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Case Report

TWIN challenges of Nephrology Acute Kidney Injury & Acute Liver Failure or Hepato-Renal Failure

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Abstract

Acute Kidney Injury (AKI) is the term that has recently replaced the term Acute Renal Failure (ARF). AKI is defined as an abrupt decrease in kidney function, which encompasses both anatomical injury (structural damage) and functional impairment (loss of function). Ascites, characterized by abnormal fluid accumulation in the peritoneal cavity, often emerges as a grim harbinger of underlying liver cirrhosis, a condition with a daunting prognosis.

Renal and liver dysfunction often present together, either as part of multiorgan failure in a critically ill patient, or because of failure of each organ independently. Three major clinical scenarios are described in which liver & renal dysfunction coexist; i) diseases simultaneously involving the liver and the kidney, or ii) a primary hepatic disorder with secondary renal dysfunction, or iii) vice versa- a primary kidney disorder and secondary liver dysfunction.

Serum-Ascites Albumin Gradient (SAAG) is used in the diagnostic workup of patients with ascites. The SAAG is a formula that calculates the difference between the albumin in the serum and the albumin in the ascitic fluid. A SAAG level of <1.1 g/dl is considered due to nonportal causes, like tuberculous peritonitis, malignancies and nephrotic syndrome in India.

Materials And Methods:

This article is based on recent case of an elderly man aged 67 years with signs of hypertension, and Pedal oedema managed with antidiuretics in February 2024. He showed radiological signs of liver inflammation in April 2024, Ascites in May 2024 and signs of Acute Kidney Injury in August 2024 and succumbed to Uraemic encephalopathy and Hepato-renal Failure in September 2024.

Outcome: Despite the possible conservative management in three district & sub-district health facilities, twice paracentesis in July and August 2024, except use of Terlipressin. He went into Uremic shock on 7th September and succumb on 8th September 2024 due to Hepatorenal syndrome (HRS), a unique form of functional pre-renal failure.

Key words: ascites albumin gradient; peritoneal fluid albumin; serum creatinine

Abbreviations

AKI= Acute Kidney Injury, ARF=Acute Renal Failure, ALF= Acute Liver Failure, HRS= Hepatorenal Syndrome, Portal Hypertension, Chronic Liver Disease, LFT= Liver Function Tests, CBC= A Complete Blood Count, PSA= Prostate-Specific Antigen (PSA) Test, Abdominal Scanning, Paracentesis (Tapping Abdominal Fluid), Serum Creatinine, Serum and Peritoneal Fluid Albumin, SAAG= Serum-Ascites Albumin Gradient,

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 failure is often multifactorial and can present as pre-renal or intrinsic renal dysfunction. Hepatorenal syndrome (HRS) is a unique form of renal failure associated with advanced liver disease or cirrhosis and is characterized by functional renal impairment without significant changes in renal histology.

Renal and liver dysfunction often present together, either as part of multiorgan failure in a critically ill patient, or because of failure of each organ independently. Three major clinical scenarios can be identified in which liver and renal dysfunction coexist; diseases simultaneously involving the liver and the kidney, or a primary hepatic disorder with secondary renal dysfunction, or vice versa [1]. Simultaneous renal and liver dysfunction share common pathogenetic mechanisms, where Renal dysfunction develops gradually, in most Liver Parenchymal inflammations. In acute infections

with leptospirosis, viral hemorrhagic fevers and acetaminophen poisoning, acute insufficiency of both organs occurs simultaneously [2]. 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 [3]. Obstructive uropathy is rare in chronic liver disease. Hepatorenal syndrome (HRS) is a unique form of functional pre-renal failure that complicates liver disease, hepatic failure or portal hypertension. In India AKI (ARF) in patients with liver disease, seems to be common. Though authentic nationally representative data is not available, a study found that 40.6% of patients with liver cirrhosis had acute kidney injury (AKI). Multiple small studies have reported the incidence of AKI in patients with liver disease ranging from 12% to 61%, using serum creatinine levels as the definition. A study of 4396 hospitalized patients reported an incidence rate of 3.1% (n = 135, Male=118, F=17) renal failure mostly males [4]. AKI Management practices in India include maintenance of volume homeostasis and correction of biochemical abnormalities are the primary goals of treatment and include correction of fluid overload with furosemide. The therapeutic paracentesis that is opted for alleviating the distressing symptoms associated with ascites by safely removing substantial volumes of ascitic fluid and correction of severe acidosis with bicarbonate administration, which becomes important as a bridge to dialysis if the patient recovers. Use of Terlipressin is limited in tertiary care facilities where multi-speciality teams' function. In India, the cost of a liver transplant can range from INR 15–33 lakh while the cost of a kidney transplant ranges from Rs. 5–15 lakh or more. The cost of both procedures can vary depending on several factors, like living donor or deceased donor, the choice of immunosuppressant medications, and additional medical services.

