients remained stopped because they began receiving a specific type of dialysis treatment called maintenance dialysis therapy. In the study, there were 118 cases of cardiovascular disease events, including 38 cases of stroke, and 48 cases of death from any cause. You can find more detailed information in Table 2. When looking at cardiovascular events and the risk of death from any cause, we found that the risk increased as the stage of chronic kidney disease (CKD) worsened, according to our initial analysis. However, these patterns disappeared when we took into account other factors that could affect the outcomes. Researchers also found significant differences in the risk depending on the underlying kidney diseases when we only looked at the initial analysis, even after considering factors that could influence the outcomes like estimated glomerular filtration rate. Only patients through CKD stage 4 or 5 at beginning of study started dialysis. There were no significant differences in the risk based on underlying renal diseases once we adjusted for other factors that could impact the results, including eGFR.

Table 1: Patient features:

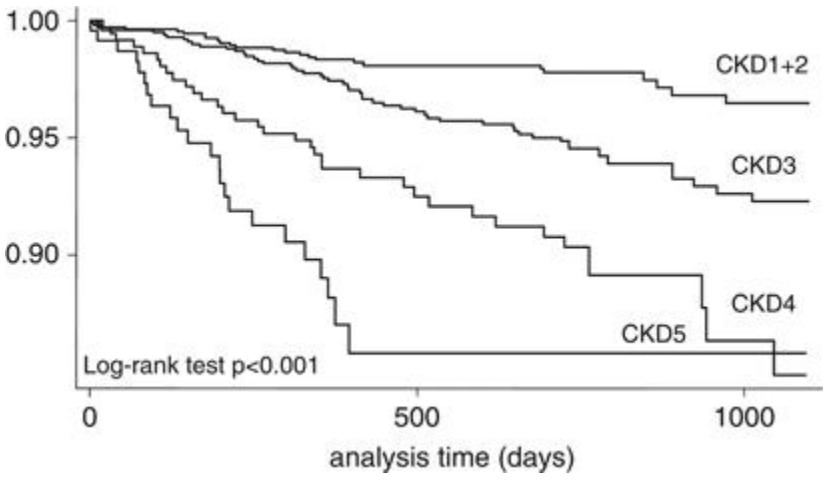
	ONs	**PRD**	**HN**	**DN**	**All**
n	462	283	1.306	643	3.695
BMI	22.9±3.7	24.2±3.8	23.5±3.8	24.1±3.8	23.4±3.8
Age (years)	70.3±11.4	58.6±15.7	66.5±12.6	60.0±16.2	55.7±16.6
Gender (male)	275 (42.8%)	262 (56.7%)	188 (66.4%)	1441 (53.5%)	716 (54.8%)
Blood pressure					
Diastolic	76.4±11.8	77.3±10.4	76.7±10.9	74.0±11.6	76.7±10.7
Systolic	134.68±17.4	129.21±15.1	136.64±17.5	130.95±16.2	129.33±15.8
Comorbidities					
Hyperlipidemia	42.2	42.6	51.6	44.6	36.8
Cardiac disease	21.2	24.7	12.8	7.5	12.3
Hypertension	72.8	93.7	89.4	70.6	77.1
Diabetes	34.2	15.5	100.0	27.4	18.0
Stroke	11.9	12.7	6.5	5.9	3.5

Management of hypertensive nephropathy typically involves a comprehensive approach aimed at controlling blood pressure and slowing the progression of kidney damage. This may include lifestyle modifications, such as adopting a healthy diet low in salt and saturated fats, regular exercise, weight management, and quitting smoking. In advanced cases, when kidney function is severely compromised, treatments such as dialysis or kidney transplantation may be necessary to maintain or replace kidney function. Regular monitoring of blood pressure, kidney function, and urine protein levels is crucial for effective management and to prevent further complications associated with hypertensive nephropathy.

