Case report

Complex Interplay of Cardiac, Hepatic, and Renal dysfunction in a patient with Extra-Hepatic Portal Vein Obstruction and Rheumatic Mitral Stenosis: A Case Report

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ABSTRACT

This case report presents a 31-year-old male with a complex interplay of cardiac, hepatic, and renal dysfunction, characterized by extra-hepatic portal venous obstruction (EHPVO), decompensated chronic liver disease (DCLD), and rheumatic heart disease (RHD) with severe mitral stenosis. The patient exhibited altered sensorium and hemodynamic instability, reflecting the intricate relationship between the heart, liver, and kidneys, often referred to as the cardio-hepato-renal axis. The initial presentation included hepatic encephalopathy, ascites, and acute kidney injury, highlighting the challenges in managing multi-organ dysfunction.

EHPVO, resulting from portal vein thrombosis, led to chronic portal hypertension and subsequent liver dysfunction, while RHD with mitral stenosis exacerbated cardiac strain and reduced renal perfusion. The clinical examination revealed significant cardiovascular findings, including elevated left atrial pressure, which contributed to pulmonary congestion and further impacted renal function. Laboratory tests indicated elevated bilirubin levels, coagulopathy, and renal impairment, consistent with the diagnosis of hepatic encephalopathy and acute kidney injury.

Management strategies included pharmacotherapy aimed at addressing hepatic encephalopathy and portal hypertension, such as lactulose and non-selective beta-blockers, along with diuretics to manage ascites. Renal support was considered to maintain adequate perfusion in light of the patient's hemodynamic instability. This case underscores the importance of a holistic and multi-disciplinary approach in managing patients with concurrent cardiac, hepatic, and renal dysfunctions, emphasizing the need for integrated strategies to address the complexities of such presentations.

Through this report, we aim to enhance understanding of the interdependencies between these organ systems and provide insights into the clinical management of complex cases involving multi-organ dysfunction.

Keywords: [Hepatic encephalopathy, EHPVO, DCLD, RHD, Portal hypertension]

1. INTRODUCTION

The intricate relationship between the heart, liver, and kidneys—often referred to as the cardio-hepato-renal axis—has garnered substantial attention in recent years due to its implications in multi-organ failure and complex management scenarios. Disruptions within this axis can precipitate a cascade of interrelated dysfunctions, where pathology in one organ amplifies the risk and severity of dysfunction in others. This interplay becomes particularly pronounced in patients with underlying chronic conditions affecting these organs, as is seen in this case involving extra-hepatic portal venous obstruction (EHPVO), decompensated chronic liver disease (DCLD), and rheumatic heart disease (RHD) with mitral stenosis (MS). Each condition poses unique pathophysiological challenges, which, in combination, create a complex clinical scenario requiring comprehensive and multi-disciplinary management.

EHPVO, primarily a disorder of the portal venous system, leads to the development of portal hypertension, often manifesting as complications such as splenomegaly, variceal bleeding, and ascites in patients from a young age. This condition, usually resulting from thrombosis of the portal vein, impairs blood flow to the liver and results in chronic portal hypertension without primary liver disease. Over time, the chronic increase in portal pressure can lead to liver dysfunction and the eventual development of DCLD, as observed in our patient. DCLD is marked by liver decompensation, including the development of hepatic encephalopathy (HE), ascites, and coagulopathy, indicating severe liver insufficiency and end-stage liver disease. Hepatic encephalopathy, characterized by altered mental status and asterixis, is often precipitated by systemic insults such as infections, gastrointestinal bleeding, or electrolyte disturbances, all of which are common in patients with portal hypertension and advanced liver disease[1– 2].

Rheumatic heart disease (RHD) remains a significant cause of valvular heart disease, particularly in developing countries, due to inadequate control of streptococcal infections[3]. Mitral stenosis (MS), a common consequence of RHD, leads to increased left atrial pressure and subsequent pulmonary congestion, placing additional strain on the heart and impacting systemic circulation. The resulting hemodynamic alterations can exacerbate portal hypertension and reduce renal perfusion, contributing to renal dysfunction and susceptibility to acute kidney injury (AKI)[4] . Moreover, the presence of RHD with MS complicates the hemodynamic stability of patients with concurrent liver disease, as both organs are highly sensitive to fluctuations in blood flow and pressure. This interdependence creates a vicious cycle where liver dysfunction exacerbates cardiovascular instability, further complicating renal function[5] .

