KIDNEY DISEASES

Dr. Annie Ninan

Associate Professor

PG Department of Home Science, Korambayil Ahamed Haji Memorial Unity Women‘s College, Manjeri, Malappuram, 676122, Kerala, India

INTRODUCTION

The structural and functional unit of the kidney, the 'nephron,' consists of a renal corpuscle (glomerulus surrounded by a Bowman capsule) and a renal tubule. Each kidney in an adult human contains around 1 million nephrons. A fenestrated endothelium forms the inner glomerular layer, followed by a layer composed of various extracellular proteins forming a meshwork called the glomerular basement membrane (GBM). The outer layer has visceral epithelial cells, podocytes, and mesangial cells. The intricate arrangement provides the basis for continuous plasma volume filtration at the glomerular level.

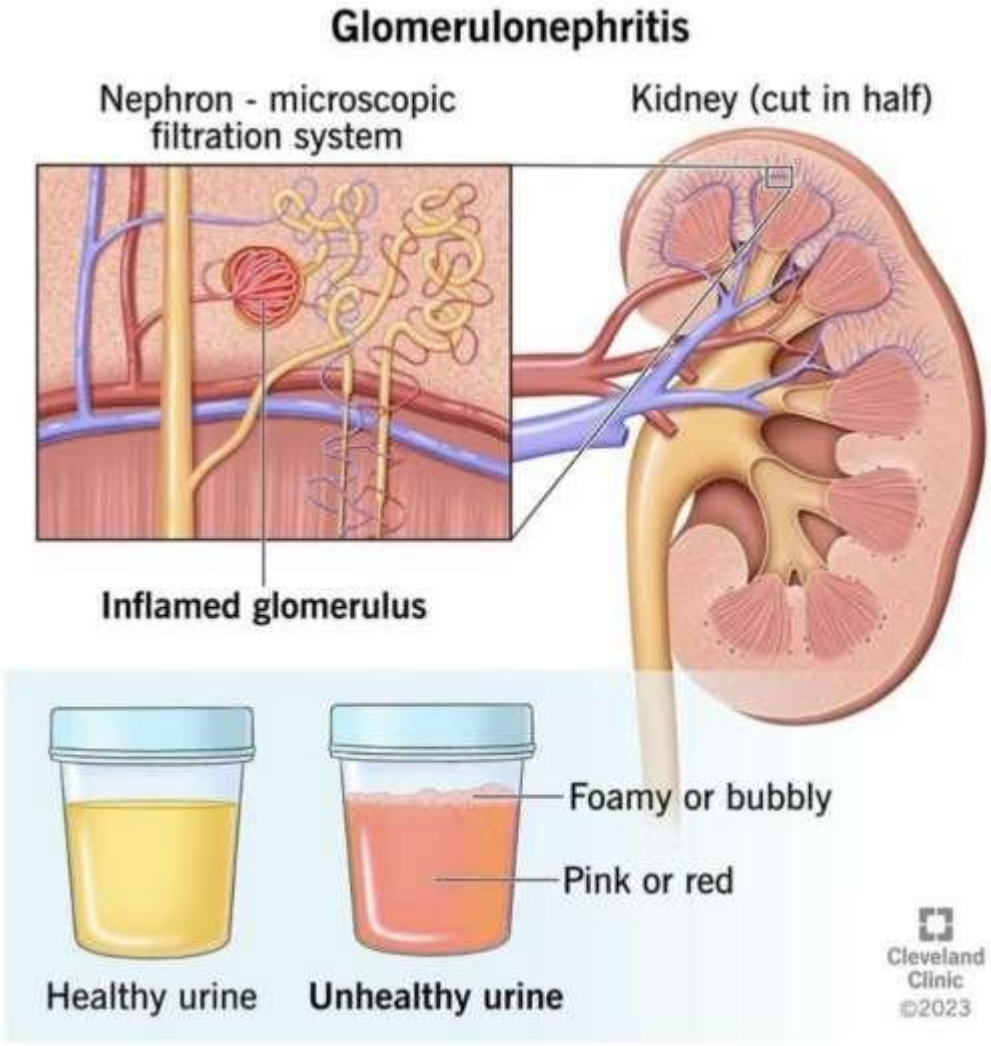
The term "glomerulonephritis" encompasses a subset of renal diseases characterized by immune-mediated damage to the basement membrane, the mesangium, or the capillary endothelium, resulting in hematuria, proteinuria, and azotemia.

