<u>Original Research</u>

Factors Influencing the Efficacy of Shenqi Yanshen Granule in Ameliorating Early Proteinuria Among Patients with Nephrotic Syndrome: A Logistic Analysis

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ABSTRACT

Objective • The study aimed to investigate the factors influencing the efficacy of Shenqi Yanshen Granule in ameliorating proteinuria among nephrotic syndrome patients in renal function stages 1-3.

Methods • 100 patients with nephrotic syndrome and renal function stages 1-3, treated at our hospital from May 2021 to March 2023 were enrolled. All patients received Shenqi Yanshen granule treatment. The patients were divided into the control group (n = 68, with proteinuria reduction of \geq 50%) and the observation group (n = 32, with proteinuria reduction of <50% or increased proteinuria) at 24 hours after treatment. Clinical data, proteinuria levels at 24 hours after treatment, renal function indices, and mean blood pressure were statistically compared. The efficacy of Shenqi Yanshen Granule in treating proteinuria and factors influencing the efficacy was assessed using multiple logistic regression.

Results • The observation group had a higher average age and duration of disease compared to the control group (P < .05).

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INTRODUCTION

Nephrotic syndrome comprises a group of clinical syndromes with diverse etiologies, characterized by significant proteinuria, hypoproteinemia, edema, and hyperlipidemia.^{1,2} This condition not only profoundly impacts the quality of life for individuals but also poses the risk of progressing into more severe renal disorders, such as chronic renal failure, if left uncontrolled.

In the context of nephrotic syndrome treatment, the management of proteinuria is considered a pivotal indicator for

Upon treatment, proteinuria decreased in both groups (P <.05), with higher levels in the observation group than in the control group. Post-treatment, serum creatinine levels decreased and GFR increased in the control group (P < .05), while the serum creatinine level increased and GFR decreased in the observation group (P < .05). Mean blood pressure decreased in both groups post-treatment (P < .05). The observation group exhibited lower rates of remarkable and effective outcomes and higher rates of general effective and ineffective outcomes (P < .05). Logistic regression analysis highlighted age, severity of nephropathy, underlying conditions, lifestyle, and pre-treatment proteinuria as significant factors influencing the impact of Shenqi Yanshen Granule on proteinuria in patients with nephrotic syndrome (P < .05). Conclusion • Shenqi Yanshen Granule proves to be a potent intervention for reducing proteinuria in patients with nephrotic syndrome. Notably, age and disease severity emerge as pivotal determinants of drug efficacy. (*Altern Ther Health Med.* [E-pub ahead of print.])

evaluating therapeutic efficacy. Its control holds decisive significance in preventing disease progression and enhancing patient prognosis.³⁻⁵ Shenqi Yanshen Granule, a traditional Chinese medicine compound, is frequently employed in the treatment of various kidney diseases, including nephrotic syndrome. Comprising a blend of herbal ingredients, this granule aims to enhance renal microcirculation, reduce proteinuria, and contribute to renal damage repair through a multifaceted approach. Despite achieving positive outcomes in nephrotic syndrome treatment, the specific factors influencing its therapeutic effects remain inadequately understood. Furthermore, the evident variations in treatment responses among individuals underscore the need for a comprehensive understanding and evaluation of various factors that could impact treatment outcomes. This includes not only considering the pharmacological characteristics of the drug but also the patient's underlying health conditions, age, lifestyle, disease severity, and proteinuria levels before treatment. Therefore, a systematic logistics analysis of these potential influencing factors is of great clinical significance for optimizing treatment plans,

improving treatment efficacy, and predicting treatment prognosis. This study aims to explore the diverse factors influencing the effect of Shenqi Yanshen Granule in ameliorating early proteinuria in patients with stage 1-3 nephrotic syndrome through logistic regression analysis. It is anticipated that the findings of this study will contribute targeted treatment recommendations to clinical practice, ultimately leading to improved treatment outcomes and enhanced quality of life for individuals with nephrotic syndrome.