Acute kidney injury, often presenting as a form of hepatorenal syndrome in patients with DCLD, reflects the vulnerability of the kidneys in the setting of impaired liver and cardiac function. Renal failure in this context is frequently precipitated by factors such as hypoperfusion, systemic vasodilation, and neurohormonal activation, all of which are common in advanced liver disease with portal hypertension and compromised cardiac output[6] . The non-oliguric renal failure observed in this patient underscores the complexity of managing AKI in the setting of multiple concurrent organ dysfunctions, where typical signs of renal compromise may be masked by altered systemic circulation and fluid dynamics[7] .

This case report aims to illustrate the challenging clinical presentation and management of a young patient with EHPVO, DCLD, severe mitral stenosis due to RHD, hepatic encephalopathy, and acute renal failure. It highlights the interdependent pathophysiological

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mechanisms linking the heart, liver, and kidneys and underscores the importance of a holistic, multi-disciplinary approach in managing such complex cases. Through this case, we aim to provide insights into the challenges and considerations involved in addressing the multi-organ dysfunctions resulting from the interplay between chronic cardiac, hepatic, and renal disease[8 – 9] .

2. PRESENTATION OF CASE

- The patient is a 31-year-old male presenting with altered sensorium following a loss of consciousness, with a history of intermittent fever for one week, abdominal distension for two months, icterus for two months, and abdominal pain for one week.

- His medical history is significant for extra-hepatic portal venous obstruction with portal hypertension since childhood, rheumatic heart disease with mitral stenosis for the past 12 years, and decompensated chronic liver disease.

- He denies any history of hematemesis, melena, constipation, decreased urine output, or seizures. He follows a mixed diet with normal bowel and bladder habits and a regular sleep pattern. He is a known alcoholic, with his last binge a month ago.

- On examination, the patient is drowsy, does not follow verbal commands, appears oriented but febrile, tachypneic, pale, and icteric, with normal jugular venous pressure. His heart rate is 100 beats per minute, and his initial systolic blood pressure was below 80 mmHg, stabilized to 90/60 mmHg with Noradrenaline at 0.1 µg/kg/min. Respiratory rate is 22 breaths per minute, capillary blood glucose is 123 mg/dL, and sPo2 is 96%. He also has bilateral pitting pedal edema.

- Cardiovascular examination revealed normal S1 and S2 with a loud S1 in the mitral area and a loud S2 in the pulmonary area accompanied by an ejection systolic murmur; there was a tapping apical impulse in the 4th intercostal space, 1/2 inch lateral to the midclavicular line, with visible pulsations over the pulmonary area and a palpable P2.

- Auscultation of the mitral area revealed normal S1 and S2 sounds, a loud S1, no S3 or S4, and a low-pitched, grade 3/4, rough rumbling mid-diastolic murmur best heard with the bell in the left lateral position with breath held in expiration, showing pre-systolic accentuation. In the tricuspid area, S1 and S2 were heard without any added sounds. The pulmonary area presented with S1 and S2 sounds, a loud P2, and a grade 3/6 ejection systolic murmur. In the aortic area, S1 and S2 were audible.

- Respiratory examination showed bilateral air entry.

- Neurological examination revealed bilateral pupils equal, reactive to light (3 mm), and bilateral flapping tremors.

- The abdominal examination was soft, with bowel sounds present, a distended abdomen with diffuse tenderness, a puffed down, everted umbilicus, equal movement in all quadrants with respiration, dilated veins on the sides, no hepatomegaly, splenomegaly extending 4 fingers below the costal margin, fluid thrill, and ascites.

