

CLINICAL AND PATHOGENETIC FACTORS OF LIVER DYSFUNCTION IN PATIENTS WITH ACUTE KIDNEY INJURY**Khikmatova Madina Furqatovna, PhD**

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Abstract. Acute kidney injury (AKI) is a systemic syndrome in which renal dysfunction interacts with distant organs through hemodynamic, inflammatory, metabolic, endothelial, and pharmacokinetic pathways. Liver test abnormalities are common in critically ill patients with AKI, but their interpretation is difficult because direct kidney-liver crosstalk frequently coexists with sepsis, shock, hypoxemia, venous congestion, surgery, malnutrition, and drug exposure. This narrative review summarizes the main clinical and pathogenetic factors associated with liver dysfunction during AKI. The evidence indicates that severe or persistent AKI, oliguria, renal replacement therapy, systemic inflammation, tissue hypoperfusion, right-sided heart failure, and exposure to potentially hepatotoxic medicines increase the probability of hepatocellular, cholestatic, or mixed biochemical patterns. Aminotransferases primarily reflect cellular injury, bilirubin and alkaline phosphatase reflect excretory and cholestatic disturbances, while albumin and the international normalized ratio require interpretation in the context of inflammation, nutrition, dilution, and anticoagulation. A clinically useful assessment should integrate baseline liver status, temporal sequence, hemodynamics, infection, medication history, laboratory trajectory, and imaging when indicated. No single laboratory marker can establish causality or fully define hepatic function in AKI.

Keywords. acute kidney injury; liver dysfunction; kidney-liver crosstalk; systemic inflammation; hypoxic hepatitis; cholestasis; drug-induced liver injury

Introduction. Acute kidney injury is defined by an abrupt increase in serum creatinine, a reduction in urine output, or both. Its clinical importance extends beyond the kidney: AKI is associated with pulmonary, cardiovascular, neurological, intestinal, and hepatic dysfunction [1-5]. In patients with AKI, abnormal liver biochemistry may represent direct renohepatic signaling, a common systemic insult affecting both organs, or an unrelated pre-existing liver disorder. This distinction is clinically important because the management of hypoxic hepatocellular injury, sepsis-associated cholestasis, venous congestion, biliary obstruction, and drug-induced liver injury is different. The term liver function tests may also be misleading: alanine aminotransferase (ALT) and aspartate aminotransferase (AST) mainly indicate cell injury, whereas bilirubin, albumin, and coagulation variables assess different excretory or synthetic dimensions.

Aim. To summarize the clinical and pathogenetic factors that contribute to liver dysfunction in patients with AKI and to formulate a practical framework for differential assessment and monitoring.

Materials and methods. A focused narrative review of PubMed-indexed articles, international guidance, and major clinical reviews available through 15 September 2026 was performed. Search concepts included acute kidney injury, renohepatic crosstalk, liver chemistry, hypoxic hepatitis, critical illness cholestasis, sepsis, venous congestion, and drug-induced liver injury. Priority was given to guidelines, large cohort studies, mechanistic reviews, and publications directly addressing distant-organ effects of AKI. Because definitions and sampling schedules varied substantially, findings were synthesized qualitatively rather than pooled statistically.

Results and discussion. The literature supports a multifactorial model. Kidney injury initiates systemic signaling through release of damage-associated molecular patterns, pro-inflammatory cytokines, activated neutrophils, oxidative stress, and endothelial dysfunction [4-7]. Experimental models demonstrate changes in hepatic cytokine expression, apoptosis, microvascular function, and drug-metabolizing pathways after renal ischemia or nephrectomy. Retained uremic solutes, acidosis, fluid overload, and altered protein binding may further modify hepatic metabolism. However, translation of these mechanisms to an individual patient requires caution, because the same critically ill patient often has sepsis, hypotension, hypoxemia, heart failure, or major surgery. These shared insults may explain liver abnormalities more strongly than kidney injury alone.

Hemodynamic and systemic determinants. Hypoperfusion and severe hypoxemia can produce a rapid hepatocellular pattern with marked AST and ALT elevation, often accompanied by increased lactate dehydrogenase and lactate. Venous congestion, especially in right-sided heart failure, increases hepatic sinusoidal pressure and may cause a mixed pattern with bilirubin elevation. Sepsis combines reduced

microcirculatory flow, endothelial activation, cytokine-mediated transporter dysfunction, and impaired bile-acid excretion. Consequently, conjugated bilirubin, alkaline phosphatase, and gamma-glutamyl transferase may rise after the initial hemodynamic insult [8,9]. The temporal sequence is therefore informative: aminotransferases may fall quickly after perfusion is restored, while cholestatic markers can peak later and normalize over days or weeks. Persistent abnormalities after stabilization require reassessment for ongoing infection, congestion, vascular disease, or biliary obstruction.