Acute forms of glomerulonephritis (GN) can result from either a primary renal cause or a secondary illness that causes renal manifestations. For instance, acute post-streptococcal glomerulonephritis (PSGN) is a typical example of acute glomerulonephritis secondary to a streptococcal infection; similarly, *Staphylococcus aureus* infection can also lead to glomerulonephritis. In recent times, however, the incidence of glomerulonephritis associated with staphylococcal has increased as opposed to the reduction of PSGN in the United States and most developed countries.

Most forms of glomerulonephritis are considered progressive disorders. Without timely therapy, progress to chronic glomerulonephritis (characterized by progressive glomerular damage and tubulointerstitial fibrosis leading to a reduced glomerular filtration rate). This leads to the retention of uremic toxins with subsequent progression into chronic kidney disease (CKD) and end-stage renal disease (ESRD) along with their associated cardiovascular diseases.

Glomerulonephritis is inflammation of the tiny filters in the kidneys (glomeruli). The excess fluid and waste that glomeruli remove from the bloodstream exit the body as urine. Glomerulonephritis can come on suddenly (acute) or gradually (chronic).

Glomerulonephritis occurs on its own or as part of another disease, such as lupus or diabetes. Severe or prolonged inflammation associated with glomerulonephritis can damage the kidneys.



ETIOLOGY

Etiological classification of glomerulonephritis can be made based on clinical presentation, ranging from severe proteinuria (>3.5 g/day) and edema qualifying for the nephrotic syndrome to a nephritic syndrome where haematuria and hypertension are more prominent while proteinuria is less pronounced.

Nephrotic Glomerulonephritis

- Minimal change disease
- Focal segmental glomerulosclerosis
- Membranoproliferative glomerulonephritis
- Membranous nephropathy
- HIV associated nephropathy
- Diabetic nephropathy
- Amyloidosis

Nephritic Glomerulonephritis

- IgA nephropathy
- Henoch Schonlein purpura (HSP)
- Post streptococcal glomerulonephritis.
- Anti-glomerular basement membrane disease
- Rapidly progressive glomerulonephritis
- Granulomatosis with polyangiitis
- Eosinophilic granulomatosis with polyangiitis
- Polyarteritis nodosa
- Idiopathic crescentic glomerulonephritis

Goodpasture syndrome

Lupus nephritis

Hepatitis C infection

Membranoproliferative glomerulonephritis (typical presentation is with acute nephritic syndrome, however, sometimes features resembling nephrotic syndrome may occur, additionally)

A more modern and widely accepted way to classify glomerulonephritis is to divide it into five forms of glomerulonephritis based on underlying immune processes. The following is the modern classification of glomerulonephritis, including pathogenic type and the disease entity associated with it:

Immune-complex GN - IgA nephropathy, IgA vasculitis, infection-related GN, lupus nephritis, and fibrillary GN with polyclonal Ig deposits

Pauci-immune GN - PR3-ANCA GN, MPO-ANCA GN, and ANCA-negative GN

Anti-glomerular basement membrane (GBM) GN - Anti-GBM GN

Monoclonal Ig GN - Proliferative GN with monoclonal Ig deposits, monoclonal Ig deposition disease, fibrillary GN with monoclonal Ig deposits, and immunotactoid glomerulopathy

C3 glomerulopathy - C3 glomerulonephritis, dense deposit disease

PATHOPHYSIOLOGY

The underlying pathogenetic mechanism common to all of these different varieties of glomerulonephritis (GN) is immune-mediated, in which both humoral as well as cell-mediated pathways are active. The consequent inflammatory response, in many cases, paves the way for fibrotic events that follow.

The targets of immune-mediated damage vary according to the type of GN. For instance, glomerulonephritis associated with staphylococcus shows IgA and C3 complement deposits.[3]

One of the targets is the glomerular basement membrane itself or some antigen trapped within it, as in post-streptococcal disease.[16] Such antigen-antibody reactions can be systemic, with

glomerulonephritis occurring as one of the components of the disease process, such as in systemic lupus erythematosus (SLE) or IgA nephropathy. On the other hand, in small vessel vasculitis, cell-mediated immune reactions are the main culprit instead of antigen-antibody reactions. Here, T lymphocytes and macrophages flood the glomeruli with resultant damage.