List 1 : The laboratory investigations are as follows

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Parameter	Observed value			Normal range	Unit
Hematology					
WBC	**14.7**↑	8.7	**12.9**↑	4.0-11.0	x103/µl
Hb	**7.8**↓	**7.3**↓	**9.7**↓	14.0-18.0	g/dl
RBC	**2.61**↓	**2.59**↓	**3.09**↓	4.5-6.0	x106/µl
HCT	**24.1**↓	**23.8**↓	**29.5**↓	36-46	%
MCV	92.3	91.9	95.5	80-100	fl
MCH	29.9	28.2	31.4	27-33	pg
MCHC	32.4	**30.7**↓	32.9	32-36	g/dl
PLT	26	28	35	150-450	x103/µl
N	**88.7**↑	**88.1**↑	**84.5**↑↓	40-60	%
L	**6.2**↓	**8.8**↓	**10.8**↓	20-40	%
M	5.1	3.1	4.7	2-8	%
Liver function tests & electrolytes					
TB	**13.9**↑	**16.3**↑	**18.6**↑	0.1-1.2	mg/dl
DB	**6.6**↑	**8.1**↑	**9.5**↑	0.0-0.3	mg/dl
AST	**90**↑	**70**↑	**53**↑	10-40	U/L
ALT	49	41	37	7-56	U/L
ALP	**295**↑	**185**↑	**180**↑	44-147	U/L
TP	6.2	**4.8**	**5.3**	6.4-8.3	g/dl
Na	**134**↓	**131**↓	141	135-145	mEq/L
K	5.0	4.7	4.3	3.5-5.1	mEq/L
PT	**27.9**↑	**37.3**↑	**26.7**↑	9.5-13.8	sec
INR	**2.27**↑	**3.15**↑	**2.1**↑	0.8-1.2	-
Albumin	**1.7**↓	**1.3**↓		3.5-5.0	g/dl
LDH	130				IU/L
Renal function tests					
Sugar	**127**	94	70	70-110	mg/dl
Urea	**96**↑	**89**↑	**61**↑	10-50	mg/dl
Creatinine	**1.4**↑	**1.5**↑	0.8	0.6-1.2	mg/dl
Ascitic fluid analysis					
Protein	0.9			0-2.5	g/dl
Sugar	**131**↑			70-110	mg/dl

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Albumin	0.3	<1.1	g/dl

- HBsAg and anti-HCV were negative, and HIV was non-reactive. Ascitic fluid culture showed no pus cells or organisms.

- The ECG indicated sinus bradycardia with inverted T waves in leads V1, V2, and V3. Chest X-ray findings included right-sided pleural effusion, left atrial enlargement, and an elevated right hemidiaphragm (Fig. 1).

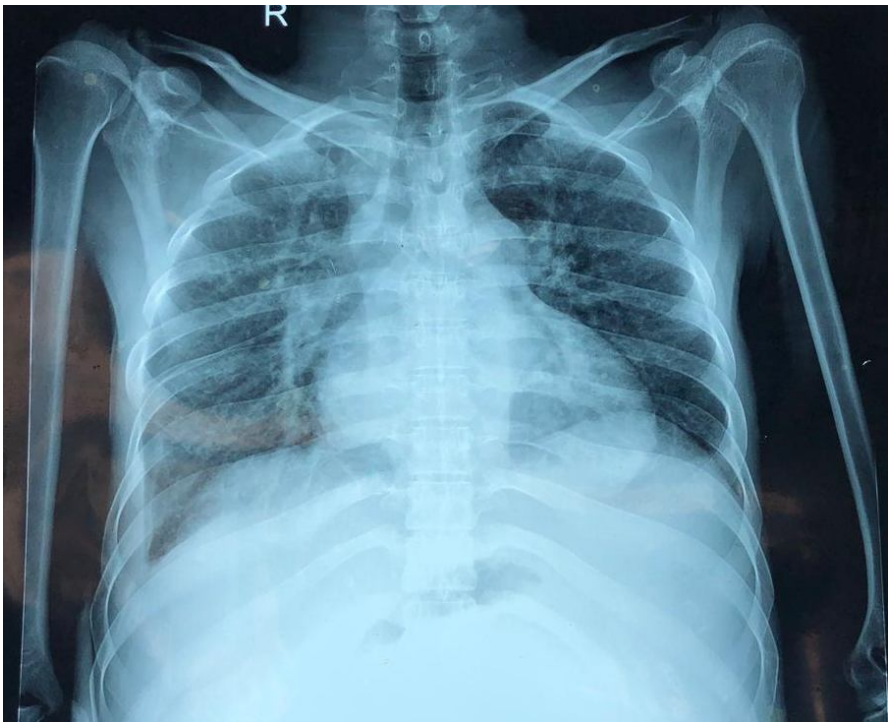

Fig. 1., Chest X-ray revealing right-sided pleural effusion, left atrial enlargement, and an elevated right hemidiaphragm.

