REVIEW ARTICLE

Immunology laboratory role of in diagnosing renal diseases

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Immune mediated injuries comprise a major bulk of renal disorders that mostly manifest as acute or chronic glomerulonephritides. Besides initial investigations for renal disorders, diagnosis of immune mediated renal diseases requires a battery of immunological tests and renal histopathology. The laboratory tests include anti-nuclear antibodies (ANA) followed by anti-double stranded deoxyribonucleic acid antibodies (anti-dsDNA) and/or anti-extractable nuclear antigens (anti-ENA), complement levels (C3, C4, factor H), rheumatoid factor (RF), C reactive proteins (CRP), anti-streptococcal antibodies including anti streptolysin-O titer (ASOT) and anti-deoxyribonuclease B (anti-DNAse B), anti-neutrophil-cytoplasmic antibodies (ANCA), anti-glomerular-basement membrane antibodies (anti-GBM), cryoglobulins detection, anti-phospholipid antibodies, nephritic factor, anti-phospholipase A2 receptor antibodies (anti-PLA2R), anti- thrombospondin type-1 domain-containing 7A (THSD7A) etc. The correct interpretation of these tests by an immunologist in collaboration with histopathologists and nephrologists is the key to an accurate diagnosis and successful management of patients with renal diseases.

A brief overview of the tests from the immunologist's perspectives for the diagnosis and monitoring of renal disorders is given in this review.

Key Words: Anti-neutrophil cytoplasmic antibodies; Anti-nuclear antibodies; anti-phospholipase A2 receptor antibodies; Anti-streptococcal antibodies; Complement proteins; C-reactive protein; Glomerulonephritis; Immunological investigations of renal diseases; Rheumatoid factor

INTRODUCTION

Customarily renal injury or failure are broadly classified as pre-renal (azotemia), post-renal (obstructive) and interstitial renal (vascular, parenchymal or tubular) diseases. Depending on the clinical course and development of renal dysfunction, renal disorders are also categorized as acute and chronic diseases [1,2].

Baseline investigations in any kind of renal disorder include complete blood picture, detailed urine report with or without culture and sensitivity, serum creatinine, glomerular filtration rate (GFR) and creatinine clearance, 24 h urinary protein excretion, fraction excretion of sodium and albumin, cystatin C and radiological investigations such as ultrasound, computed tomography scanning etc. [3,4].

Most of the renal diseases result due to immune mediated injury mainly manifesting as glomerulonephritides (GN) [4]. GN can be primary or it may be a part of other autoimmune disorders such as systemic lupus erythematosus (SLE) with multiple organ involvement or vasculitis [5]. Immunopathogenesis of GN involves activation of complement cascades and coagulation pathways, recruitment of inflammatory cells and release of proinflammatory cytokines. Other important mechanisms include failure of apoptosis and intraglomerular hemodynamic changes. Progression to fibrosis and scarring depends upon the rate of antigen clearance or their persistence [1,5].

The immunological investigations for workup of patients presenting acutely or with chronic GN include anti-nuclear antibodies (ANA) followed by anti-double stranded deoxyribonucleic acid antibodies (anti-dsDNA) and/ or anti-extractable nuclear antigens antibodies (anti-ENA), complement levels (mostly C3 and C4), rheumatoid factor (RF), C reactive proteins (CRP), anti-streptococcal antibodies such as anti-streptolysin O titer (ASOT) and anti-deoxyribonuclease B (anti-DNAse B), anti-neutrophil cytoplasmic antibodies (ANCA), anti-glomerular basement membrane antibodies (anti-GBM), cryoglobulins detection and characterization, anti-phospholipid antibodies (APLA), nephritic factor and recently added anti-phospholipase A2 receptor antibodies (anti-PLA2R). Some of these tests are done routinely while others are done depending upon the presenting clinical features or histopathological findings and other laboratory parameters [5-10].

The value of these tests (immunological laboratory parameters) will be discussed in detail with their clinical association. The overview of the tests to evaluate immune dysregulation with renal manifestations is given in Table 1. Table 2 summarizes the clinical and laboratory features in various types of GN.

Table 1: Overview of laboratory tests done in patients with renal diseases.