Case Report:

Mr. S Murthy aged about 67 years, from Challkere in Karnataka, consulted a physician in Belagavi, Karnataka, on one of his visits to his married daughter on 12 February 2024 with the complaints of abdominal discomfort, difficulty in micturition and swelling of feet and poor appetite. A routine general examination revealed pallor, hypertension 156/102 mm hg, slight tenderness in right upper quadrant of the abdomen. A routine urine analysis did not indicate any infection, A complete blood count (CBC) had shown Iron deficiency anaemia with 10.5% Hb, Blood urea (24 mg/dl) and Creatinine (1.0 mg/dl), all in normal ranges. A prostate-specific antigen (PSA) test and Liver function test biomarkers did not reveal anything suspicious of either liver or Kidney functions. He was prescribed Dytor 20 mg (a diuretic) half tablet twice a day, Tab Envas 2.5 mg (antihypertensive), Tab. Urimax 0.4 mg once day (alpha adrenergic antagonist) for BPH one tab every night and Tab Detox (for indigestion) after lunch every day. In a follow up visit after about 2 months on 8 April 2024, except for the reduction of pedal oedema, there was no improvement in general condition. This time the routine clinical examination revealed BP under control (132/89 mm Hg). Repeat routine urine and blood biomarkers and abdominal and Pelvic Scanning was ordered. Key abnormal findings recorded in the scanning report were i) Liver showed normal size with coarse eco-structure and surface nodularity ii) Gall bladder distended with a few Calculi largest measuring about 3.6mm in diameter with No GB wall thickening and pericholecystic oedema iii)Urinary bladder was also moderately distended and mild thickening of the wall measuring 5.2 mm with internal echoes & 2-3 tandem calculi largest measuring 6.9x3.5mm. iv) Pre-voiding urine volume was 246 ml and post-voiding residual urine of 126 ml. v) Prostate enlarged measuring 4.4x3.8x4.6 cm and a volume of 41.5cc. vi) Blood PSA level was raised to 0.54 (0.00-0.40) vii) Liver function biomarkers were in normal ranges. He was advised to continue the same treatment.