These initiating events activate common inflammatory pathways, i.e., the complement system and coagulation cascade. The generation of pro-inflammatory cytokines and complement products, in turn, results in the proliferation of glomerular cells. Cytokines such as platelet-derived growth factor (PDGF) are also released, ultimately causing glomerulosclerosis. This event is seen in those situations where the antigen is present for longer periods, for example, in hepatitis C viral infection. When the antigen is rapidly cleared, as in post-streptococcal GN, the resolution of inflammation is more likely.

Structural Changes

Structurally, cellular proliferation causes an increase in the cellularity of the glomerular tuft due to the excess of endothelial, mesangial, and epithelial cells. The proliferation may be of two types:

Endocapillary - within the glomerular capillary tufts

Extracapillary - in the Bowman space, including the epithelial cells

In extra-capillary proliferation, parietal epithelial cells proliferate to cause the formation of crescents, characteristic of some forms of rapidly progressive glomerulonephritis.

Thickening of glomerular basement membrane appears as thickened capillary walls on light microscopy. However, on electron microscopy, this may look like a consequence of the thickening of the basement membrane proper, for instance, diabetes or electron-dense deposits either on the epithelial or endothelial side of the basement membrane. There can be various types of electron-dense deposits corresponding to an area of immune complex deposition, such as subendothelial, subepithelial, intramembranous, and mesangial. (See the images below)

Features of irreversible injury include hyalinization or sclerosis that can be focal, diffuse, segmental, or global.

Functional Changes

Functional changes include the following:

Proteinuria

Haematuria

Reduction in creatinine clearance, oliguria, or anuria

Active urine sediments, such as RBCs and RBC casts

This leads to intravascular volume expansion, edema, and systemic hypertension.

SYMPTOMS

Signs and symptoms of glomerulonephritis may vary depending on whether you have the acute or chronic form and the cause. You may notice no symptoms of chronic disease. Your first indication that something is wrong might come from the results of a routine urine test (urinalysis).

Glomerulonephritis signs and symptoms may include:

Pink or cola-coloured urine from red blood cells in your urine (haematuria).

Foamy or bubbly urine due to excess protein in the urine (proteinuria).

High blood pressure (hypertension).

Fluid retention (edema) with swelling evident in your face, hands, feet and abdomen.

Urinating less than usual.

Nausea and vomiting.

Muscle cramps.

Fatigue.

CAUSES

Many conditions can cause glomerulonephritis. Sometimes the disease runs in families and sometimes the cause is unknown. Factors that can lead to inflammation of the glomeruli include the following conditions.

Infections

Infectious diseases can directly or indirectly lead to glomerulonephritis. These infections include:

Post-streptococcal glomerulonephritis. Glomerulonephritis may develop a week or two after recovery from a strep throat infection or, rarely, a skin infection caused by a streptococcal bacterium (impetigo). Inflammation occurs when antibodies to the bacteria build up in the glomeruli. Children are more likely to develop post-streptococcal glomerulonephritis than are adults, and they're also more likely to recover quickly.

Bacterial endocarditis. Bacterial endocarditis is an infection of the inner lining of your heart's chambers and valves. It isn't clear whether the inflammation in the kidneys is the result of immune system activity alone or other factors.

Viral kidney infections. Viral infections of the kidney, such as hepatitis B and hepatitis C, cause inflammation of the glomeruli and other kidney tissues.

HIV. Infection with HIV, the virus that causes AIDS, can lead to glomerulonephritis and progressive kidney damage, even before the onset of AIDS.

Autoimmune diseases

Autoimmune diseases are illnesses caused by the immune system attacking healthy tissues. Autoimmune diseases that may cause glomerulonephritis include:

Lupus. A chronic inflammatory disease, systemic lupus erythematosus can affect many parts of your body, including your skin, joints, kidneys, blood cells, heart and lungs.

Goodpasture's syndrome. In this rare disorder, also known as anti-GBM disease, the immune system creates antibodies to tissues in the lungs and kidneys. It can cause progressive and permanent damage to the kidneys.