Tests	Association
ANA[1], anti-dsDNA[2], anti-ENA[3]	Autoimmune/connective tissue disorders such as lupus nephritis, systemic sclerosis, Sjögren's syndrome, inflammatory dermatomyositis
Anti-neutrophil cytoplasmic antibodies (ANCA)	Rapidly proliferative GN; Pauci immune glomerulonephritis, pulmonary-renal syndrome
Anti-glomerular basement membrane antibodies (anti-GBM)	Rapidly proliferative GN; Anti-GBM disease, pulmonary-renal syndrome

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Complement assays C3 and C4	All types of GN; especially required in monitoring of lupus nephritis, post-infectious/ post streptococcal GN, cryoglobulinemic GN, aHUS
ASOT[4], anti-DNAse B[5]	Post-streptococcal GN
Rheumatoid factor (RF)	Lupus nephritis, systemic sclerosis, vasculitis causing GN such as cryoglobulinemic GN, rheumatoid arthritis with or without renal involvement
C-reactive protein (CRP)	For monitoring of all inflammatory conditions. In differentiating acute LN from other causes of GN and infections
Cryoglobulins detection	Cryoglobulinemic GN; idiopathic or secondary
Anti-phospholipid antibodies (APLA)	Antiphospholipid syndrome causing renal APS
Anti-PLA2R[6]	Idiopathic membranous GN
Serum immunoglobulins	Multiple myeloma with renal manifestation , Henoch Schonlein purpura
Immunofixation electrophoresis	Multiple myeloma with renal manifestation
HBsAg[7], anti-HCV[8]	In all patients as a routine work up and especially in suspected cases of polyarteritis nodosa and cryoglobulinemic vasculitis.

[1]=anti-nuclear antibodies, [2]=anti-double stranded deoxyribonucleic acid antibodies, [3]=anti-extractable nuclear antigens, [4]=anti-streptolysin O titer, [5]=anti-deoxyribonuclease B antibodies, [6]=anti-phospholipase A2 receptor antibodies, [7]=hepatitis B surface antigen, [8]=anti-hepatitis C virus antibodies.

Table 2: Laboratory Findings in Immune Mediated Renal Diseases.

Disease	Renal involvement	Autoantibodies	Complement proteins	Other proteins	Other supportive laboratory features	References
APSGN[1]	5-52% of RPGN[2]	Anti-streptococcal antibodies (ASOT[34]	C3 mostly low, sometime C3 and C4 both low. Normal C3 and C4 do not rule out APSGN[1]	CRP[5]	Mild anemia, Hematuria with or without significant proteinuria	[7,11]
Anti-GBM[6]	10-20% of RPGN[2]	Anti-GBM[6]	Normal C3 and C4	CRP[5]	Hematuria ± proteinuria, Renal biopsy: linear deposition of IgG and C3 on GBM[6]	[12]
ANCA[78]	74% of RPGN[2], GPA[9]: 70-80%, MPA[10]: 90-100%, eGPA[11]:45%	C- and P-ANCA[7], anti-PR3[12], anti-MPO[13]	Normal to high C3 and C4	CRP[5]	Paucimmune, necrotizing and or crescentic GN[8], RPGN[2], usually preceded by upper respiratory infections, nasal polyps and nasal septum involvement in GPA[9] and eGPA[11], h/o asthma in eGPA[11]	[13-15]
Henoch Schonlein Purpura	20-50%	Negative for autoantibodies, ASOT[3]	C3 may be low	High IgA levels	Non-thrombotic purpura , arthralgia and positive throat cultures of group A β-hemolytic Streptococcus, Renal biopsy: mesangial hypercellularity, endocapillary proliferation, necrosis, cellular crescents, and leukocyte infiltration	[11,16]
Lupus Nephritis	40-75% of SLE[14]	Positive ANA[15], anti-ds DNA[16], anti-ENA[17] (anti-Sm[18], -SSA[19] ± SSB[20], -ribosomal P protein, -PCNA[21], etc.)	Low C3 and C4	Normal or low CRP[5]	Nephritic and/or nephritic syndrome. Renal biopsy: Immunoglobulins and complement deposition	[17,18]
Renal APS[22]	2.7% of APS[22] 30% of SLE[14] with APLA[23], 78% of catastrophic APS[22]	Persistence of APLA[25]	C3 and C4 may be low	Other coagulation proteins such as protein C and protein S may be low	Hypertension, Hematuria, proteinuria, renal dysfunction, Renal biopsy; TMA[26], thrombosis, infarction	[19-21]
Renal involvement in other connective tissue disorders	Sjogren's: 4.2-88%, SSc[27]: 5%, Inflammatory dermatomyositis: 20-23%	Sjogren's; anti-SSA[19] and SSB20, SSc[27]: anti-Scl-70, CENPB[28], anti-RNA polymerase III Antibodies, anti-Pm/Scl[29], Inflammatory myositis: anti-Jo1, anti-Pm/Scl[29]	Complements may be low in Sjogren's	High CRP[5]	Sjogren's: Type 1, Renal tubular acidosis, TIN[30], CGN[31], SSc[23]: TMA[26], renal crises in 5%, Inflammatory dermatomyositis: proximal muscle weakness, elevated muscle enzymes, electromyographic alterations, malignancies (9.4% to 32% in DM[32]& 4.4 to 17% in PM[33] patients) Renal biopsy: MPGN34, membranous, FSGS[35], CGN[31], TIN[30]	[17,22,23]