- On assessment of diagnosis, The patient is experiencing hepatic encephalopathy (grade II-III) as evidenced by altered sensorium, drowsiness, and bilateral flapping tremors (asterixis). His history of decompensated chronic liver disease (DCLD), indicated by elevated total bilirubin (13.9 mg/dL) and direct bilirubin (6.6 mg/dL), significantly supports this diagnosis. Additionally, the prolonged prothrombin time (PT) (27.9 seconds) and elevated International Normalized Ratio (INR) (2.27), alongside low albumin levels (1.7 g/dL), confirm liver dysfunction contributing to the encephalopathy.

- The presence of extra-hepatic portal venous obstruction (EHPVO) with portal hypertension is substantiated by the distended abdomen with ascites, visible superficial abdominal veins (caput medusae), and the patient's history of portal hypertension since childhood. The ascitic fluid analysis shows low protein levels (0.9 g/dL) and a low serum-ascites albumin gradient (SAAG), indicating portal hypertension as the likely cause of the ascites.

- Rheumatic heart disease (RHD) with severe mitral stenosis is evidenced by the cardiovascular examination findings of a loud S1, a rough rumbling mid-diastolic murmur, and signs of pulmonary congestion noted on the chest X-ray. The elevated heart rate (tachycardia at 100 bpm) and initial hypotension (systolic blood pressure < 80 mmHg) suggest hemodynamic instability, indicating shock.

- The laboratory results indicate acute kidney injury (AKI) characterized by elevated creatinine levels of 1.4 mg/dL and urea levels of 96 mg/dL. These findings are consistent with renal failure, likely due to volume depletion from ascites and potential hepatorenal syndrome. Although the patient is non-oliguric, the renal function has been previously compromised, highlighting the need for ongoing monitoring and supportive management.

Overall, the correlation between the clinical presentations and laboratory findings strongly supports the assessments of hepatic encephalopathy, decompensated chronic liver disease, EHPVO with portal hypertension, severe mitral stenosis due to RHD, shock, and acute kidney injury.

3. DISCUSSION

The interplay between cardiac, hepatic, and renal dysfunction is a complex clinical scenario, especially in a patient with extra-hepatic portal venous obstruction (EHPVO) and rheumatic mitral stenosis. Understanding this interplay is crucial for effective management strategies tailored to address multi-organ dysfunction.

1) Cardiac Dysfunction in the Context of Rheumatic Mitral Stenosis

Rheumatic heart disease (RHD), particularly in developing countries, significantly contributes to mitral stenosis (MS), leading to various cardiovascular complications. In our case, the patient's history of RHD with MS was confirmed by clinical examination findings, such as a loud first heart sound (S1) and a mid-diastolic murmur, both of which indicate increased left atrial pressure and subsequent pulmonary congestion. Elevated left atrial pressure can lead to pulmonary hypertension, increasing the workload on the right heart and contributing to right heart failure [1].

i. Pharmacotherapeutic Management:

In patients with MS, diuretics such as furosemide can help manage volume overload and pulmonary congestion, improving symptoms and cardiac output[4]. Anticoagulation therapy, particularly with warfarin or direct oral anticoagulants, may be indicated to prevent thromboembolic events associated with atrial fibrillation, which can occur due to left atrial enlargement [10]. Additionally, beta-blockers can help manage heart rate and reduce myocardial oxygen demand, which may be beneficial in cases of heart failure or significant arrhythmias [11].

ii. Surgical Options:

Surgical interventions such as balloon mitral valvuloplasty or mitral valve replacement should be considered, especially in symptomatic patients with significant stenosis, as timely intervention can significantly improve hemodynamics and mitigate complications related to right heart failure [12].

iii. Lifestyle Modifications:

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Patients are advised to maintain a low-sodium diet to help manage fluid retention, engage in regular physical activity as tolerated, and avoid excessive fluid intake. Weight management can also reduce the strain on the heart, improving overall cardiovascular health.