IgA nephropathy. Immunoglobulin A (IgA) is an antibody that's a first line of defense against infectious agents. IgA nephropathy occurs when deposits of the antibody accumulate in the glomeruli. The inflammation and subsequent damage may go undetected for a long time. The most common symptom is blood in the urine.

Vasculitis

Vasculitis is inflammation of blood vessels. Types of vasculitis that can cause glomerulonephritis include:

Polyarteritis. This form of vasculitis affects medium and small blood vessels in many parts of your body, including the kidneys, skin, muscles, joints and digestive tract.

Granulomatosis with polyangiitis. This form of vasculitis, formerly known as Wegener's granulomatosis, affects small and medium blood vessels in your lungs, upper airways and kidneys.

Sclerotic conditions

Some diseases or conditions cause scarring of the glomeruli that results in poor and declining kidney function. These include:

High blood pressure. Long-term, poorly managed high blood pressure can cause scarring and inflammation of the glomeruli. Glomerulonephritis inhibits the kidney's role in regulating blood pressure.

Diabetic kidney disease (diabetic nephropathy). High blood sugar levels contribute to scarring of the glomeruli and increase the rate of blood flow through the nephrons.

Focal segmental glomerulosclerosis. In this condition, scarring is scattered among some of the glomeruli. This may be the result of another disease, or it may occur for no known reason.

Other causes

Infrequently, chronic glomerulonephritis runs in families. One inherited form, Alport syndrome, also might impair hearing or vision.

Glomerulonephritis is associated with certain cancers, such as gastric cancer, lung cancer and chronic lymphocytic leukaemia.

COMPLICATIONS

Glomerulonephritis affects the ability of nephrons to filter the bloodstream efficiently. The breakdown in filtering results in:

Accumulation of wastes or toxins in the bloodstream.

Poor regulation of essential minerals and nutrients.

Loss of red blood cells.

Loss of blood proteins.

Possible complications of glomerulonephritis include:

Acute kidney failure. Acute kidney failure is the sudden, rapid decline in kidney function, often associated with an infectious cause of glomerulonephritis. The accumulation of waste and fluids can be life-threatening if not treated promptly with an artificial filtering machine (dialysis). The kidneys often resume typical function after recovery.

Chronic kidney disease. Persistent inflammation results in long-term damage and declining function of the kidneys. Chronic kidney disease is generally defined as kidney damage or decreased function for three or more months. Chronic kidney disease may advance to end-stage kidney disease, which requires either dialysis or a kidney transplant.

High blood pressure. Damage to the glomeruli from inflammation or scarring can lead to increased blood pressure.

Nephrotic syndrome. Nephrotic syndrome is a condition in which there is too much blood protein in urine and too little in the bloodstream. These proteins play a role in regulating fluids

and cholesterol levels. A drop in blood proteins results in high cholesterol, high blood pressure and swelling (edema) of the face, hands, feet and abdomen. In rare instances, nephrotic syndrome may cause a blood clot in a kidney blood vessel.

DIAGNOSIS

Blood

Complete blood count - A decreased haematocrit may suggest a dilutional type of anemia. In the background of an infectious cause, pleocytosis may be apparent.

Serum electrolytes - Potassium levels may be raised in patients with severe renal impairment.

Renal function tests - BUN and creatinine levels are raised, demonstrating a degree of renal impairment. In addition, the glomerular filtration rate (GFR) may be low.

Liver function tests - May point towards the underlying etiology.

Immunoglobulins

C-reactive protein (CRP)

Electrophoresis

Complement (C3, C4 levels) - Differentiation may allow the provider to narrow the differentials. Low complement levels indicate the following diseases: cryoglobulinemia, systemic lupus erythematosus, infective (bacterial) endocarditis, and shunt nephritis. Certain renal disorders may also be considered, such as membranoproliferative GN or post-streptococcal GN. Normal complement levels suggest an underlying abscess, polyarteritis nodosa, Henoch-Schönlein purpura, Goodpasture syndrome, idiopathic rapidly progressive GN, immune complex disease, and immunoglobulin G or immunoglobulin A nephropathy. Chauvet et al. reported that in patients with new-onset nephritis and low C3 levels, anti-factor B autoantibodies might help distinguish new-onset post-streptococcal GN from hypocomplementemic C3 glomerulonephritis.