Cryoglobulinemic Glomerulo nephritis	20-40%	Negative in essential mixed cryoglobulinemia, In secondary mixed cryoglobulinemia, autoantibodies related to CTDs[36] may be present	Complements are usually low	Cryoglobulins, positivity for anti-HCV[37]	Medium to small vessel vasculitis causing arthralgia, thrombocytopenia and weakness. Renal histopathology may show cryoglobulin deposition, MPGN[34]or TMA[26]	[25]

1=acute post streptococcal glomerulonephritis, 2=rapidly progressive glomerulonephritis, 3=anti-streptolysin O titer , 4=anti-deoxyribonuclease B, 5=C-reactive protein, 6=glomerulobasement membrane, 7=anti-neutrophil cytoplasmic antibodies, 8=glomerulonephritis, 9=granulomatosis with polyangiitis, 10=microscopic polyangiitis, 11=eosinophilic granulomatosis with polyangiitis, 12=proteinase 3, 13=myeloperoxidase, 14=systemic lupus erythematosus, 15=anti-nuclear antibodies, 16=double stranded deoxyribonucleic acid antibodies , 17=extractable nuclear antigens, 18=anti-Smith antibodies, 19= Sjogren's syndrome antigen A, 20=Sjogren's syndrome antigen B, 21=proliferating cell nuclear antigen, 22=antiphospholipid syndrome, 23=anti-phospholipid antibodies, 24=beta-2 microglobulin, 25=lupus anticoagulant, 26=thrombotic microangiopathy,27=systemic sclerosis, 28=Centromere Protein B, 29=polymyositis/systemic sclerosis,30=tubulointerstitial nephritis, 31=crescentic glomerulonephritis, 32=dermatomyositis, 33=polymyositis, 34=membranoproliferative glomerulonephritis, 35=focal segmental glomerulosclerosis, 36=connective tissue diseases, 37=anti-hepatitis C virus antibodies.

ANA, anti-dsDNA and anti-ENA

ANA are the hallmark of most of the connective tissue disorders [25]. These are detected by various methods such as indirect immunofluorescent (IFA) assay using Hep-2 cell lines or rat tissue (liver, kidney, stomach) as substrate, enzyme linked immunosorbent assay (ELISA) and immunodiffusion techniques, etc. The widely accepted assay for ANA detection is IFA using Hep-2 cell lines. The sensitivity of the assay is higher with this method especially for diagnosing SLE but at the expense of specificity [26].

Renal involvement occurs in various connective tissue disorders including SLE, systemic sclerosis (SScl), Sjogren's syndrome (SS), inflammatory myositis [27,28] and others [17]. The histopathological evidence and detection of ANA followed by anti-dsDNA and anti-ENA antibodies has become the mainstay to make a final diagnosis of GN [5,29,30].

ANA can be positive in various other clinical conditions besides autoimmune disorders. They are also present in 5-10% of healthy individuals in low titers [31]. Therefore ANA results should be interpreted carefully in association with clinical features, other laboratory results and histopathological findings in GN patients.

Anti-dsDNA antibodies are detected most preferably by IFA using *Crithidia luciliae* as substrate. Other methods for anti-dsDNA detection including ELISA and agglutination assays are either less specific or less sensitive [32].