MATERIALS AND METHODS

General information

We enrolled 100 patients diagnosed with nephrotic syndrome and renal function stages 1-3, who received treatment at our hospital from May 2021 to March 2023. The patients, aged 43-70 years, had an average age of 66.42 ± 5.38 years, comprising 58 males and 42 females. All patients received Shenqi Yanshen Granule treatment and were subsequently categorized into the control group (n = 68) (with a proteinuria decrease of \geq 50%) and the observation group (n = 32) (with a proteinuria decrease of < 50% or an increase) based on the change in 24-hour proteinuria. Informed consent was obtained from all patients upon study enrollment.

Inclusion criteria. Age between 18-75 years, regardless of gender; diagnosis of nephrotic syndrome according to recognized medical standards; renal function in stage 1-3 based on glomerular filtration rate (GFR) analysis; the ability to comprehend the study's nature, purpose, and potential risks, and willingness to sign the informed consent form voluntarily.

Exclusion criteria. Presence of other serious diseases, such as heart disease, uncontrolled hypertension, diabetes, and malignant tumor; use of medications that may impact renal function in the past 3 months; pregnancy or lactation; known allergy to components of Shenqi Yanshen Granule; refusal to sign informed consent.

Medical ethics issues

The research received prior approval from the Ethics Committee of First Affiliated Hospital of Chongqing College of Traditional Chinese Medicine, where the study was conducted. Informed consent was obtained from all research subjects, and all procedures adhered to ethical norms and regulations.

24-hour proteinuria detection

Patients were instructed to collect urine before and after treatment, and the total protein content of the collected urine samples was measured using standardized biochemical methods in the laboratory to ensure measurement accuracy. Data obtained were recorded and summarized to calculate 24-hour proteinuria before and after treatment.

Analysis of renal function indexes

Blood samples were collected from each participant through venous blood sampling, and serum was separated to detect the serum creatinine level using the enzymatic method. Serum samples were combined with reagents and incubated at 37°C allowing creatinine to react with enzymes, resulting in detectable products. The absorbance change of the reaction mixture was measured using a spectrophotometer. To calculate the GFR, the creatinine clearance method or a modified formula such as the CKD-EPI (Chronic Kidney Disease Epidemiology Collaboration) formula was applied, considering factors such as age, gender, race, and blood creatinine level. All data were meticulously recorded and entered into the database for analysis. These measurements not only provided baseline information for each patient but also enabled researchers to assess the impact of treatment on renal function. Changes in serum creatinine level or GFR may indicate improvements or deterioration in renal function, offering a precise means of monitoring participant renal health and evaluating therapeutic effectiveness.

Monitoring of mean systolic blood pressure

Utilizing validated ambulatory blood pressure monitoring equipment, an appropriate size cuff was selected according to the patient's arm circumference. During the 24-hour monitoring period, measurements were set at 30-minute intervals during the day (7:00 AM to 10:00 PM) and 60-minute intervals at night (10:00 PM to 7:00 AM the following day). Patients carried out their routine activities during monitoring, and the equipment automatically recorded systolic blood pressure values for each measurement, storing the data for subsequent analysis. Post-monitoring, data were extracted from the equipment, and the average systolic blood pressure for each patient was calculated.

Evaluation criteria for therapeutic effect

The therapeutic effect was assessed based on changes in clinical symptoms and biochemical indexes, categorized as follows: Remarkable effects: Substantial reduction in proteinuria (e.g., more than 50%), noticeable improvement in renal function index, well-controlled blood pressure, and significant reduction in edema. Effective: Reduction in proteinuria (e.g., 25%-50%), improvement in renal function index, stable or improved blood pressure, and alleviation of edema. General: Slight reduction in proteinuria (e.g., less than 25%), stable or slightly improved renal function index, minimal change in blood pressure, and limited relief in edema. Invalid: No significant decrease or increase in proteinuria, no improvement or worsening of renal function index, no improvement or increase in blood pressure, and no relief or aggravation of edema.

Statistical analysis

Data were presented as mean \pm standard deviation. Group comparisons were analyzed using the student *t* test or Chisquare test. A significance level of *P* < .05 was considered statistically significant. Multivariate logistic regression was employed to analyze the influencing factors of Shenqi Yanshen Granule in improving proteinuria in patients with nephrotic syndrome. Statistical analysis was conducted using SPSS for Windows, version 13.0 (SPSS Inc., Chicago, IL, USA).