Autoantibodies, such as antinuclear antibodies (ANA), anti-neutrophil cytoplasmic antibodies (ANCA), and anti-ds-DNA, anti-glomerular basement membrane (GBM) to rule out collagenopathy as the underlying cause of GN.

Blood culture - Blood culture is indicated when there is a fever, immunosuppression, intravenous drug abuse, indwelling catheters, or shunts.

Ant streptolysin O titer (ASOT) increases in 60 to 80% of cases. The rise begins in one to three weeks, peaks in three to five weeks, and returns to baseline in six months. It is unrelated to the severity, duration, and prognosis of renal disease.

Hepatitis serology - As infectious hepatitis can lead to glomerulonephritis of various types

Urine

The urine is usually dark, and the specific gravity is more than 1.020 with RBCs and RBC casts. The 24-hour urinary protein excretion and creatinine clearance may help establish the degree of renal impairment and proteinuria. The following parameters are usually helpful:

Microscopy, culture, and sensitivity

Bence Jones protein

Albumin to creatinine or protein to creatinine ratio

RBC casts

Imaging

Chest X-ray (helps to see for evidence of pulmonary hemorrhage, if any)

Renal ultrasound (helps in assessing the size and anatomy for biopsy)

Renal Biopsy

The examination of glomerular lesions via a renal biopsy provides the diagnosis of glomerulonephritis by answering the following queries:

Approximate proportion of involved glomeruli (focal vs. diffuse)

Approximate involvement of each glomerulus (segmental vs. global)

Presence of hypercellularity

Any evident sclerosis

Any deposits on immunohistology (immunoglobulins, light chains, complement)

Electron microscopy findings - precise localization of deposits. Exact ultrastructural appearance. Podocyte appearance

Presence of tubulointerstitial inflammation, atrophy, or fibrosis

Evident vessel-related pathology

DIETARY RECOMMENDATIONS

1. Control Protein Intake

Consuming moderate amounts of high-quality protein is important, but excessive protein can strain the kidneys. The recommended amount varies depending on the individual but typically ranges between 0.6 and 0.8 grams of protein per kilogram of body weight. Thus, good sources of high-quality protein include lean meats, poultry, fish, eggs, dairy products, and plant-based sources like legumes and tofu.

2. Limit Sodium (Salt) Intake

Excess sodium can lead to fluid retention and high blood pressure, which can worsen kidney function. But to control your BP you can follow high blood pressure diet plan. Always aim to consume less than 2300 milligrams of sodium per day.

Also, try not to include processed and packaged foods, as they tend to be high in sodium. Instead, choose fresh, whole foods and season meals with herbs, spices, and lemon juice to enhance flavor.

3. Monitor Fluid Intake

In some cases of glomerulonephritis, fluid intake may need to be restricted to manage swelling or fluid buildup. However, your healthcare provider will guide you on the appropriate amount of fluid to consume daily.

4. Control Blood Pressure

High blood pressure can further damage the kidneys. Also, follow a low-sodium diet, maintain a healthy weight, limit alcohol consumption, and engage in regular physical activity to help manage blood pressure.

5. Manage Potassium and Phosphorus Intake

Depending on the severity of glomerulonephritis and kidney function, it may be necessary to restrict potassium and phosphorus intake. Foods high in potassium include bananas, oranges, tomatoes, potatoes, and dairy products. Thus, foods high in phosphorus include dairy products, legumes, nuts, and whole grains. Your healthcare provider will advise you on the appropriate levels for your specific condition.

6. Consume A Balanced Diet

Focus on consuming a variety of fruits, vegetables, whole grains, and healthy fats. These foods provide essential vitamins, minerals, and antioxidants that support overall health.

7. Consider Dietary Modifications

Depending on individual circumstances, additional dietary modifications may be recommended, such as limiting oxalate-rich foods (e.g., spinach, rhubarb) or reducing the intake of certain types of fats. Your healthcare provider or dietitian can provide guidance based on your specific needs.