2) Hepatic Dysfunction and Its Management

In patients with EHPVO, portal hypertension leads to various hepatic complications, including ascites and hepatic encephalopathy (HE). The patient presented with ascites, asterixis, and altered sensorium, indicative of HE, which has been substantiated by previous studies emphasizing the need for early recognition and management of HE in patients with liver dysfunction [8].

i. **Pharmacotherapeutic Management:**
Management strategies for HE typically include addressing precipitating factors such as infections, electrolyte imbalances, and gastrointestinal bleeding. Lactulose is commonly used to reduce ammonia levels, while rifaximin can be added to prevent recurrence of HE [6]. Additionally, for portal hypertension, non-selective beta-blockers (such as propranolol or nadolol) can be employed to reduce portal pressure by decreasing cardiac output and splanchnic blood flow, thereby lowering the risk of variceal bleeding [13].

ii. Management of Portal Hypertension:

a) Non-Selective Beta-Blockers: These are first-line agents for preventing variceal bleeding in portal hypertension, effective in reducing portal pressure [14].
b) Diuretics: Agents like spironolactone can be used to manage ascites, helping to decrease fluid retention and reduce abdominal pressure [15].
c) Endoscopic Procedures: Variceal ligation or sclerotherapy may be necessary for patients with significant varices to prevent bleeding [16].
d) Surgical Options: For patients with refractory ascites or significant portal hypertension, procedures such as transjugular intrahepatic portosystemic shunt (TIPS) may be indicated to reduce portal pressure and improve liver function [7].

iii. Lifestyle Modifications:
Dietary modifications should include a low-protein diet to reduce ammonia production, while also monitoring for malnutrition due to hepatic dysfunction. Regular follow-ups with a hepatologist are vital for managing liver health and monitoring for complications [9].

3) Renal Dysfunction in the Context of Hepatic and Cardiac Failure

Acute kidney injury (AKI) in this patient, reflected by elevated creatinine and urea levels, underscores the renal vulnerability associated with hepatic dysfunction and cardiac instability. The concept of hepatorenal syndrome, as detailed by Boyer and Sanyal, demonstrates that renal impairment in liver disease often stems from splanchnic vasodilation and reduced renal perfusion [17]. This patient's non-oliguric renal failure complicates the clinical picture, as hemodynamic stability must be restored to improve renal outcomes.

i. Pharmacotherapeutic Management:
Maintaining adequate renal perfusion is crucial. Administering intravenous fluids and avoiding nephrotoxic agents such as nonsteroidal anti-inflammatory drugs (NSAIDs) is essential [18]. In some cases, vasopressors may be required to support renal blood flow in the setting of severe hypotension. Additionally, managing hyperkalemia may be necessary, particularly if renal function continues to decline, and can be achieved through the use of agents such as calcium gluconate, insulin with glucose, and sodium bicarbonate [19].

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ii. Supportive therapy:
In cases of acute kidney injury secondary to hepatorenal syndrome, continuous renal replacement therapy (CRRT) may be indicated to support renal function while addressing underlying hepatic issues [5].

iii. Lifestyle Modifications:
Encouraging patients to maintain a balanced diet with adequate hydration, while monitoring for signs of fluid overload, is critical. Regular exercise and avoidance of alcohol can help protect renal function.

Interconnectedness of Multi-Organ Dysfunction:

The complexities of multi-organ dysfunction in this case demonstrate how dysfunction in one organ can lead to cascading failures in others. This phenomenon is particularly evident in patients with portal hypertension and RHD, where the combined effects exacerbate renal insufficiency and HE.

Supporting this view, Vilstrup et al. highlight that management of hepatic encephalopathy requires a holistic approach that considers the overall clinical status, integrating cardiac and renal parameters to optimize outcomes [9].

Summary of Management Strategies

Cardiac Management:

- Early intervention in mitral stenosis through balloon valvuloplasty or surgical repair should be considered, especially in patients with concurrent liver disease to optimize hemodynamics [12].
- Pharmacotherapy: Use of diuretics for fluid management, anticoagulants for thromboembolic prevention, and beta-blockers for rate control.
- Lifestyle: Low-sodium diet and regular exercise.

Hepatic Management:

- Close monitoring for precipitating factors of HE and utilizing lactulose or rifaximin for symptomatic relief are essential [6].
- Portal Hypertension Management: Use of non-selective beta-blockers, diuretics, and endoscopic interventions to manage complications [7].
- Surgical Options: Consideration of TIPS for refractory cases.
- Lifestyle: Dietary modifications and regular hepatology follow-ups.

