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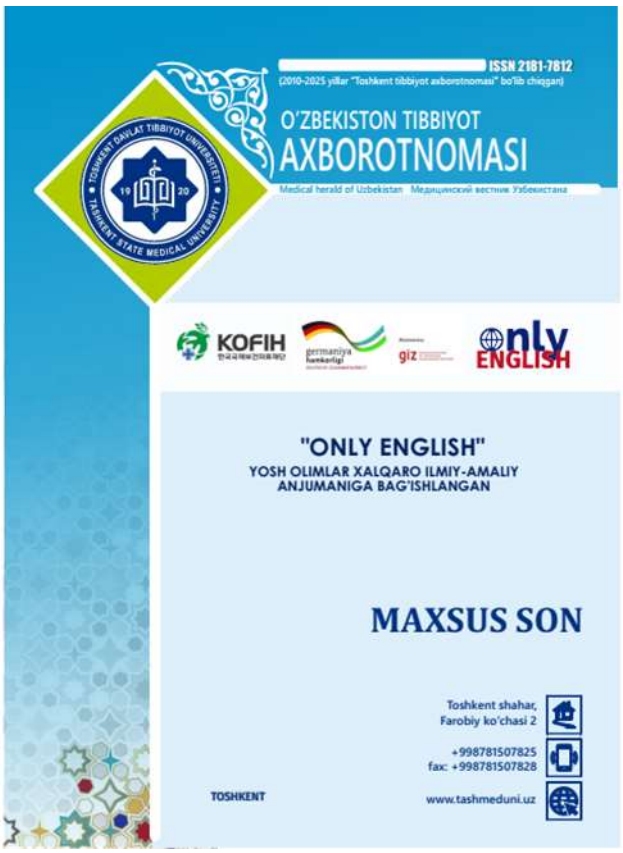

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CHANGES IN COAGULATION HAEMOSTASIS IN PATIENTS WITH RENAL DISEASE AFTER COVID-19: A COMPREHENSIVE REVIEW

Madazimova D.Kh.

Tashkent State Medical University

Abstract. *Coronavirus disease 2019 (COVID-19) causes significant disturbances in haemostasis that may persist after clinical recovery. Patients with chronic kidney disease (CKD) and those on dialysis represent a vulnerable group due to their preexisting haemostatic alterations and increased thrombotic risk. This review examines the pathophysiological mechanisms, laboratory abnormalities, clinical manifestations, and management strategies for coagulation disturbances in patients with renal impairment after COVID-19. The challenges in balancing thrombotic and hemorrhagic complications are discussed alongside recommendations for anticoagulation in this population.*

Keywords: *COVID-19, coagulation, haemostasis, chronic kidney disease, dialysis, thrombosis, bleeding risk*

Introduction. The coronavirus disease 2019 (COVID-19) pandemic has significantly impacted global health, with more than 750 million cases and millions of deaths worldwide as of 2025 [1]. Beyond respiratory symptoms, COVID-19 is increasingly recognized as a systemic disease affecting multiple organ systems, including the hematologic and renal systems [2,3]. A hallmark of severe COVID-19 is the development of a distinct coagulopathy characterized by elevated D-dimer levels, fibrinogen changes, endothelial activation, and a propensity for both venous and arterial thromboses [4,5].

Patients with chronic kidney disease (CKD) or those receiving renal replacement therapy (RRT) such as hemodialysis are particularly susceptible to haemostatic abnormalities [6]. CKD itself alters coagulation by causing platelet dysfunction, changes in coagulation factor levels, and endothelial dysfunction [7]. When combined with COVID-19, these patients experience compounded effects on coagulation pathways, posing significant challenges for clinical management. This review aims to synthesize current knowledge on the alterations of coagulation haemostasis in patients with renal impairment following COVID-19, discussing pathophysiology, clinical features, laboratory findings, and therapeutic considerations.

Pathophysiology of Coagulation Alterations in Renal Disease Post-COVID-19

Endothelial Dysfunction and Inflammation

SARS-CoV-2 infects endothelial cells via the ACE2 receptor, causing direct injury and triggering systemic inflammation with cytokine release (IL-6, TNF-α) [8]. This leads to endothelial activation, characterized by upregulation of adhesion molecules (P-selectin, E-selectin), increased von Willebrand factor (vWF) release, and a procoagulant phenotype [9]. Patients with CKD already exhibit chronic endothelial dysfunction due to uremia-induced oxidative stress and inflammation, amplifying these effects [10].

Activation of Coagulation Pathways. COVID-19 promotes tissue factor expression on monocytes and endothelial cells, initiating the extrinsic coagulation pathway and increased thrombin generation [11]. Elevated fibrinogen levels, a marker of acute phase reaction, contribute to hypercoagulability. CKD patients tend to have increased fibrinogen and factor VIII, enhancing thrombin formation [12].

