# Kidney diseases secondary to liver diseases

**Essay**

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in Internal Medicine

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بسم الله الرحمن الرحيم

( رَبِّ أَوْزِعْنِي أَنْ أَشْكُرَ نِعْمَتَكَ الَّتِي أَنْعَمْتَ عَلَيَّ وعَلَى والِدَيَّ وأَنْ أَعْمَلَ صَالِحاً تَرْضَاهُ وأَدْخِلْنِي بِرَحْمَتِكَ فِي عِبَادِكَ الصَّالِحِينَ )

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*Mohamed Abd El Hamid Mahdy*

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# ABBREVIATIONS

| | |
|---|---|
| / | Per. |
| **AA** | Amyloid A. |
| **A2RA** | Angiotensin II receptor antagonist. |
| **ACE** | Angiotensin converting enzyme. |
| **ACA** | Anti-cardiolipin antibodies. |
| **ADCLF** | Acute decompensation of chronic liver disease. |
| **ADH** | Anti diuretic hormone. |
| **AKI** | Acute kidney injury. |
| **Alb** | Albumin. |
| **ALF** | Acute liver failure. |
| **ANCA** | Anti neutrophil cytoplasmic antibody. |
| **ANP** | Atrial natriuretic peptitide. |
| **ARF** | Acute renal failure. |
| **ATN** | Acute tubular necrosis. |
| **AVP** | Arginine vasopressin. |
| **BUN** | Blood urea nitrogen. |
| **CICs** | Circulating immune complexes. |
| **CKD** | Chronic kidney disease. |
| **CNIs** | Calcineurin Inhibitors. |
| **Cr** | Creatinine. |
| **CRF** | Chronic renal failure. |
| **CRRT** | Continuous renal replacement therapy. |
| **ESRD** | End stage renal disease. |
| **EM** | Electron microscopy. |
| **FHF** | Fulminant hepatic failure. |
| **FSGS** | Focal segmental glomerulosclerosis. |
| **GBM** | Glomerular basement membrane. |
| **GFR** | Glomerular filtration rate. |
| **gm** | Gram. |
| **HBV** | Hepatitis B virus. |
| **HBcAg** | Hepatitis B core antigen. |
| **HBsAg** | Hepatitis B surface antigen. |
| **HbeAg** | Hepatitis B envelope antigen. |
| **HCV** | Hepatitis C virus. |
| **HD** | Haemodialysis. |
| **HRS** | Hepatorenal syndrome. |
| **IC** | Immune complex. |

# ABBREVIATIONS (Cont.)

| | |
|---|---|
| **IF** | Immunofluorescent. |
| **IgA** | Immunoglobulin A. |
| **ICP** | Intracranial pressure. |
| **IFN** | Interferon. |
| **IL** | Interleukin. |
| **KDOQI** | Kidney Disease Outcomes Quality Initiative. |
| **Kcal** | Kilocalorie. |
| **Kg** | Kilogram. |
| **LCM** | Laser capture micro dissection. |
| **MAP** | Mean arterial pressure. |
| **MARS** | Molecular adsorbent recirculating system. |
| **MCGN** | Mesangiocapillary glomerulonephritis. |
| **MDRD** | Modification of Diet in Renal Disease. |
| **MELD** | Model for end stage liver disease. |
| **MMF** | Mycophenolate mofetil. |
| **MN** | Membranous nephropathy. |
| **MPGN** | Membranoproliferative Glomerulonephritis. |
| **MU** | Million units. |
| **NCPF** | Noncirrhotic portal fibrosis. |
| **NK** | Natural killer cells. |
| **NKF** | National kidney foundation. |
| **NKT** | Natural killer T lymphocyte. |
| **NO** | Nitric oxide. |
| **NS** | Nephrotic syndrome. |
| **NSAIDs** | Non-steroidal anti-inflammatory drugs. |
| **OLT** | Orthotopic liver transplantation. |
| **PAN** | Polyarteritis Nodosa. |
| **PTDS** | Post-transplant diabetes mellitus. |
| **RAAS** | Renin angiotensin aldosteron system. |
| **RBF** | Renal blood flow. |
| **RES** | Reticuloendothelial system. |
| **SBP** | Spontaneous bacterial peritonitis. |
| **SLE** | Systemic lupus erythematosus. |
| **SNS** | Sympathetic nervous system. |
| **SRS** | Spleno-renal shunt. |
| **SRTR** | the Scientific Registry of Transplant Recipients. |
| **SVR** | Systemic vascular resistance. |
| **TIPS** | Transjugular intrahepatic portosystemic shunt. |
| **TLR** | Tool- like receptor. |
| **TMA** | Thrombotic microangiopathy. |
| **WHO** | World Health Organization. |

# Introduction and Aim of the Work

# INTRODUCTION

Renal dysfunction is common in liver diseases, either as part of multiorgan involvement in acute illness or secondary to advanced liver disease. The presence of renal impairment in both groups is a poor prognostic indicator. Renal dysfunction is often multifactorial and can present as pre-renal or intrinsic renal dysfunction. Obstructive or post renal dysfunction only rarely complicates liver disease **(Betrosian et al., 2007).**

Renal diseases secondary to liver diseases can be classified according to different types of liver diseases, such as: Cirrhosis of liver, Acute or Chronic Viral Hepatitis, Obstructive jaundice, Noncirrhotic portal fibrosis following spleno-renal shunt surgery, alcoholic hepatitis, fulminant hepatic failure, hepatocellular carcinoma and chronic Budd-Chiari Syndrome **(Indian J Nephrol, 2001)**.