In mid-May 2024 in his hometown of Challakere, he noticed bloating abdomen and swelling of the feet. When the abdominal distension was discomforting, he consulted a local Physician on 26 June 2024 and Liver function tests were repeated. This time showed the reports were indicating abnormal biomarkers (normal range in parenthesis) – i) Serum Creatinine-2.0 (0.6-1.6), Na-122 (136-145) and Chorides-92 (97-111), Serum Bilirubin-3.4 mg/dl (0-1.3), Direct Bilirubin -0.8 mg/dl (0.0-0.3) Indirect Bilirubin -2.6 mg (0.2-1.0), Alkaline Phosphate-145 u/l (41-137) & Gamma GT GGT)-51 u/ l (0-50) a first indication of Liver dysfunction. He was put on a dozen drugs liver, kidney, prostate. A repeat Biomarkers tests on 21 July 2024 showed a bit improvement in i) Creatintine-1.5, Na-124. However, the abdominal distension had increased discomforting him, therefore, about 1 Liter abdominal fluid was tapped. There was a temporary relief but soon abdomen starting bulging again. Another repeat Biomarkers test on 21 August 2024, showed His Hb% - 9.1g/dl and serum Creatinine was 1.6mg/dl. The liver function biomarkers worsened further as T. bilirubin was 5.1, Direct Bilirubin-0.9, Indirect Bilirubin -4.2, SGOT-79, SGPT-52 (all higher than upper limits) and Serum Globulin-1.9 gm/dl (lower than lower limit of 2.3) indicating Liver failure. This time however, 2 Liters of abdominal fluid was tapped again. He was more comfortable this time for almost 2 weeks. Come September 2024 he started complaining of fatigue to the extent of inability walk in the house itself. On 7 September 2024, he suddenly became disoriented, confused, unable to swallow fluids and retention of urine. local Physician advised admitting him to medical College Hospital (MCH) as he found the patient's condition critical. The same afternoon he was admitted in an ICU of a private Medical College Hospital in Chitradurga. On admission his BP recorded 86/54 mm Hg. At the MCH the biomarkers read Blood Urea 118 mg/dl (10-45), Serum Creatinine-5.4 mg/dl (0.7-1.5), Sodium-134 mmol/l (135-155), Potassium -5.8 mmol/L (3.5-5.5), Chlorides-112 mmol /L (98-107), all elevated. All LFT biomarkers were off the mark too e.g., T Bilirubin-3.1 mg/dl, (0-1.2) D Bilirubin-0.4 (0-0.3), IBilirubin-2.7mg/dl (0-1.5), Total Protein -5.6 gm /dl (6.0-8.3), Albumin-1.9 gm/dl, (3.4-4.5) were reduced, and Globulin 3.7 gm/dl (2.0-3.5) was raised, SGOT-239 u/L (0-46), SGPT-91 U/L (0-49) were more than double, Hb%-8.6 g/l had come down further. The Albumin level in Peritoneal fluid was 2.1 gm/dl. With SAAG working out to be 1.9/2.1= 0.905, a diagnosis of Hepatorenal failure consequent to AKI, was made and led to Hypovolemic shock, and anuria, and the patient died on the early morning of 8th September 2024.

It was concluded that the patient went into Uremic encephalopathy, a cerebral dysfunction caused by the accumulation of toxins due to acute or chronic renal failure, as estimated glomerular filtration rate was below 05 mL/min.

Discussions:

The global incidence of renal failure in acute liver failure (ALF) or acute exacerbation of Chronic Liver failure varies from 40% to 85%, depending on the aetiology. Paracetamol poisoning leads the renal failure in up to 75% of patients in the absence of ALF. In non-paracetamol cases the incidence of renal failure is usually accompanied by worsening encephalopathy (leading to confusion etc) and is associated with a poor outcome. Uremic encephalopathy is a cerebral dysfunction caused by the accumulation of toxins due to acute or chronic renal failure. This condition typically develops in patients with acute or chronic renal failure whose estimated glomerular filtration rate is below 15 mL/min.

In India Acute renal failure (ARF) in patients with advanced liver disease, seems to be common. A study found that 40.6% of patients with liver cirrhosis had acute kidney injury (AKI). The incidence of ARF in patients with liver disease ranges from 12% to 61% when serum creatinine levels are used as the definition. A study of 4396 hospitalized patients reported an incidence rate of 3.1% (n = 135, Male=118, F=17) renal failure mostly males [4].

There are some factors that make it difficult to accurately measure serum creatinine levels in patients with cirrhosis like Muscle atrophy, Increased renal tubular secretion, Increased volume of distribution, and Elevated bilirubin. This is explained by the fact that patients with cirrhosis tend to have false low serum creatinine levels due to decreased hepatic creatinine synthesis and decreased skeletal muscle mass. ARF in patients with cirrhosis frequently accompanies complications such as hypovolemia from gastrointestinal bleeding or excessive diuretic therapy, administration of nephrotoxic drugs/contrast agents, or development of Hepatorenal shock HRS as was in our case. The probability of the occurrence of HRS in patients with cirrhosis and ascites at 1 and 5 years is 18% and 39%, respectively, with mortality approaching 100% in type I HRS without specific therapy. The median survival time in patients without liver transplantation was only 12 d

after diagnosis in one study [6,7]. However, there seems to be an improvement with terlipressin and albumin therapy, which of course was not attempted in our case. In patients with cirrhosis admitted to hospital with acute upper gastrointestinal haemorrhage, development of ARF forms an independent predictive factor for death.