Anti-ENA antibodies can be detected by double immunodiffusion, counter current immunoelectrophoresis, ELISA and immunoblot assays. Detection of these autoantibodies are helpful in distinguishing various connective tissue disorders associated with renal manifestations such as anti-Scl-70 for diagnosing SScl, anti-Jo1 and anti-Pm/Scl for inflammatory myositis [33,34], anti-Sm for SLE and anti-SSA and anti-SSB for SLE or SS based on clinical features. In rare cases of ANA negative SLE, identification of anti-ribosomal P protein (anti-P antibodies) and rarely anti-SSA antibodies become very helpful in reaching a correct diagnosis. However, with ANA detection by IFA using Hep-2 cells, a negative ANA with positive anti-SSA is now a rarity. The characterization of ANA for their specific antigens is more important in GN patients with significant proteinuria [26].

Anti-phospholipid antibodies (APLA)

APLA are associated with antiphospholipid syndrome (APS). The syndrome is characterized by the manifestations of recurrent arterial and venous thrombosis in the presence of APLA. The most important antibodies, included in the classification criteria of APS are anti-beta-2 GP1antibodies (anti-β2GP1), anti-cardiolipin antibodies (aCL) and lupus anticoagulant (LA). Complete work-up of APS require detection of LA and screening and isotypes (IgG, IgM and IgA) detection of anti-β2GP1 & aCL. These antibodies should be present persistently when tested 12 weeks apart with fresh samples [19,35].

APS can be primary or it can be secondary when found with other autoimmune disorders. Renal APS include renal vessel thrombosis, renal artery stenosis, thrombotic microangiopathy, renal ischemia and anti-phospholipid nephropathies [20,36,37]. APLA are present in around 50% of SLE patients with or without APS [38]. Presence of APLA is associated with increased severity of lupus nephritis (LN) in these patients [20,39].

Anti-neutrophil cytoplasmic antibodies (ANCA)

ANCA are associated with a spectrum of small vessel vasculitides or can have renal limited disease. There are two types of ANCA detected by IFA using human neutrophils as substrate. The c-ANCA gives a cytoplasmic staining with specificity for proteinase-3 (PR-3) antigens on ELISA while p-ANCA give a perinuclear staining of human neutrophils and have specificity for myeloperoxidase (MPO) antigens on ELISA [40].

ANCA account for 90% cases of pauci-immune, crescentic lesions in the glomeruli that present as rapidly progressive GN (RPGN). Assays for both c- and p-ANCA patterns by IFA and anti-PR3 and anti-MPO IgG by ELISA are required to diagnose ANCA associated GN. An early diagnosis and prompt patient management is required in ANCA associated renal diseases to save the progression to end stage renal failure [41].

ANCA associated vasculitides and GN include granulomatosis with polyangiitis (GPA), formerly called Wegener's granulomatosis (WG), microscopic polyangiitis (MPA) and eosinophilic granulomatosis with polyangiitis (EGPA) or Churg Strauss syndrome. GPA is characterized by granulomatous inflammation of small vessels predominantly involving upper and lower respiratory tracts with mostly c-ANCA and anti-PR3 positivity [42]. In MPA, there is non-granulomatous inflammation of small vessels mostly presenting as palpable purpura, mononeuritis multiplex, gastrointestinal vasculitis and renal failure with p-ANCA and anti-MPO positivity. EGPA occurs in asthmatics and characteristically associated with peripheral eosinophilia, high serum IgE levels and mostly anti-MPO positivity [43,44].

Anti-glomerular basement membrane antibodies (anti-GBM)

Anti-GBM are associated with anti-GBM disease (renal limited) and Good Pasteur's disease (pulmonary-renal syndrome). It accounts for 10-20% cases of RPGN. Anti-GBM bind to alpha 3 chain of type IV collagen found in the specialized basement membranes of the kidneys and lungs. On histopathology, there is focal necrotizing GN and crescent formation with linear deposition of IgG with or without C3 along the glomerular capillary wall and glomerular basement membrane (GBM). Co-existence of ANCA with anti-GBM usually indicates vasculitis as the primary disease with better prognosis [45].

Anti-streptococcal antibodies

Anti-streptococcal antibodies are heterogeneous that are formed against various streptococcal antigens. These include ASOT, anti-DNAse B, anti-nucleotide adenine dinucleotide (anti-NAD) and anti-streptokinase (ASKase) in high titers [46].

Post-streptococcal GN is the most important and commonest cause of post-infectious GN that usually manifests in children as facial edema, hematuria, hypertension and acute renal failure. It follows either pharyngitis or skin infections with a β-hemolytic nephritogenic strain of streptococcus, occurring one to 12 weeks after initial infection [5].