**G**lomerulonephritis associated with cirrhosis and other chronic active hepatitis is a secondary IgA nephropathy. Glomerulonephritis usually is clinically silent and characterized by microhematuria, proteinuria and glomerular deposition of IgA in nearly all cases. Glomerulopathies in patients of cirrhosis of liver occur in 50 to 100% of cases. **(Noel et al., 1987)**

**A**cute viral hepatitis and hepatitis B infection associated nephropathies can be classified into three major forms: membranous nephropathy, membrano-proliferative Glomerulonephritis and polyarteritis nodosa.

***M**embranous Nephropathy **(MGN)***: Hepatitis B virus can induce subepithelial immune deposits containing HbeAg and anti-Hbe antibody responsible for MGN leading to proteinuria and the nephrotic syndrome.

***M**embranoproliferative Glomerulonephritis**:*** associated with HBV is an immune complex disease characterized by deposition of circulating antigen antibody complex in the mesangium and sub endothelial space. Clinically the disease manifests with proteinuria and microscopic hematuria with a progressive course and deterioration of renal function over few months to few years similar to idiopathic MPGN.

***P**olyarteritis Nodosa **(PAN)***: Medium vessel vasculitis, like PAN can be induced by HBV in which circulating antigen-antibody complexes are deposited in the sub endothelium. HBV association has been reported in 10percent of the cases **(Levy et al., 1991)**.

**H**epatitis C Virus (HCV) related nephropathies: Three patterns of renal disease have been recognized: Glomerular, Vasculitic, Tubulointerstitial.

***Glomerular lesions***: either Cryoglobulinaemic or non-Cryoglobulinaemic.

1-Cryoglobulinaemic lesions are: Membranoproliferative, Immunotactoids, Fibrillary, and Amyloidosis.

2-Non- Cryoglobulinaemic lesions are: Membranoproliferative, Mesangial proliferative, Membranous, Focal segmental sclerosis.

***Vasculitic lesions:*** either Cryoglobulinaemic or non-Cryoglobulinaemic.

***Tubulointerstitial lesions*** are due to HCV interstitial nephritis **(Garini et al., 2005).**

**I**n Obstructive jaundice: the kidney becomes the main excretory pathway for biliary products. Therefore, the jaundice patient is critically dependent on kidney for survival. In such a situation if renal function declines due to pre renal reasons, the

hyperbilirubinemia is associated with high risk of developing acute renal failure.

Mechanism responsible for ARF in obstructive jaundice is multifactorial; such as (i) endotoxemia (ii) hyperbilirubinemia (iii) increased serum levels of bile salts (iv) renovascular fibrin deposition (v) alterations in systemic and renal hemodynamics and (vi) fluid depletion **(Parks et al., 1994).**

**I**n non-cirrhotic portal fibrosis (NCPF), increased incidence of Glomerulonephritis has been described particularly following splenorenal shunt surgery. 32% of patients develop nephrotic syndrome after splenorenal shunt surgery in five years. Renal histology in these cases showed MPGN (8.5%), mesangial proliferative Glomerulonephritis (9%), no change (3%) and sclerosing Glomerulonephritis (1.5%). Immunofluorescence revealed Glomerular IgA2 deposition in all cases indicating IgA was derived from gastrointestinal tract **(Dach et al., 1997).**

**Hepatorenal syndrome** is a unique form of functional renal failure that often complicates advanced liver disease. The syndrome is characterized by intense intrarenal vasoconstriction in the presence of vasodilatation of Systemic and splanchnic circulation, which triggers a reduction in peripheral vascular resistance and a decrease in effective systemic circulatory volume, despite an overall expanded total extracellular fluid volume.

Two patterns of HRS can be identified: Type 1 HRS is characterized by a rapidly progressive reduction of renal function, Type 2 HRS is characterized by a more benign course with a stable reduction in GFR over weeks to months, accompanying diuretic-resistant ascites and avid sodium retention **(Wong ., 2002).**

## Aim of the work

The aim of this work is to write a review about the prevalence, clinical features, pathogenesis, and methods of diagnosis and suggested management of renal diseases secondary to liver disorders.

# Review of Literature

# Acute renal dysfunction in liver diseases

***INTRODUCTION:***

Renal dysfunction in this setting usually develops gradually, with the exception of certain infections such as leptospirosis, some viral hemorrhagic fevers and toxin-mediated injuries such as acetaminophen poisoning, which cause acute insufficiency of both organs **(Eckardt, 1999).**

Renal failure secondary to liver dysfunction is generally functional in nature and occurs in the absence of significant alterations in renal histology (pre-renal).However, intrinsic renal abnormalities can also complicate acute or chronic liver disease (intrinsic renal failure) **(Moreau and Lebrec ,2003).**

Obstructive uropathy that leads to postrenal acute renal failure only rarely develops in chronic liver disease (papillary necrosis in alcoholic liver disease, bleeding in the urinary tract due to severe coagulopathy) Hepatorenal syndrome(HRS) is a unique form of functional renal failure (pre-renal) that often complicates advanced liver disease, hepatic failure or portal Hypertension **(Guevara and Gines, 2005).**

***EPIDEMIOLOGY:***

The incidence of renal failure in acute liver failure (ALF) varies from 40% to 85%, depending on the etiology; paracetamol poisoning leads to renal failure in up to75% of patients. Renal failure following paracetamol overdose may also occur in the absence of ALF, and has a good prognosis. In non-paracetamol cases the incidence of renal failure is usually accompanied by worsening encephalopathy and is associated with a poor outcome **(Eguia and Materson, 1997).**

Acute renal failure (ARF) in patients with cirrhosis, particularly with advanced liver disease, seems to be common;