Pathophysiology Of Renal Failure (Arf) In Liver Disease

The development of ARF in liver parenchymal inflammation & cirrhosis is complex, as it is a culmination of interactions between changes in the systemic arterial circulation, portal hypertension, activation of vasoconstrictors and suppression of vasodilatory factors acting on the renal circulation [2,4]. Portal hypertension is more pronounced in those with cirrhosis than in ALF [4]. The renal dysfunction is the result of systemic arterial vasodilation, preceded by increased release of endogenous vasodilator- nitric oxide, which escapes from the splanchnic to the systemic circulation through portosystemic shunts. [1]. The systemic vasodilation leads to a reduction in systemic vascular resistance (SVR) and consequent high cardiac output and hyperdynamic circulation, but this increase in cardiac output becomes inadequate to compensate for the drop in SVR, especially in ALF, resulting in hypotension with mean arterial pressure (MAP) commonly falling to 60-70 mmHg, as was in our case. That was due to the pressure-dependent part of the autoregulatory curve of renal blood flow. In healthy individuals, autoregulation of RBF occurs until the renal perfusion pressure falls below 60-70 mmHg. Altered renal vascular autoregulation, as seen in sepsis. In some patients with cirrhosis, the presence of cardiomyopathy and congestive cardiac failure render them susceptible to renal compromise secondary to hypoperfusion and I suspect our case also had this mechanism contributing though he was not alcoholic [1,4]. The therapeutic paracentesis that was opted in the reported case is a powerful tool for alleviating the distressing symptoms associated with ascites by safely removing substantial volumes of ascitic fluid. Diagnostic paracentesis provides a clue to the origins of ascites and rule out peritoneal fluid infection, but accessibility to such a test in sub-district level labs is still scarce in India. Ascites, characterized by abnormal fluid accumulation in the peritoneal cavity, emerges as a grim harbinger of underlying liver cirrhosis, with a daunting prognosis.

Serum-ascites albumin gradient (SAAG) has been used extensively in the diagnostic workup of patients with ascites. The SAAG is a formula that calculates the difference between the albumin in the serum and the albumin in the ascitic fluid. A SAAG level of <1.1 g/dl is considered due to nonportal causes like malignancies, tuberculous peritonitis, and nephrotic syndrome [6]. A SAAG of <1.1 g/dl among elderly with Cirrhosis of liver by radiological features as was in our reported case, or clinical, or histological, criteria. The Nonportal hypertension causes of low SAAG in India are likely to be tuberculous peritonitis, bacterial peritonitis, peritoneal carcinomatosis, nephrogenesis ascites, chylous and pancreatic ascites. A SAAG <1.1 g/dl in patients without cirrhosis is more likely to be helpful in indicating ARF than in patients with Cirrhosis. A repeat paracentesis as part of the workup to ARF [6]. The indications, contraindications, and potential complications of paracentesis, underscores the crucial role of an interprofessional team in managing patients with ascites, as early diagnosis and intervention can significantly impact patient outcomes. In a world where liver cirrhosis remains a leading cause of ascites, like India understanding the nuances of paracentesis becomes an essential skill for healthcare professionals. Complications of ascitic fluid tapping: Hypotension after large volume fluid removal, Persistent leakage of ascitic fluid at the needle insertion site., Abdominal wall hematoma or bleeding, Wound infection, Spontaneous hemoperitoneum. Irrespective of the type of renal failure, renal hypoperfusion is the central pathogenetic mechanism, due either to reduced perfusion pressure or increased renal vascular resistance. Volume expansion, avoidance of precipitating factors and treatment of underlying liver disease constitute the mainstay of therapy to prevent and reverse renal impairment. Splanchnic vasoconstrictor agents, such as terlipressin, along with volume expansion, and early placement of transjugular intrahepatic portosystemic shunt (TIPS) may be effective in improving renal function in HRS. Continuous renal replacement therapy (CRRT) and molecular absorbent recirculating system (MARS) in selected patients may be lifesaving while awaiting liver transplantation. The normal homeostatic response to vasodilation is activation of i) the renin-angiotensin-aldosterone system (RAAS), ii) the sympathetic nervous system (SNS), and iii) arginine-vasopressin (AVP) which leads to intense vasoconstriction and salt and water retention, to maintain blood pressure and perfusion of vital organs. [2,4]. Other vasoconstrictors, such as eicosanoids, endothelin's, thromboxane A2 and leukotrienes may further exacerbate this [6].