Renal Management:

- Maintaining fluid balance and considering CRRT in severe AKI can help manage renal complications arising from liver dysfunction [5].
- Pharmacotherapy: Avoidance of nephrotoxins, administration of fluids, and managing electrolyte imbalances.
- Lifestyle: Hydration management and monitoring for fluid overload.

Holistic Approach:

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- A multi-disciplinary approach integrating cardiology, hepatology, and nephrology expertise is crucial for managing such complex cases effectively [9].

4. CONCLUSION

This case underscores the critical need for integrated management strategies in patients with complex multi-organ dysfunction, emphasizing that a thorough understanding of the interrelated pathophysiological mechanisms is essential for optimal patient outcomes.

COMPETING INTERESTS

Authors have declared that no competing interests exist.

CONSENT

The participation was on a voluntary basis and written consent was obtained from the individual who participated in this case report.

ETHICAL APPROVAL (WHERE EVER APPLICABLE)

As per international standards or university standards written ethical approval has been collected and preserved by the author(s).

REFERENCES

1. Dhiman RK, Chawla YK. Endemic extrahepatic portal vein obstruction in India: history, pathophysiology and management. World J Gastroenterol. 2010;16(6):1856-66.

2. Sarin SK, Agarwal SR. Extrahepatic portal vein obstruction. Semin Liver Dis. 2002;22(1):43-58.

3. Carapetis JR, Steer AC, Mulholland EK, Weber M. The global burden of group A streptococcal diseases. Lancet Infect Dis. 2005;5(11):685-94.

4. Reddy S, Singh J, Aggarwal R, et al. Mitral stenosis: diagnosis and management. Tex Heart Inst J. 2014;41(4):437-44.

5. Jalan R, Williams R. Acute-on-chronic liver failure: pathophysiological basis of therapeutic options. Blood Purif. 2002;20(3):252-61.

6. Ginès P, Schrier RW, Arroyo V, et al. Hepatorenal syndrome. Nat Rev Dis Primers. 2009;5:1014-25.

7. Boyer TD, Sanyal AJ. The liver and kidney in chronic liver disease. In: Zakim D, Boyer TD, editors. Hepatology: a textbook of liver disease. 1st ed. Philadelphia: Elsevier; 2016. p. 829-64.

8. Bajaj JS. Review article: the modern management of hepatic encephalopathy. Aliment Pharmacol Ther. 2010;31(5):537-47.

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9. Vilstrup H, Amodio P, Bajaj J, et al. Hepatic encephalopathy in chronic liver disease: 2014 practice guideline by AASLD and EASL. Hepatology. 2014;60(2):715-35.

10. Lip GY, Lane DA, Apostolakis S, et al. Anticoagulation in atrial fibrillation. J Cardiovasc Med (Hagerstown). 2010;11(2):103-14.

11. Palaniappan R, Rao SK, Rajan S, et al. Current management of mitral stenosis. J Cardiovasc Dis Res. 2015;6(4):201-6.

12. Sutherland FW, Pearson AC, Mihaljevic T, et al. Surgical management of mitral stenosis: an update. Curr Cardiol Rep. 2013;15(6):367.

13. Chalasani N, Imperiale TF, Ismail A, et al. Portal hypertension: current management and future perspectives. Am J Gastroenterol. 2009;104(10):2374-86.

14. Kim SY, Lee JH, Kim DJ, et al. Management of portal hypertension. Hepatology. 2014;60(1):90-7.

15. Runyon BA. Introduction to the special issue on ascites. Hepatology. 2004;39(1):1-4.

16. Moini M, Kanthasamy A. Transjugular intrahepatic portosystemic shunt (TIPS): indications and complications. Clin Gastroenterol Hepatol. 2017;15(7):983-92.

17. Rathi P, Vasudevan D. Acute kidney injury in liver disease: a review. Indian J Nephrol. 2014;24(6):313-20.

18. Schrier RW, Wang W. Acute renal failure and its consequences. N Engl J Med. 2004;351(2):171-9.

19. Hsu CY, Chertow GM. A physician's guide to acute kidney injury. Nat Rev Nephrol. 2008;4(1):16-21.

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