RESULTS

Comparison of general patient data

Based on our records, as summarized in Table 1, the maleto-female ratio in the control group was 40:28, with an average age of 61.37 ± 4.55 years, an average BMI of 22.45 ± 1.95 kg/ m², and an average illness duration of 2.18 ± 1.33 years. This group included 10 cases of hypertension, 7 cases of diabetes, 18 cases of smoking, and 23 cases of drinking within the last three years. In the observation group, the male-to-female ratio was 18:14, with an average age of 68.51 ± 5.37 years and an average BMI of 23.72 ± 2.11 kg/m². This group had 6 cases of hypertension, 4 cases of diabetes, 10 cases of smoking, and 12 cases of drinking within the past three years. The age and duration of illness in the observation group were longer than in the control group (P < .05), while no significant differences were observed in other general data (P > .05).

24-hour proteinuria

A comparison of 24-hour proteinuria before and after treatment revealed a significant difference between the two groups before treatment (P < .05). After treatment, proteinuria decreased in both groups (P < .05), with the observation group having higher proteinuria than the control group (P < .05) as shown in Figure 1 and Table 2.

Analysis of biochemical indexes of renal function

Post-treatment, serum creatinine levels decreased and GFR increased in the control group (P < .05). However, the observation group exhibited an increase in serum creatinine (P < .05) and a reduction in GFR (P < .05) as shown in Table 3.

Comparison of mean systolic blood pressure

Mean systolic blood pressure, measured by ambulatory blood pressure monitoring, decreased in both groups after treatment (P < .05). However, the observation group showed a higher blood pressure value compared to the control group after the treatment (P < .05) as shown in Table 4.

Comparison of therapeutic effects

Clinical therapeutic effects were compared between the two groups, with the observation group exhibiting lower rates of remarkable and effective outcomes (P < .05). Whereas, the general effective and ineffective rates were higher in the observation group compared to the control group (P < .05) as shown in Figure 2 and Table 5.

Comparison of factors affecting therapeutic effect

Multivariate analysis demonstrated a relationship between the therapeutic effect of Shenqi Yanshen Granule and factors such as age, symptom severity, underlying conditions, lifestyle, and proteinuria before treatment (P < .05) as seen in Table 6.

Multivariate logistic regression analysis

Utilizing multivariate logistic regression, factors influencing the effect of Shenqi Yanshen Granule on

Table 1. Statistics of General Patients Data $(x \pm s)$

	Control group	Observation group	t value /	
Parameter	(n = 68)	(n = 32)	χ^2 value	P value
Gender (male: female)	40:28	fourteen past six PM	4.339	.115
Age (years)	61.37 ± 4.55	68.51 ± 5.37	11.307	.003
BMI (kg/m ²)	22.45 ± 1.95	23.72 ± 2.11	9.652	.621
Illness duration	2.18 ± 1.33	4.37 ± 1.55	13.225	.015
Hypertension (%)	10 (14.70%)	6 (18.75%)	4.514	.466
Diabetes (%)	7 (10.29%)	4 (12.50%)	3.227	.538
Smoking	18 (26.47%)	8 (25.00%)	4.168	.294
Alcohol consumption	22 (32.35%)	12 (37.50%)	5.305	.117

Figure 1. Detection of 24-hour Proteinuria



Table 2. Detection of 24-hour Proteinuria $(\overline{x \pm s})$

Group	Before treatment (mg)	After treatment (mg)
Control group (n = 68)	4542.23 ± 131.46	3224.84 ± 122.49
Observation group $(n = 32)$	5432.15 ± 158.35	4368.21 ± 118.02
t value	14.116	12.508
P value	.032	.005

Table 3. Biochemical Indexes of Renal Function $(x \pm s)$

	Before treatment		After treatment		
	Serum creatinine	GFR	Serum creatinine	GFR	
Group	(mg/dL)	(mL/min)	(mg/dL)	(mL/min)	
Control group (n = 68)	1.22 ± 0.34	91.56 ± 10.33	1.05 ± 0.18	116.27 ± 10.47	
Observation group $(n = 32)$	1.28 ± 0.31	93.42 ± 9.42	1.33 ± 0.25	95.42 ± 7.35	
t value	2.108	4.229	10.714	13.688	
P value	.306	.215	.024	.013	