RBF is kept within normal limits in the early stage of the liver disease, due to the release of certain local vasodilators such as prostaglandins. As the liver disease progresses, there is extreme vasoconstriction of the renal vascular bed that predisposes the kidneys to development of HRS [2]. The presence of tense ascites may further impair renal perfusion. The continuing vasoconstriction and raised vascular resistance results in contraction of the mesangium, with a reduction in glomerular surface area, leading to acute tubular necrosis. It was inferred that our reported case went into Hypovolemic shock (HVS), which is an emergency condition in due to fluid loss because of tapping abdominal fluid, in quick succession, that made the heart unable to pump enough blood to the body. This type of shock can cause many organs to stop working. Clinicians classify HVS in 4 stages, Class 1: Volume loss up to 15% of total blood volume, approximately 750 mL, Class 2: Volume loss from 15% to 30% 750 mL to 1500 mL, Class 3: Volume loss from 30% to 40% 1500 mL to 2000 mL and Class 4: Volume loss over 40% of total blood volume. In our case the nearly 2.5 Liters of fluid tapping probably causes Hypovolemic shock leading to heart, liver and Kidney functions inadequate and patient died on the early morning of 8 September 2024.Terlipressin is a medication that helps improve kidney function in patients with hepatorenal syndrome (HRS), a kidney problem that can occur in patients with severe liver disease. Terlipressin decreases the neurohormonal response and improve circulatory dysfunction and lower plasma creatinine levels. It can increase survival rates and reverse functional renal failure, however, has serious side effects like respiratory failure, ischemic events, and bradycardia. Mild side effects include nausea and vomiting. As it is not recommended for patients with baseline S Cr levels greater than 5 mg/dL, it was not tried in reported case. In India multiple brand names include Erliso (Wockhardt), Terlyz: (Sun Pharma), Terlistat: (Samarth Life), Terloc: (Cadila), Thinwes (Biocon) & Vextop (H & I). As an alternative to bolus injection, terlipressin can be administered as a continuous intravenous (IV) infusion with a starting dose of 2 mg of terlipressin acetate/24 hours and increased to a maximum of 12 mg of terlipressin acetate/24 hours.A prospective analysis of 221 patients with liver disease and ARF to determine the aetiology, reported 66 developing ARF secondary to various liver disease i) cirrhosis (n = 29, mortality 8, risk factors-older age $p < 0.01$, grade III/IV encephalopathy $p < 0.05$), ii) fulminant hepatic failure (n = 25, mortality 15, risk factor-prolonged prothrombin time $p < 0.01$), and iii) obstructive jaundice (n = 12, mortality 7, risk factor-sepsis $p < 0.01$). In these three groups the factors leading to ARF were volume depletion (24), gastrointestinal bleed (28), sepsis (34), drugs (27) [aminoglycosides (9) and NSAID (18)] along with hyperbilirubinemia [7]. In India liver injury is mostly due to i) malaria (n = 37, mortality 15, risk factors-higher bilirubin $p < 0.001$, higher creatinine $p < 0.05$, anuria $p < 0.05$ and dialysis dependency $p < 0.05$), ii) sepsis (n = 36, mortality 22, risk factors-age $p < 0.001$, higher bilirubin $p < 0.01$, oliguria $p < 0.05$), iii) hypovolemia with ischemic hepatic injury (n = 14, mortality 5, risk factors-higher creatinine $p < 0.05$ and SGPT $p < 0.01$), iv) acute pancreatitis (n = 12 mortality 4, risk factors-higher bilirubin $p < 0.001$, higher SGPT $p < 0.01$, dialysis dependency $p < 0.05$), v) rifampicin toxicity (n = 10, no mortality), vi) paroxysmal nocturnal haemoglobinuria (n = 3, no mortality), vii) $CuSO_4$ poisoning (n = 3 mortality 2), viii) post abortal (n = 11, mortality 6, risk factors higher creatinine $p < 0.05$ and SGPT $p < 0.01$), ix) ARF following delivery including HELLP syndrome (n = 12, mortality 4, risk factors-higher bilirubin $p < 0.01$ and SGPT $p < 0.01$), and of x) uncertain aetiology (n= 14 mortality 4). 133 patients (60.2%) required haemodialysis hemodiafiltration or peritoneal dialysis. ARF associated with liver disease is having high mortality (42.5%). Avoidance of dehydration, hypotension, nephrotoxic drugs and sepsis, with promote dialytic support are necessary to reduce mortality and morbidity. Global CHANCE study presented at the European Association for the Study of the Liver's annual meeting, patients with severe acute-on-chronic liver failure (ACLF) face a higher risk of dying while waiting for a liver transplant compared to those