Table 2: Probability of basic renal illnesses in all individuals as endpoints for CVD, stroke, and death:

renal disease	Stroke	Death	CVD	Multivariate analysis		Univariate analysis	
				HR	95% CI	HR	95% CI
DN	7	12	29	5.93	2.80–12.52	10.88	6.29–18.84
PRD	4	10	11	1.00		2.01	
ONs	13	9	13	2.22	1.22–4.05	3.17	1.78–5.62
HN	14	13	26	3.33	1.82–6.09	7.12	4.18–12.14

Figure 1:



DISCUSSION:

This study wanted to understand how kidney diseases affect the occurrence of cardiovascular events and death before starting dialysis treatment. The researchers looked at the results of 2720 patients with chronic kidney disease (CKD) who were receiving outpatient care at 11 kidney clinics [16]. They followed these patients for about 22.6 months and found that there were differences in frequency of cardiovascular events also deaths amongst patients having diverse types of kidney diseases, even after considering other factors that could influence the results, such as kidney function [17]. The study showed that patients with a type of kidney disease called HN were at a higher risk of cardiovascular events and death, except for those with diabetic nephropathy. Patients with ONs and PRD were also at higher risk compared to other types of kidney diseases [18]. However, when it came to starting chronic dialysis treatment, the researchers did not find substantial changes based on the type of kidney disease [19]. The increased risk of cardiovascular disease among CKD patients is influenced by both traditional factors like high blood pressure, diabetes, high cholesterol, and smoking, as well as non-traditional factors like problems with fluid balance, abnormal calcium and phosphate levels, anemia, poor nutrition, increased inflammation and oxidative stress, and the buildup of harmful substances in the body due to kidney problems [20]. So basically, people with blood vessel problems are believed to experience faster damage to their blood vessels as their chronic kidney disease (CKD) gets worse. High blood pressure is a major risk factor for cardiovascular disease (CVD) in the general population, and it makes sense that people with long-term hypertension may have a higher chance of developing CVD and facing a higher risk of death if they also have non-diabetic kidney disease [21]. There are a few reasons why people with primary renal disease (PRD) may have better outcomes when it comes to CVD. First, many PRD patients have a specific kidney condition called immunoglobulin A nephropathy, and treatment with glucocorticoids doesn't increase their risk of CVD. These patients also had better control over their blood pressure compared to others [22]. Furthermore, the presence of blood vessel problems was not as common among pre-dialysis PRD patients, especially in comparison to children with kidney disease. This shows that the stage of CKD alone cannot accurately predict who is at high danger of CVD without considering specific kind of kidney disease. Those findings propose that persons through non-diabetic kidney disease should be the main focus of efforts to prevent cardiovascular disease [23-25].

In this study, we found that the different types of kidney diseases did not affect how often dialysis was needed, even after considering other factors like kidney function. However, dialysis was only given to individuals having chronic kidney disease (CKD). This supports idea that CKD is main reason for dialysis, as recommended in guidelines. There were some issues in the study that could have affected the results [26]. Firstly, the individuals remained selected from nephrology hospitals, which might have caused a bias towards patients who followed their medical treatment better and had manageable factors like high urea levels and BP. Secondly, individuals having hypertension or diabetes who had proteinuria before study and answered to treatment were excepted unless their kidney function was very low [27]. This means that diabetes or high blood pressure patients included in the study may have been harder to treat

with standard methods. This confrontation could have made their results worsen, even though we considered positive findings for proteinuria. Lastly, we didn't have data on microalbuminuria in this study. Since microalbuminuria is known to be important clinically, more research is needed to understand its impact on these patients [28-30].

CONCLUSION:

In short, this study showed that people with HN (Hypertensive Nephropathy) have very higher chance of experiencing cardiovascular events and dying associated to non-diabetic CKD (chronic kidney disease) patients. This emphasizes how important HN is in a medical setting.

REFERENCES:

