In the name of Allah

Kidney disease associated with hepatitis B virus infection

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Chronic Kidney Disease and Hepatitis B Virus (HBV) Infection

- **Global Impact:**

  Chronic kidney disease is an increasing public health concern worldwide.

  Hepatitis B virus (HBV) affects around 400 million individuals globally and is a significant cause of liver disease and cancer.

- **Extra-Hepatic Manifestations:**

  Up to **20%** of HBV-infected patients experience **extra-hepatic** manifestations.

  These manifestations occur in both **acute** and **chronic** HBV infections.

- **Related Conditions:**
  1. **Mixed Cryoglobulinemia Vasculitis:** A condition where abnormal proteins in the blood lead to inflammation.
  2. **Polyarteritis Nodosa:** A serious blood vessel disease causing damage to small and medium-sized arteries.
  3. **Renal Disease:** The most common HBV-related renal disease is membranous nephropathy.

- **Membranous Nephropathy:**

  Predominantly affects individuals in the **Asian continent**.

  Characterized by changes in the kidney's structure leading to protein leakage in the urine.

- **Contributing Factors to Renal Injury:**

  Insulin Resistance: A condition where cells fail to respond to insulin properly.

  Oxidative Stress: An imbalance between free radicals and antioxidants in the body.

Common HBV-Related Kidney Diseases:

1. **Membranous Nephropathy**
2. **Membranoproliferative Glomerulonephritis (MPGN)**
3. **Polyarteritis Nodosa (PAN)**

Additional Associated Kidney Diseases:

- Mesangial proliferative glomerulonephritis
- Immunoglobulin A (IgA) nephropathy
- Crescentic glomerulonephritis
- Focal segmental glomerulosclerosis (FSGS)
- Minimal change disease
- Amyloidosis

- **Prevalence and Vaccination:**

Kidney disease related to HBV is more common in **endemic areas** (infancy and early childhood infections).

Lower frequency in the United States and Western Europe due to lower chronic HBV infection prevalence and reduced childhood infections.

Hepatitis B vaccination has reduced the incidence of HBV-related membranous nephropathy and MPGN.

Diagnostic Indicators:

Patients with HBV-related kidney disease are typically test positive for:

1. Hepatitis B surface antigen (**HBsAg**)
2. Hepatitis B core antibody (**anti-HBc**)
3. Hepatitis B e antigen (**HBeAg**) in membranous nephropathy cases.

Many have mild to moderate serum aminotransferase elevation, even without active hepatitis.

- **Pathogenesis:**

Documented through hepatitis B **antigen-antibody complexes** found in kidney lesions via immunofluorescence microscopy.

Involves **deposition of immune complexes** leading to inflammatory pathways activation.

Types of HBV-Related Kidney Diseases

1. Membranous Nephropathy:

***Presentation*: Proteinuria**, often nephrotic range; more **microscopic hematuria** and lower complement levels compared to idiopathic forms.

***Histologic Clues*: Mesangial cell proliferation and immune deposits**.

***Prevalence*:** Common in **children**; often resolves **spontaneously**, especially with **HBeAg to anti-HBe seroconversion.**

***Adults*: Less** common spontaneous resolution; progressive kidney deterioration possible.

2. Membranoproliferative Glomerulonephritis (MPGN):

***Presentation*: Hematuria** (dysmorphic red blood cells, red blood cell casts), **variable proteinuria**, **reduced GFR**, **hypertension**.

***Pathogenesis*: Deposition of antigen-antibody complexes** in mesangium and subendothelial space.

- **Comparison: HBV is a rare cause** of **mixed cryoglobulinemia**, unlike hepatitis C.

3. Polyarteritis Nodosa (PAN):

***Nature*:** Necrotizing vasculitis affecting small- and medium-sized vessels; involves multiple organs.

***Kidney Involvement*:** Variable degrees of **reduced GFR**, **hypertension**.

***Timing*:** Typically occurs **within four months after HBV infection onset**.

***Comparison*:** Clinical features similar to **idiopathic PAN**.

Diagnosis

- ***Suspected Cases:***
  - Patients with **acute or chronic HBV infection** and clinical/laboratory features suggestive of **glomerular disease** (proteinuria, hematuria, AKI, kidney function deterioration, hypertension, edema).
  - Important in **endemic areas** with higher HBV prevalence.
  - **Kidney biopsy** often required for confirmation.
- ***Testing:***
  - **Patients with unknown HBV status showing nephrotic syndrome or glomerulonephritis should be tested for HBsAg and anti-HBc.**
  - Positive tests warrant further investigation for anti-HBs, HBeAg, anti-HBe, and HBV DNA.
  - Consider concurrent **HCV** or **HIV** infection.

- ***Presumptive Diagnosis*:**
  - **HBsAg positive** with **biopsy-proven** membranous nephropathy, MPGN, or PAN, especially in children from endemic areas or adults without other identifiable causes.
  - Confirming etiologic role of HBV may be challenging due to required diagnostic techniques' availability.

- ***Therapeutic Considerations:***
  - Glucocorticoids, cytotoxic, or immunomodulatory agents **may not benefit** patients with **HBV**-associated kidney disease.
  - Such therapies can lead to reactivation of HBV replication, hepatitis flares, and liver failure if used without antiviral therapy.

Treatment

- ***Antiviral Therapy*:**

  Indicated for patients with **detectable HBV DNA or positive HBeAg**.

  Reduces proteinuria and induces seroconversion.

- ***Therapy Choices*:**

  Interferon Alfa: Preferred in **children** and **young adults**; **avoid in RPGN**.

  Nucleoside/Nucleotide Analogs: Preferred in **older adults** and **non-interferon candidates**. **Entecavir** or **tenofovir** is preferred.

- ***Rapidly Progressive Glomerulonephritis (RPGN):***
  - **Antiviral therapy** (nucleoside/nucleotide analog) **with high-dose glucocorticoids and possible immunosuppressants** (cyclophosphamide or rituximab).
  - **Monitor HBV DNA levels** for at least six months post-therapy.

- ***Polyarteritis Nodosa (PAN):***
  - **Mild PAN:** Antiviral therapy alone.
  - **Severe PAN:** Antiviral therapy with glucocorticoids and plasmapheresis.

- ***Regimens:***
  - **Glucocorticoids:** Prednisone, tapered over **four to six months**.
  - **Plasmapheresis: 6-10** sessions over **two to three weeks**.
  - **Avoid cyclophosphamide addition in HBV-associated PAN**.

- ***Patients with Concomitant HCV Infection* :**

Initial Therapy

- **Combination of direct-acting antivirals for HCV and nucleoside/nucleotide analogs for HBV**.
- **Direct-acting antivirals** for HCV preferred over interferon due to better tolerance and higher sustained virologic response.