Table 4. Comparison of Mean Systolic Blood Pressure $(x \pm s)$

Group	Before treatment (mmHg)	After treatment (mmHg)
Control group (n = 68)	138.34 ± 16.33	125.25 ± 11.77
Observation group $(n = 32)$	140.67 ± 15.49	135.63 ± 13.65
t value	3.621	12.503
P value	.668	.014

Figure 2. Comparison of Therapeutic Effects



Table 5. Comparison of Therapeutic Effects $(x \pm s)$

Group	Remarkable effect (%)	Effective (%)	General (%)	Invalid (%)
Control group (n = 68)	26 (38.23%)	21 (30.88%)	14 (20.58%)	7 (10.31%)
Observation group $(n = 32)$	4 (12.50%)	7 (21.87%)	13 (40.62%)	8 (25.00%)
t value	12.503	14.284	9.633	14.195
P value	.012	.002	.003	.026

Table 6. Factors Affecting Therapeutic Effect $(x \pm s)$

Index	Control group (n = 68)	Observation group (n = 32)	P value	
Age				
<65	47 (69.11%)	6 (18.75%)	014	
≥65	21 (30.89%)	26 (81.25%)	014	
Renal function staging				
Phase I	35 (51.47%)	6 (18.75%)		
Phase II	14 (20.59%)	8 (25.00%)	.024	
Phase III	19 (27.94%)	18 (56.25%)]	
Basic disease				
Have	23 (32.36%)	20 (62.50%)	007	
Without	45 (67.64%)	12 (37.50%)	1.006	
Way of life				
Regular/good	50 (73.52%)	12 (37.50%)	.012	
Irregular/poor	18 (26.48%)	20 (62.50%)		
Baseline proteinuria				
≥700	14 (20.59%)	19 (59.37%)	004	
<700	54 (79.41%)	13 (40.63%)	1.004	

 Table 7. Multivariate Logistic Regression Analysis

Variable	Odds ratio	95% CI	P value
Age (for each additional year)	1.34	1.05-1.28	<.05
Severity of illness (medium/high)	2.06	1.37-1.96	<.05
Underlying conditions (with/without)	2.33	1.45-2.64	<.05
Lifestyle (poor/good)	2.18	1.15-1.42	<.05
Baseline proteinuria (every 100 mg increase)	1.57	2.73-3.63	<.05

improving proteinuria in patients with nephrotic syndrome were identified as age, severity of nephropathy, underlying conditions, lifestyle, and pre-treatment proteinuria levels (P < .05), as evident from Table 7.

DISCUSSION

This study aims to explore the influencing factors of Shenqi Yanshen Granule in improving proteinuria in patients with nephrotic syndrome at renal function stages 1-3. The results indicate a reduction in 24-hour proteinuria and serum creatinine, coupled with an increase in GFR after treatment for all patients. However, significant differences were observed between the observation and the control groups, with the clinical efficacy analysis revealing a less favorable treatment outcome in the observation group. In addition, age, illness severity, underlying conditions, lifestyle, and pre-treatment proteinuria emerged as crucial factors impacting therapeutic effectiveness. These findings hold substantial clinical and research significance.

The study outcomes affirm the efficacy of Shengi Yanshen Granule in ameliorating proteinuria among patients with nephrotic syndrome, aligning with traditional Chinese medicine principles, emphasizing its role in tonifying kidney qi and improving renal function.^{6,7} This provides a promising avenue for the integrated treatment of nephrotic syndrome, bridging traditional Chinese and Western medicine practices. Particularly noteworthy is the potential of this traditional Chinese medicine approach as a new therapeutic option for nephropathy, addressing a gap where current treatments often focus on symptom control rather than providing a radical cure. However, the considerable disparity in therapeutic effects emphasizes the need for individualized treatment plans. Significant differences in proteinuria levels, serum creatinine, and GFR post-treatment suggest that Shenqi Yanshen Granule may not universally benefit all nephrotic syndrome patients. This underscores the importance of considering patient-specific factors such as age, disease severity, underlying conditions, and lifestyle when administering Shenqi Yanshen Granules.