1. Wu, J. C., Wang, X. J., Zhu, J. H., Huang, X. Y., Liu, M., Qiao, Z., ... & Yi, F. (2023). GPR97 deficiency ameliorates renal interstitial fibrosis in mouse hypertensive nephropathy. *Acta Pharmacologica Sinica*, 1-11.
2. Mikkelsen, H., Vikse, B. E., Eikrem, O., Scherer, A., Finne, K., Osman, T., & Marti, H. P. (2023). Glomerular proteomic profiling of kidney biopsies with hypertensive nephropathy reveals a signature of disease progression. *Hypertension Research*, *46*(1), 144-156.
3. Kurkowski, S. C., Thimmesch, M. J., Elkhider, O., & Abdelgadir, Y. (2023). A Rare Presentation of IgA Nephropathy in a 62-Year-Old Hispanic Female. *Cureus*, *15*(5).
4. Kurkowski, S. C., Thimmesch, M. J., Elkhider, O., & Abdelgadir, Y. (2023). A Rare Presentation of IgA Nephropathy in a 62-Year-Old Hispanic Female. *Cureus*, *15*(5).
5. Ochiai, K., Mochida, Y., Nagase, T., Fukuhara, H., Yamaguchi, Y., & Nagase, M. (2023). Upregulation of Piezo2 in the mesangial, renin, and perivascular mesenchymal cells of the kidney of Dahl salt-sensitive hypertensive rats and its reversal by esaxerenone. *Hypertension Research*, *46*(5), 1234-1246.
6. Du, X., Ma, X., Tan, Y., Shao, F., Li, C., Zhao, Y., ... & Wang, X. (2023). B cell-derived anti-beta 2 glycoprotein I antibody mediates hyperhomocysteinemia-aggravated hypertensive glomerular lesions by triggering ferroptosis. *Signal Transduction and Targeted Therapy*, *8*(1), 103.
7. Li, J., Hu, G., Liu, W., Cao, X., Chen, G., Peng, F., ... & Peng, C. (2023). Patchouli alcohol against renal fibrosis of spontaneously hypertensive rats via Ras/Raf-1/ERK1/2 signalling pathway. *Journal of Pharmacy and Pharmacology*, rgad032.
8. Jo, R., Shibata, H., Kurihara, I., Yokota, K., Kobayashi, S., Murai-Takeda, A., ... & Itoh, H. (2023). Mechanisms of mineralocorticoid receptor-associated hypertension in diabetes mellitus: the role of O-GlcNAc modification. *Hypertension Research*, *46*(1), 19-31.
9. Seetharaman, R., Advani, M., Mali, S., & Pawar, S. (2023). A drug utilisation pattern in non-dialysis patients of diabetic nephropathy in a government-run tertiary care hospital in South-Asia. *Journal of Basic and Clinical Physiology and Pharmacology*, (0).

10. Hata, S., Ushigome, E., Hosomi, Y., Yoshimura, T., Takegami, M., Kitagawa, N., ... & Fukui, M. (2023). Impact of continued high blood pressure on the progression of diabetic nephropathy after 10 years: KAMOGAWA-HBP study. *Hypertension Research*, 1-10.
11. Guo, T., Jiang, H., Tang, F., Ma, R., Wang, Z., Chen, J., ... & Yu, J. (2023). Angiotensin Receptor Neprilysin Inhibition mediates Renal Protection by ARNI (Sacubatril Valsartan) in Rats with Spontaneous Hypertension.
12. Gao, Y., Liu, B., Guo, X., Nie, J., Zou, H., Wen, S., ... & Liang, H. (2023). Interferon regulatory factor 4 deletion protects against kidney inflammation and fibrosis in deoxycorticosterone acetate/salt hypertension. *Journal of Hypertension*, *41*(5), 794-810.
13. Rahim, M. A., Haque, W. M. M. U., Afsana, F., Zaman, S., & Iqbal, S. (2023). Risk Factors for Diabetic Nephropathy among Newly Detected Type 2 Diabetic Patients Attending a Tertiary Care Hospital of Bangladesh. *Journal of Bangladesh College of Physicians and Surgeons*, *41*(1), 15-21.
14. Ramani, N., Whittier, W. L., & Korbet, S. M. (2023). IgA Nephropathy (IgAN) with Crescents: A single center experience. *American Journal of Nephrology*.
15. Ndulue, C. N., Jisieike-Onuigbo, N. N., Okwesa, N. J., Anyanor, A., Ozuemba, B. C., Osakwe, N., ... & Odenigbo, C. U. (2023). Clopidogrel-induced thrombotic thrombocytopenic purpura: a case report. *African Health Sciences*, *23*(1), 592-5.
16. Chen, S., Liao, D., Yang, M., & Wang, S. (2023). Anticoagulant-related nephropathy induced by direct-acting oral anticoagulants: Clinical characteristics, treatments and outcomes. *Thrombosis Research*, *222*, 20-23.
17. Bahrampour, N., Mirzababaei, A., Hosseininasab, D., Abaj, F., Clark, C. C., & Mirzaei, K. (2023). High intake of dietary phytochemical index may be related to reducing risk of diabetic nephropathy: a case–control study. *BMC nutrition*, *9*(1), 14.
18. Liu, S., Zhao, Y., Lu, S., Zhang, T., Lindenmeyer, M. T., Nair, V., ... & Huber, T. B. (2023). Single-cell transcriptomics reveals a mechanosensitive injury signaling pathway in early diabetic nephropathy. *Genome Medicine*, *15*(1), 1-19.
19. Berbari, A. E., Daouk, N. A., & Nasr, E. M. (2023). Coexistence of Diabetes Mellitus and Hypertension. In *Blood Pressure Disorders in Diabetes Mellitus* (pp. 3-17). Cham: Springer International Publishing.
20. Ozbeyaz, N. B., Gokalp, G., Algul, E., Sahan, H. F., Aydinyilmaz, F., Guliyev, I., & Kalkan, K. (2023). H2FPEF Score and Contrast-Induced Nephropathy in Patients With Acute Coronary Syndrome Undergoing Percutaneous Coronary Intervention. *Angiology*, *74*(2), 181-188.
21. Ikwuka, A. O., Virstyuk, N. G., Luchko, O. R., & Kobitovych, I. (2023). Heterogeneity Of Renal Pathogenicity On The Background Of Asymptomatic Hyperuricemia In Patients With Dual Metabolic Syndrome Diseases (Essential Hypertensive Disease and Type 2 Diabetes Mellitus). *Clinical Trials and Clinical Research*, *1*(1).