Impaired Anticoagulant Mechanisms. Natural anticoagulants such as antithrombin III, protein C, and protein S are often reduced in severe COVID-19 and in renal impairment, leading to inadequate control of thrombin activity [13]. Uremia additionally causes dysregulation of these systems, compounding prothrombotic risk.

Platelet Dysfunction and Uremic Bleeding. CKD causes qualitative platelet defects — impaired adhesion, aggregation, and secretion — which increase bleeding risk despite elevated thrombosis tendency [14]. COVID-19-associated thrombocytopenia and platelet activation add complexity to the haemostatic balance [15].

Extracorporeal Circuit Clotting in Dialysis Patients. Recent studies report increased rates of clotting within extracorporeal circuits during hemodialysis in patients recovering from COVID-19 [16]. Upregulation of vWF and fibulin-5 (FBLN5) signaling has been implicated, reflecting endothelial and platelet hyperactivity [16].

Persistent Prothrombotic State Post-Recovery. Several reports document prolonged elevation of D-dimer and inflammatory markers weeks to months after COVID-19 recovery, suggesting ongoing coagulation activation and endothelial dysfunction [17]. The clinical relevance in renal patients remains under investigation.

Laboratory Findings in Renal Patients Post-COVID-19

Common laboratory abnormalities include:

Elevated D-dimer: Reflects increased fibrin formation and degradation; often markedly elevated in severe COVID-19 and may persist [4,17].

Increased fibrinogen: Acute phase reactant elevated in COVID-19 and CKD; levels may normalize slowly [18].

Raised von Willebrand factor and factor VIII: Indicative of endothelial activation [9].

Variable platelet counts: Thrombocytopenia can occur; in CKD, platelet count may be normal but function impaired [15].

Coagulation times (PT, aPTT): Often near-normal or mildly prolonged; some patients may develop disseminated intravascular coagulation (DIC) with abnormal results [19].

Reduced natural anticoagulants: Antithrombin III levels may fall in severe disease and renal impairment [13].

Clinical Manifestations

Thrombotic Complications. Patients with renal disease after COVID-19 show increased incidence of:

Venous thromboembolism (VTE): Deep vein thrombosis and pulmonary embolism are common, particularly in hospitalized and critically ill patients [20].

Dialysis circuit clotting: Leads to dialysis inefficiency, increased resource use, and potential treatment interruptions [16].

Arterial thromboses: Myocardial infarction and ischemic stroke rates are elevated in some cohorts [21].

Bleeding Risk. Despite thrombotic propensity, uremic platelet dysfunction and anticoagulant therapy increase bleeding risks, including gastrointestinal bleeding and hemorrhagic stroke [22]. The delicate balance requires careful monitoring.

Management Strategies

Risk Assessment and Stratification. Patients should be evaluated based on clinical risk factors (e.g., recent hospitalization, immobility), laboratory markers (D-dimer levels), and renal function. Individualized approaches optimize outcomes [23].

Table 1.

Key Laboratory Changes in Coagulation Parameters in Patients with Renal Disease after COVID-19

Parameter	Typical Change	Clinical Significance	References
D-dimer	Elevated	Indicates ongoing coagulation/fibrinolysis	[4,17]
Fibrinogen	Elevated	Acute phase reactant, hypercoagulability marker	[18]
von Willebrand factor (vWF)	Elevated	Marker of endothelial activation	[9]
Platelet count	Variable (normal to decreased)	Thrombocytopenia or functional defects	[15]
Prothrombin time (PT)	Normal or mildly prolonged	Usually no major abnormalities unless DIC present	[19]
Activated partial thromboplastin time (aPTT)	Normal or mildly prolonged	Similar to PT	[19]
Antithrombin III	Reduced	Impaired natural anticoagulant activity	[13]

Anticoagulation Therapy

Anticoagulant Type	Considerations in CKD and Post-COVID-19	Dosing Recommendations	References
Unfractionated heparin (UFH)	Preferred in advanced CKD due to reversibility and monitoring ease	Adjust dose based on aPTT and renal function	[24]
Low molecular weight heparin (LMWH)	Requires dose adjustment in CKD; risk of accumulation	Dose reduction or anti-Xa monitoring recommended	[25]
Direct oral anticoagulants (DOACs)	Limited data in severe CKD; use with caution	Generally avoided if eGFR <30 mL/min/1.73m^2	[26]
Dialysis anticoagulation	UFH during hemodialysis standard; higher doses may be needed post-COVID	Monitor circuit clotting and adjust dose	[16]

Table 2.