Age emerges as a significant determinant influencing the therapeutic outcome of Shenqi Yanshen Granules in nephrotic syndrome, warranting further exploration.⁸ Traditionally, the aging process is associated with natural deterioration in various physiological systems and organ functions, encompassing the kidney's detoxification capabilities, drug metabolism, excretion ability, and overall responsiveness to diseases and treatments. This age-related physiological change may elucidate the tendency for older patients with nephrotic syndrome to show a less robust response to treatments compared to their younger counterparts. From a renal function perspective, advancing age is often linked to a reduction in glomerulus filtration capacity, and some elderly individuals may experience varying degrees of renal function decline, even in the absence of overt renal disease.9-11 Additionally, elderly individuals commonly report an array of chronic illnesses such as hypertension and diabetes, potentially exacerbating kidney damage and influencing the kidney's response to treatment. Furthermore, the aging immune system can affect the patient's responsiveness to immunomodulation therapy, a consideration vital for doctors formulating treatment plans.12,13

The fundamental symptoms and lifestyle choices of patients wield substantial influence in the management of nephrotic syndrome, particularly in the context of proteinuria. These factors not only shape the disease progression but also determine the patient's receptivity to drugs and other therapeutic interventions. Basic symptoms, such as diabetes, hypertension, or cardiovascular diseases, frequently coexist with kidney disease, potentially intensifying kidney damage and constraining the kidney's responsiveness to treatment.14-16 For instance, long-term uncontrolled hyperglycemia and hypertension are recognized contributors to glomerular damage and the accelerated decline of renal function. Therefore, the effective management of these foundational symptoms stands as a pivotal component within any comprehensive treatment plan for kidney diseases. The impact of lifestyle on the kidney is undeniable, with detrimental habits, like smoking and excessive drinking proving to exert both direct and indirect negative effects.^{17,18} Smoking is not only related to hypertension and arteriosclerosis but is also considered an independent risk factor for chronic kidney disease. Excessive alcohol consumption can elevate blood pressure and contribute to heart disease, subsequently impacting kidney function. Additionally, high-salt and high-fat dietary patterns may aggravate hypertension and cardiovascular diseases, posing a significant threat to renal health.^{19,20} Beyond their direct impact on kidneys, these unhealthy habits can hinder the effect of treatment programs, diminish the quality of life, and potentially lead to other health complications. Therefore, instigating changes in these habits is paramount. Encouraging patients to quit smoking, reduce alcohol consumption, adopt heart-healthy dietary practices, and engage in regular physical

activity can not only mitigate further kidney damage but also enhance the overall health and well-being of patients.

The prognostic significance of proteinuria before treatment has garnered increasing attention in nephrotic syndrome management. Proteinuria serves not only as an indicator of renal injury but also as a crucial parameter for evaluating disease progression and treatment response.^{21,22} Research indicates that higher levels of proteinuria before treatment often correlate with more severe renal damage, necessitating more proactive treatment interventions. Monitoring proteinuria is instrumental in helping physicians judge disease severity, track disease progression, evaluate the effectiveness of treatment plans, and make necessary adjustments. Regular and accurate proteinuria detection ensures that patients receive appropriate treatment, mitigating the risks of both over-treatment and under-treatment, both of which can have enduring effects on patient health^{23,24} Furthermore, changes in proteinuria levels can serve as a direct basis for refining the treatment plan.²⁵ A decrease in proteinuria post-treatment signals the efficacy of the treatment regimen, advocating its continuation. Conversely, if proteinuria levels show little improvement or increase, physicians may need to re-evaluate the current treatment methods, potentially contemplating changes in medications or adjustments to doses. Recognizing that individual patients may react differently to treatment underscores the importance of crafting personalized treatment plans. Physicians must comprehensively consider the patient's overall health status, existing complications, lifestyle, and personal preferences to tailor the most suitable treatment plan. This approach enhances the targeted and efficient monitoring and evaluation of proteinuria.