Glomerular injury occurs due to anti-streptococcal antibodies that may bind to implanted antigens in the glomerulus. These antibodies may also cross react with glomerular structures that mimic streptococcal antigens [46]. In-situ immune complexes are formed that activate complement cascade by alternate pathway of complement activation, however, mannose binding lectin (MBL) or classical pathway may also be involved [11,47].

On histopathology, diffuse proliferative GN with immune-staining for C3 and IgG is seen in the mesangium and along capillary walls [7].

Anti-phospholipase A2 receptor antibodies (anti-PLA2R), anti-thrombospondin type-1 domain-containing 7A (anti-THSD7A) and other anti-podocyte antibodies

Recently identification of certain autoantibodies associated with primary membranous GN (pMN) has greatly improved the diagnosis of this disease. These antibodies include anti-PLA2R, anti-THSD7A, anti-neutral endopeptidase (anti-NEP) and anti-bovine serum albumin (anti-BSA) detected by either western blot, IFA or ELISA [48].

Anti-PLA2R antibodies have a high specificity (nearly 100%) and sensitivity around 70% for pMN. These autoantibodies are directed against M-type PLA2R, expressed normally on podocytes [49]. Anti-PLA2R are of IgG4 subclass and correlate well with remission and response to therapy [48,50,51].

Anti-THSD7A is also directed to the antigens present on podocytes named THSD7A. These antibodies can be detected in 2-5% of pMN, negative for anti-PLA2R. Anti-NEP and anti-BSA antibodies can be detected in children with pMN, however their clinical utility is not well established yet [48].

Complement levels

Complements are plasma proteins that provide protection against infections and autoimmunity. Complement activation is involved in most of the renal injury with or without low complement (C3 and C4) levels in the blood [52]. Usually classical or alternate pathways of complement activation are described in the pathogenesis of GN. C3 is found low in both pathways of complement activation while C4 is low in classical pathway complement activation [52,53].

The complement (C3 and C4) estimation assays are very useful not only in the diagnosis but monitoring of disease activity in various GN including LN, post-infectious GN, membranoproliferative GN (MPGN) and dense deposit disease (DDD). C3 is also found low sometimes in Henoch Schonlein purpura (HSP) [16,54]. Estimation of factor H, an alternate pathway complement regulatory protein, is done for the diagnosis of atypical hemolytic uremic syndrome (aHUS), MPGN type II and DDD. The complement protein assays are usually measured either by immunonephlometry or ELISA [53,55].

Anti-complement antibodies

The autoantibodies against various complement proteins or activated enzymes have been found in MPGN and DDD. These include C3 nephritic factor (C3NeF), C4 nephritic factor (C4NeF), anti-factor H (anti-fH), anti-factor B(anti-fib) and anti-C1q antibodies [56].

C3 Nef is an autoantibody of IgG or IgM isotype that prevents physiological decay of alternate pathway C3 convertase (C3Bb). These are of two types, properdin dependent (stabilizes C5 convertase as well) and properdin independent [56,57]. C4 NeF stabilizes classical pathway C3 convertase [58]. Anti-factor B antibodies have been detected in few

patients presenting with DDD. Autoantibodies against the complement regulator, factor H are detected in some patients with aHUS [56,59].

Various assays are in use to detect these antibodies. Detection of anti-fH and anti-fB can be done by ELISA, but assays for nephritic factors are not very sensitive neither specific. This is because of the variability in antigenic epitopes recognized by these autoantibodies [56,58].

Cryoglobulins

Cryoglobulins are paraproteins comprising of abnormal immunoglobulins that precipitate at temperatures below 37°C. They are strongly associated with hepatitis C virus (HCV) infection [60] but may be found in other infections, various autoimmune disorders or may be idiopathic [24,61].

Cryoglobulin detection requires stringent temperature control. The cryocrit or cryoprecipitate concentration does not correlate with the severity of vasculitis. However it is used for disease monitoring. Positive samples are characterized by immunofixation. Type II mixed cryoglobulins are associated with severe disease [61].

Rheumatoid factors (RFs)

RFs are autoantibodies against IgG molecule. The target antigenic epitope is in the Fc region of the molecule at the interface of Cγ2 and Cγ3. Under physiological conditions and in certain infections, polyclonal IgM-RFs are produced by CD5+Bcells that help in the removal of immune complexes and maintenance of immune homeostasis [62,63]. Pathological RFs are produced in rheumatoid arthritis, mixed cryoglobulinemia, chronic autoimmune diseases and certain infections. These pathological RFs are usually monoclonal and may be of other isotypes besides IgM (IgG, IgA or IgD) [63].