REFERENCES

- Stahl RA, Hoxha E. [Glomerulonephritis]. Dtsch Med Wochenschr. 2016 Jul;141(13):960-8. [PubMed]
- Wang SY, Bu R, Zhang Q, Liang S, Wu J, Liu XZS, Cai GY, Chen XM. Clinical, Pathological, and Prognostic Characteristics of Glomerulonephritis Related to Staphylococcal Infection. Medicine (Baltimore). 2016 Apr;95(15):e3386. [PMC free article] [PubMed]

- Khalighi MA, Al-Rabadi L, Chalasani M, Smith M, Kakani S, Revelo MP, Meehan SM. Staphylococcal Infection-Related Glomerulonephritis With Cryoglobulinemic Features. Kidney Int Rep. 2018 Sep;3(5):1128-1134. [PMC free article] [PubMed]
- Satoskar AA, Parikh SV, Nadasdy T. Epidemiology, pathogenesis, treatment and outcomes of infection-associated glomerulonephritis. Nat Rev Nephrol. 2020 Jan;16(1):32-50. [PubMed]
- Wen YK, Chen ML. The significance of atypical morphology in the changes of spectrum of postinfectious glomerulonephritis. Clin Nephrol. 2010 Mar;73(3):173-9. [PubMed]
- Politano SA, Colbert GB, Hamiduzzaman N. Nephrotic Syndrome. Prim Care. 2020 Dec;47(4):597-613. [PubMed]
- Davin JC, Coppo R. Henoch-Schönlein purpura nephritis in children. Nat Rev Nephrol. 2014 Oct;10(10):563-73. [PubMed]
- Ozkok A, Yildiz A. Hepatitis C virus associated glomerulopathies. World J Gastroenterol. 2014 Jun 28;20(24):7544-54. [PMC free article] [PubMed]
- Couser WG, Johnson RJ. The etiology of glomerulonephritis: roles of infection and autoimmunity. Kidney Int. 2014 Nov;86(5):905-14. [PubMed]
- Sethi S, Fervenza FC. Standardized classification and reporting of glomerulonephritis. Nephrol Dial Transplant. 2019 Feb 01;34(2):193-199. [PubMed]
- Wetmore JB, Guo H, Liu J, Collins AJ, Gilbertson DT. The incidence, prevalence, and outcomes of glomerulonephritis derived from a large retrospective analysis. Kidney Int. 2016 Oct;90(4):853-60. [PubMed]
- Schena FP, Nistor I. Epidemiology of IgA Nephropathy: A Global Perspective. Semin Nephrol. 2018 Sep;38(5):435-442. [PubMed]
- 13.Usui J, Tawara-Iida T, Takada K, Ebihara I, Ueda A, Iwabuchi S, Ishizu T, Iitsuka T, Takemura K, Kawamura T, Kaneko S, Sakai K, Kai H, Gomibuchi T, Nagata M, Kobayashi M, Koyama A, Suka M, Radhakrishnan J, Yamagata K. Temporal Changes in Post-Infectious Glomerulonephritis in Japan (1976-2009). PLoS One. 2016;11(6):e0157356. [PMC free article] [PubMed]
- Anochie I, Eke F, Okpere A. Childhood acute glomerulonephritis in Port Harcourt, Rivers State, Nigeria. Niger J Med. 2009 Apr-Jun;18(2):162-7. [PubMed]

- Becquet O, Pasche J, Gatti H, Chenel C, Abély M, Morville P, Pietrement C. Acute post-streptococcal glomerulonephritis in children of French Polynesia: a 3-year retrospective study. Pediatr Nephrol. 2010 Feb;25(2):275-80. [PubMed]
- 16.Mosquera J, Pedreañez A. Acute post-streptococcal glomerulonephritis: analysis of the pathogenesis. Int Rev Immunol. 2021;40(6):381-400. [PubMed]
- Lech M, Anders HJ. The pathogenesis of lupus nephritis. J Am Soc Nephrol. 2013 Sep;24(9):1357-66. [PMC free article] [PubMed]
- Jennette JC, Falk RJ, Hu P, Xiao H. Pathogenesis of antineutrophil cytoplasmic autoantibody-associated small-vessel vasculitis. Annu Rev Pathol. 2013 Jan 24;8:139-60. [PMC free article] [PubMed]