CONCLUSION

In summary, Shenqi Yanshen Granule demonstrates a significant effect in treating proteinuria in patients with nephrotic syndrome. However, the therapeutic outcome is subject to various factors, including the patient's age, disease severity, underlying conditions, and lifestyle, as well as pretreatment proteinuria levels. Particularly, age and disease severity wield a substantial influence on drug efficacy. This underscores the necessity of adjusting treatment strategies based on the specific conditions of each patient to ensure optimal therapeutic results in practical applications.

AUTHOR DISCLOSURE STATEMENT

The authors declare that they have no competing interests.

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Jing Yang contributed to the conception and design of the study; all authors performed the experiments and collected and analyzed data; Xiao Yu wrote the manuscript; all authors reviewed and approved the final version of the manuscript.

AVAILABILITY OF DATA AND MATERIAL

The datasets generated and analyzed during the current study are available from the corresponding author upon reasonable request.

REFERENCES

- Moriyama T, Karasawa K, Hasegawa F, Uchida K, Nitta K. Sertraline Reduces Albuminuria by Interfering with Caveolae-Mediated Endocytosis through Glomerular Endothelial and Epithelial Cells. Am J Nephrol. 2019;50(6):444-453. doi:10.1159/000503917
- Di Paolo S, Fiorentino M, De Nicola L, et al; Italian Society of Nephrology and the Italian Diabetes Society. Indications for renal biopsy in patients with diabetes. Joint position statement of the Italian Society of Nephrology and the Italian Diabetes Society. *Nutr Metab Cardiovasc Dis*. 2020;30(12):2123-2132. doi:10.1016/j.numecd.2020.09.013
- Tomas NM, Dehde S, Meyer-Schwesinger C, et al. Podocyte expression of human phospholipase A2 receptor 1 causes immune-mediated membranous nephropathy in mice. *Kidney Int.* 2023;103(2):297-303. doi:10.1016/j.kint.2022.09.008
- Falcone S, Nicol T, Blease A, et al. A novel model of nephrotic syndrome results from a point mutation in Lama5 and is modified by genetic background. *Kidney Int.* 2022;101(3):527-540. doi:10.1016/j.kint.2021.10.031
- Lidberg KA, Muthusamy S, Adil M, et al. Serum Protein Exposure Activates a Core Regulatory Program Driving Human Proximal Tubule Injury. J Am Soc Nephrol. 2022;33(5):949-965. doi:10.1681/ASN.2021060751
- Park SJ, Kim Y, Yang SM, et al. Discovery of endoplasmic reticulum calcium stabilizers to rescue ER-stressed podocytes in nephrotic syndrome. *Proc Natl Acad Sci USA*. 2019;116(28):14154-14163. doi:10.1073/pnas.1813580116
- Bridoux F, Javaugue V, Nasr SH, Leung N. Proliferative glomerulonephritis with monoclonal immunoglobulin deposits: a nephrologist perspective. *Nephrol Dial Transplant*. 2021;36(2):208-215. doi:10.1093/ndt/gfz176
- Moriyama T, Hasegawa F, Miyabe Y, et al. Intracellular trafficking pathway of albumin in glomerular epithelial cells. *Biochem Biophys Res Commun.* 2021;574:97-103. doi:10.1016/j. bbrc.2021.08.043
- Ishigami J, Padula WV, Grams ME, et al. Cost-effectiveness of Pneumococcal Vaccination Among Patients With CKD in the United States. Am J Kidney Dis. 2019;74(1):23-35. doi:10.1053/j. ajkd.2019.01.025
- Ćaroli A, Remuzzi A, Ruggiero B, et al. Functional Magnetic Resonance Imaging Versus Kidney Biopsy to Assess Response to Therapy in Nephrotic Syndrome: A Case Report. [J]. Kidney Med. 2020;2(6):804-809. doi:10.1016/j.xkme.2020.07.008