without ACLF [8]. The study revealed that among patients with ACLF grades 2 or 3 (Group 1), 28% died or were delisted while waiting for a liver transplant, compared to 16% of patients with ACLF 0 or 1 and a Model for End-Stage Liver Disease (MELD) score greater than 20 (Group 2). In a separate group with severe ACLF who were evaluated for the waitlist but not listed (Group 3), 85% died, with the main cause of liver disease being alcohol-associated cirrhosis, in contrast to 56% in Group 1 and 48% in Group 2. The interim analysis included outcomes for 823 patients from 66 liver transplant centres across 21 countries in Asia, Europe, Latin America, and North America. Study reported that the risk of death post-transplant for patients with ACLF grades 2 or 3 was not significantly different from those with decompensated cirrhosis.

Conclusion:

Acute Kidney Injury (AKI) is the term that has recently replaced the term ARF. AKI is defined as an abrupt (within hours) decrease in kidney function, which encompasses both injury (structural damage) and impairment (loss of function). It is a syndrome that rarely has a sole and distinct pathophysiology. AKI is commonly encountered in patients with decompensated cirrhosis, and it is associated with unfavorable outcomes. Among factors specific to cirrhosis, hepatorenal syndrome type 1, also referred to as hepatorenal syndrome-AKI, is the most salient and unique aetiology. Patients with cirrhosis are vulnerable to traditional causes of AKI, such as prerenal azotaemia, acute tubular injury, and acute interstitial nephritis. Other less common aetiologies of AKI specifically related to chronic liver disease are abdominal compartment syndrome, cardiorenal processes linked to cirrhotic cardiomyopathy and Porto-pulmonary hypertension, and cholemic nephropathy. Albumin-based volume resuscitation is recommended in prerenal AKI. Acute tubular injury and acute interstitial nephritis are managed with supportive care, withdrawal of the offending agent, and, potentially, corticosteroids in acute interstitial nephritis. Large-volume paracentesis and diuretics are indicated to relieve intra-abdominal hypertension and renal vein congestion.

References:

1. Epstein M. (1995). Liver disease. Textbook of nephrology. Williams & Wilkins. pp. 1105–1107.
2. Renal failure in liver disease. Intensive Care Med.; 25:5–14.
3. Alex P Bedrossian, (2007). Acute renal dysfunction in liver diseases, World J Gastroenterol. Nov 14; 13(42): 5552-5559, Online
4. S Sural, (2000). Acute renal failure associated with liver disease in India: aetiology and outcome, et.al, Ren Fail,22(5):623-634.
5. Acute Kidney Injury in Patients with Liver Disease, C., Giuseppe et.al, CJASN 17(11),
6. E Khand Walla. The utility of evaluating low serum albumin gradient ascites in patients with cirrhosis.
7. Incidence, clinical predictors & outcome of ARF among North Indian trauma patients, Medha, et.al, J Emerg Trauma Shock. 2013 Jan-Mar; 6(1).
8. Severe Acute-On-Chronic Liver Failure Increases Mortality Risk.