RF is a very useful test in the diagnostic workup and monitoring of GN. These auto antibodies have been reported to be involved in the pathogenesis of various GN including LN, IgA nephropathy, membranous GN [64], ANCA associated GN [65,66] and cryoglobulinemic GN with or without HCV [61,67]. Various assays are available to detect RF including latex agglutination assay, ELISA, immunonephlometry and multiplexed immunoassays [63].

C-reactive proteins (CRP)

CRP is an acute phase protein that increases several folds non-specifically in response to infections and inflammation and hence is a very useful surrogate marker in these conditions. In blood, it starts increasing in six to 12 h and peak at 19 h and is not influenced by other blood proteins or cellular constituents. Moreover, its concentration decreases more rapidly than erythrocyte sedimentation rate at the decline of inflammation or infection. Therefore, it is a much more reliable inflammatory marker for disease monitoring [68,69].

CRP is included in the diagnostic testing repertoire of GN and monitoring the response to treatment. In SLE patients, CRP helps to differentiate between active LN disease and infections [69-72].

Immunoglobulins, immunofixation electrophoresis (IFE) and free light chain assay

There is a polyclonal increase in serum immunoglobulins in chronic infections and autoimmune diseases [73]. This may also be reflected in immune mediated renal disorders [22]. However in GN patients with glomerular damage, serum IgG is often found low due to their urinary excretion [74]. In HSP, serum IgA is usually found high, though not used as a surrogate diagnostic marker [11,16].

The utility of serum immunoglobulins mainly lies in multiple myeloma (MM) along with serum and urine electrophoresis and immunofixation and free light chain assay [75].

In MM and monoclonal gammopathy of renal significance (MGRS), electrophoresis determines the presence of monoclonal proteins in the

form of M spike which is then characterized by immunofixation [76]. Recently serum free light chain assay has become an integral part of the diagnostic work-up and for monitoring and determining prognosis of patients with monoclonal gammopathy. Its role becomes more important in non-secretory multiple myeloma and light chain disease. It is more sensitive than urine protein electrophoresis and IFE (for Bence Jones proteins) [77,78].

Serum IgG subclasses

There are four IgG subclasses including IgG1-IgG4. The utility of serum IgG subclass in renal diseases lies in the determination of IgG4 when there is a suspicion of IgG4 related renal disease (IgG4-RD). This is a recently recognized entity characterized by storiform fibrosis and dense lymphoplasmacytic infiltrates, mostly as tubulointerstitial nephritis. As IgG4 is increased in many other disorders including autoimmune diseases, vasculitis and malignancies, therefore it is important to use this test judicially only when there is a clinical suspicion of IgG4-RD. moreover this test is interpreted along with the histopathological findings of the organ involved [79,80].

Viral markers

Certain viruses are implicated in renal diseases as they cause immune dysregulation, resulting in immune complex formation and deposition with subsequent complement activation [81].

Hepatitis C virus (HCV) and hepatitis B virus (HBV) infections are associated with various forms of GN including cryoglobulinemic GN, MPGN and polyarteritis nodosa causing pauci immune GN. Therefore, anti-HCV and HBV surface antigen (HBs Ag) detection tests are done routinely in these patients [82].

Human immunodeficiency virus (HIV) is also associated with renal pathology, either directly or indirectly due to co-infections or as side effects of anti-retroviral therapy. HIV associated nephropathy (HIVAN) is mostly found in African-American population. KIDGO (Kidney disease: improving global outcomes) has given pathological classification and guidelines for the management of these patients [83]. It is to be noted that in the setting of certain risk factors and characteristics histopathological features, anti-HIV testing should be done for better patient management.

Less commonly Epstein Barr virus (EBV) can also cause acute or chronic kidney disease. Therefore in case of infectious mononucleosis and renal manifestation, consider EBV infection also and keep it in your investigating repertoire [45,81].

CONCLUSION

Immunology laboratory has a very important role in the diagnosis and monitoring of disease in patients with renal disorders especially with GN. Immunopathologist have a very big responsibility in proper interpretation of the results in correlation with clinical features that affects patient management. It is important that immunologists, histopathologists and nephrologists or treating physicians should collaborate with each other for proper diagnosis and management of the patient with renal diseases.

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