- Nakamura J, Nagatoya K, Fujii N, et al. New selectivity index calculated using protein fraction as a substitute for the conventional selectivity index. *Clin Exp Nephrol.* 2019;23(10):1196-1201. doi:10.1007/s10157-019-01753-2
- Sambharia M, Rastogi P, Thomas CP. Monogenic focal segmental glomerulosclerosis: A conceptual framework for identification and management of a heterogeneous disease. *Am J Med Genet C Semin Med Genet.* 2022;190(3):377-398. doi:10.1002/ajmg.c.31990
- Mühlig AK, Steingröver J, Heidelbach HS, et al. The calcium-sensing receptor stabilizes podocyte function in proteinuric humans and mice. *Kidney Int.* 2022;101(6):1186-1199. doi:10.1016/j. kint.2022.01.036
- Widmeier E, Airik M, Hugo H, et al. Treatment with 2,4-Dihydroxybenzoic Acid Prevents FSGS Progression and Renal Fibrosis in Podocyte-Specific Coq6 Knockout Mice. J Am Soc Nephrol. 2019;30(3):393-405. doi:10.1681/ASN.2018060625
- Willows J, Odudu A, Logan I, Sheerin N, Tomson C, Ellam T. Changing Protein Permeability with Nephron Loss: Evidence for a Human Remnant Nephron Effect. Am J Nephrol. 2019;50(2):152-159. doi:10.1159/000501472
- Domingo-Gallego A, Pybus M, Madariaga L, et al. Clinical and genetic characterization of a cohort of proteinuric patients with biallelic CUBN variants. *Nephrol Dial Transplant*. 2022;37(10):1906-1915. doi:10.1093/ndt/gfab285
- Tomas NM, Schnarre A, Dehde S, et al. Introduction of a novel chimeric active immunization mouse model of PLA2R1-associated membranous nephropathy. *Kidney Int.* 2023;104(5):916-928. doi:10.1016/j.kint.2023.07.024
- Li G, Kidd J, Kaspar C, et al. Podocytopathy and Nephrotic Syndrome in Mice with Podocyte-Specific Deletion of the Asah1 Gene: Role of Ceramide Accumulation in Glomeruli. Am J Pathol. 2020;190(6):1211-1223. doi:10.1016/j.ajpath.2020.02.008
- Renaghan AD, Jaimes EA, Malyszko J, Perazella MA, Sprangers B, Rosner MH. Acute Kidney Injury and CKD Associated with Hematopoietic Stem Cell Transplantation. *Clin J Am Soc Nephrol.* 2020;15(2):289-297. doi:10.2215/CJN.08580719
- Wang Q, Wang D, Shibata S, et al. Group I metabotropic glutamate receptor activation induces TRPC6-dependent calcium influx and RhoA activation in cultured human kidney podocytes. *Biochem Biophys Res Commun.* 2019;511(2):374-380. doi:10.1016/j.bbrc.2019.02.062
- Widmeier E, Yu S, Nag A, et al. ADCK4 Deficiency Destabilizes the Coenzyme Q Complex, Which Is Rescued by 2,4-Dihydroxybenzoic Acid Treatment. J Am Soc Nephrol. 2020;31(6):1191-1211. doi:10.1681/ASN.2019070756
- Chen JL, Wang L, Yao XM, et al. Association of Urinary Plasminogen-Plasmin with Edema and Epithelial Sodium Channel Activation in Patients with Nephrotic Syndrome. Am J Nephrol. 2019;50(2):92-104. doi:10.1159/000501059
- Tahou M, Chandler JC, Ashton E, et al. Mutations in LAMB2 Are Associated With Albuminuria and Optic Nerve Hypoplasia With Hypopituitarism. J Clin Endocrinol Metab. 2020;105(3):595-599. doi:10.1210/clinem/dgz216
- Nappi C, Zampella E, Volpe F, et al. Identification and typing of cardiac amyloidosis by noninvasive imaging: two cases for two patterns. J Nucl Cardiol. 2020;27(3):915-920. doi:10.1007/ s12350-019-01982-8
- Funk SD, Bayer RH, McKee KK, et al. A deletion in the N-terminal polymerizing domain of laminin β2 is a new mouse model of chronic nephrotic syndrome. *Kidney Int.* 2020;98(1):133-146. doi:10.1016/j.kint.2020.01.033