22. Mambelli, E., Gasperoni, L., Maldini, L., Biagetti, C., & Rigotti, A. (2023). Sotrovimab in SARS-COV-2 chronic hemodialysis patients in the Omicron era. Is intradialytic administration feasible? Report of 4 cases. *Journal of Nephrology*, *36*(3), 669-672.
23. Lv, R., Xu, L., Che, L., Liu, S., Wang, Y., & Dong, B. (2023). Cardiovascular-renal protective effect and molecular mechanism of finerenone in type 2 diabetic mellitus. *Frontiers in Endocrinology*, *14*.
24. Mambelli, E., Gasperoni, L., Maldini, L., Biagetti, C., & Rigotti, A. (2023). Sotrovimab in SARS-COV-2 chronic hemodialysis patients in the Omicron era. Is intradialytic administration feasible? Report of 4 cases. *Journal of Nephrology*, *36*(3), 669-672.
25. Luo, M., Luo, S., Xue, Y., Chang, Q., Yang, H., Dong, W., ... & Cao, S. (2023). Aerobic exercise inhibits renal EMT through promoting irisin expression in SHR. *iScience*, 105990.
26. Lv, R., Xu, L., Che, L., Liu, S., Wang, Y., & Dong, B. (2023). Cardiovascular-renal protective effect and molecular mechanism of finerenone in type 2 diabetic mellitus. *Frontiers in Endocrinology*, *14*.
27. Etta, P. K., & Madhavi, T. (2023). Are renal microvascular lesions the novel histological predictors in IgA nephropathy. *Indian Journal of Pathology and Microbiology*, *66*(1), 216.
28. Morimoto, N., Mori, T., Shioji, S., Taguchi, T., Watanabe, H., Sakai, K., ... & Uchida, S. (2023). Rapidly progressive IgA nephropathy with membranoproliferative glomerulonephritis-like lesions in an elderly man following the third dose of an mRNA COVID-19 vaccine: a case report. *BMC nephrology*, *24*(1), 1-9.
29. Du, Y., Xu, T., Luo, D., Wang, Y., Yin, H., Liu, C., & Li, S. (2023). Perfluorooctane sulfonate-induced apoptosis in kidney cells by triggering the NOX4/ROS/JNK axis and antagonism of cannabidiol. *Environmental toxicology*.
30. Adani, A. A., Siyad, M. O., Adan, A. M., & Jeele, M. O. O. (2023). Prevalence and Determinants of Hypothyroidism in Patients on Routine Hemodialysis in Somalia: A Cross-Sectional Study.