Patient-related and treatment-related factors. Advanced age, chronic kidney disease, diabetes, obesity, pre-existing liver disease, heart failure, malnutrition, and repeated episodes of AKI reduce physiological reserve. AKI severity and duration, oliguria, fluid accumulation, and need for renal replacement therapy identify patients with a high systemic illness burden. Drug exposure is particularly important. Reduced renal clearance can increase concentrations of active metabolites; hypoalbuminemia changes the unbound fraction of highly protein-bound drugs; and inflammation may suppress hepatic enzymes and transporters. Antibiotics, antifungal agents, analgesics, anticonvulsants, contrast agents, herbal products, and multiple-drug combinations should be placed on a precise timeline. A temporal association alone is not proof of drug-induced liver injury, but failure to improve after hemodynamic stabilization should trigger structured causality assessment [10].

Clinical phenotypes and interpretation. A hepatocellular phenotype is characterized by predominant aminotransferase elevation and should prompt assessment of shock, hypoxemia, vascular occlusion, viral hepatitis, autoimmune disease, muscle injury, and toxic exposure. A cholestatic phenotype is dominated by conjugated bilirubin and alkaline phosphatase and requires evaluation for sepsis-associated cholestasis, congestion, parenteral nutrition, medication effects, or mechanical obstruction. Mixed patterns broaden the differential diagnosis. Isolated hypoalbuminemia is nonspecific because it reflects inflammation, capillary leak, dilution, nutrition, and protein loss. An increased international normalized ratio may indicate impaired synthesis but can also result from anticoagulants, vitamin K deficiency, or disseminated intravascular coagulation. Baseline values, peak abnormality, direction of change, and concordance with the clinical course are more useful than a single isolated result [8,10,11].

Practical monitoring. At recognition of AKI, clinicians should document prior liver disease, alcohol and metabolic risk, hemodynamic events, infection, surgery, transfusion, medication changes, and herbal exposure. Baseline and serial measurements should include creatinine, urine output, ALT, AST, bilirubin fractions, alkaline phosphatase, albumin, and coagulation variables when clinically relevant. Creatine kinase helps identify a muscle source of AST, while lactate and lactate dehydrogenase support the assessment of hypoxic injury. Ultrasonography is indicated when jaundice progresses, pain or fever is present, or obstruction and congestion are suspected. The interval for repeated testing should be individualized according to AKI stage, liver phenotype, treatment changes, and direction of the laboratory trajectory.

Conclusion. Liver dysfunction in AKI is usually multifactorial. Direct kidney-liver crosstalk may contribute through inflammation, oxidative stress, endothelial injury, uremic retention, and altered drug metabolism, but shared causes such as sepsis, shock, hypoxemia, congestion, surgery, and medication exposure frequently dominate the clinical picture. Reliable interpretation requires integration of baseline reserve, injury phenotype, temporal sequence, laboratory dynamics, and clinical context. Simultaneous monitoring of renal and hepatic trajectories can identify reversible causes early and reduce both diagnostic error and medication-related harm.

References

1. Kidney Disease: Improving Global Outcomes (KDIGO) Acute Kidney Injury Work Group. KDIGO clinical practice guideline for acute kidney injury. *Kidney Int Suppl.* 2012;2(1):1-138.
2. Kellum JA, Romagnani P, Ashuntantang G, Ronco C, Zarbock A, Anders HJ. Acute kidney injury. *Nat Rev Dis Primers.* 2021;7:52.
3. Hoste EAJ, Bagshaw SM, Bellomo R, et al. Epidemiology of acute kidney injury in critically ill patients: the multinational AKI-EPI study. *Intensive Care Med.* 2015;41:1411-1423.
4. Grams ME, Rabb H. The distant organ effects of acute kidney injury. *Kidney Int.* 2012;81:942-948.
5. Doi K, Rabb H. Impact of acute kidney injury on distant organ function: recent findings and potential therapeutic targets. *Kidney Int.* 2016;89:555-564.
6. Bonavia A, Stiles N. Renohepatic crosstalk: a review of the effects of acute kidney injury on the liver. *Nephrol Dial Transplant.* 2022;37:1218-1228.
7. Matsuura R, Doi K, Rabb H. Acute kidney injury and distant organ dysfunction: network system analysis. *Kidney Int.* 2023;103:1041-1055.

8. Horvatits T, Drolz A, Trauner M, Fuhrmann V. Liver injury and failure in critical illness. *Hepatology*. 2019;70:2204-2215.
9. Drolz A, Jager B, Wewalka M, et al. Outcome and features of acute kidney injury complicating hypoxic hepatitis at the medical intensive care unit. *Ann Intensive Care*. 2016;6:61.
10. Andrade RJ, Chalasani N, Bjornsson ES, et al. Drug-induced liver injury. *Nat Rev Dis Primers*. 2019;5:58.
11. Newsome PN, Cramb R, Davison SM, et al. Guidelines on the management of abnormal liver blood tests. *Gut*. 2018;67:6-19.