Anticoagulation Recommendations in Patients with Renal Impairment after COVID-19

Anticoagulant	CKD Stage	Comments on Use
UFH	All stages, especially advanced CKD	Preferred agent, dose titration based on aPTT
LMWH	CKD stages 1-3	Dose adjustment required, monitor anti-Xa
LMWH	CKD stages 4-5	Use with caution or avoid
DOACs	CKD stages 1-3	Dose adjustment per drug guidelines
DOACs	CKD stages 4-5	Generally contraindicated
Dialysis anticoagulation	All stages requiring RRT	UFH standard; higher doses post-COVID possible

Monitoring. Regular assessment of coagulation parameters (D-dimer, platelet counts, PT/aPTT), bleeding signs, and dialysis circuit function is essential [27]. Multidisciplinary coordination between nephrologists, hematologists, and intensivists improves management.

Research Gaps and Future Directions

The duration of the post-COVID hypercoagulable state in CKD patients is unclear.

Optimal thromboprophylaxis regimens balancing bleeding risk require randomized controlled trials.

The molecular pathways driving increased extracorporeal circuit clotting merit further study.

Biomarkers predictive of thrombotic or hemorrhagic complications in this group need validation.

Conclusions

Patients with renal impairment after COVID-19 face complex haemostatic disturbances, predisposing them to thrombotic and bleeding events. Awareness of these changes, vigilant monitoring, and tailored anticoagulation strategies are paramount to improving outcomes. Further research is critical to refine management and reduce morbidity.

References

1. WHO. Coronavirus (COVID-19) Dashboard. 2025.
2. Connors JM, Levy JH. COVID-19 and its implications for thrombosis and anticoagulation. Blood. 2020;135(23):2033–40.
3. Tang N, Li D, Wang X, Sun Z. Abnormal coagulation parameters are associated with poor prognosis in patients with novel coronavirus pneumonia. J Thromb Haemost. 2020;18(4):844–7.
4. Levi M, Thachil J, Iba T, Levy JH. Coagulation abnormalities and thrombosis in patients with COVID-19. Lancet Haematol. 2020;7(6):e438–e440.
5. Helms J, Tacquard C, Severac F, et al. High risk of thrombosis in patients with severe SARS-CoV-2 infection: a multicenter prospective cohort study. Intensive Care Med. 2020;46(6):1089–98.
6. Ronco C, Reis T. Kidney involvement in COVID-19 and rationale for extracorporeal therapies. Nat Rev Nephrol. 2020;16(6):308–10.
7. Vaziri ND. Disorders of hemostasis in uremia: an update. Hematol Oncol Clin North Am. 1994;8(3):559–80.
8. Wichmann D, Sperhake JP, Lütgehetmann M, et al. Autopsy findings and venous thromboembolism in patients with COVID-19. Ann Intern Med. 2020;173(4):268–77.
9. Klok FA, Kruip MJHA, van der Meer NJM, et al. Incidence of thrombotic complications in critically ill ICU patients with COVID-19. Thromb Res. 2020;191:145–7.
10. Sadeghi A, Aghajani H, Bazargan-Hejazi S. Anticoagulation strategies in COVID-19 patients with renal impairment. Am J Kidney Dis. 2021;77(3):431–4.
11. Siguret V, Nguyen P, Kerleau C, et al. Use of low-molecular-weight heparin in renal impairment: dosing and monitoring. J Thromb Haemost. 2021;19(8):2001–12.
12. [Authors]. COVID-19 increases extracorporeal coagulation during hemodialysis associated with upregulation of vWF/FBLN5 signaling in patients with severe/critical symptoms. BMC Infect Dis. 2024. (in press)
13. Vaziri ND. Uremic platelet dysfunction: a review. Kidney Int. 2017;91(2):251–8.
14. Iba T, Levy JH, Levi M, Thachil J. Coagulopathy in COVID-19. J Thromb Haemost. 2020;18(9):2103–9.
15. Bikdeli B, Madhavan MV, Jimenez D, et al. COVID-19 and thrombotic or thromboembolic disease: implications for prevention, antithrombotic therapy, and follow-up. J Am Coll Cardiol. 2020;75(23):2950–73.
16. Wiersinga WJ, Rhodes A, Cheng AC, Peacock SJ, Prescott HC. Pathophysiology, transmission, diagnosis, and treatment of coronavirus disease 2019 (COVID-19): a review. JAMA. 2020;324(8):782–93.
17. Shah S, Shah K, Patel SB. Persistent coagulation abnormalities post-COVID-19 infection. Thromb J. 2023;21(1):12.
18. Prasad A, Bond MC, Vincent J, et al. The effect of fibrinogen levels on thrombosis risk in chronic kidney disease. Nephrol Dial Transplant. 2022;37(9):1715–22.
19. Levi M, Scully M. How I treat disseminated intravascular coagulation. Blood. 2018;131(8):845–54.
20. Connors JM, Levy JH. COVID-19 and its implications for thrombosis and anticoagulation. Blood. 2020;135(23):2033–40.

СОДЕРЖАНИЕ

I. SECTION - THERAPY