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CHANGES IN PLATELET HEMOSTASIS IN POST-COVID SYNDROME

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Abstract. Post-COVID syndrome (also referred to as post-acute sequelae of SARS-CoV-2 infection, PASC) is characterized by persistent, heterogeneous symptoms that may continue for months after the acute infection. A growing body of evidence suggests that dysregulated hemostasis—particularly sustained platelet activation and thromboinflammatory signaling—can persist beyond viral clearance and may contribute to microvascular dysfunction, impaired tissue perfusion, and fluctuating systemic inflammation.

Keywords: post-COVID syndrome; PASC; platelet activation; thromboinflammation; platelet–leukocyte aggregates.

INTRODUCTION

The acute phase of COVID-19 highlighted how a respiratory viral infection can become a systemic vascular disease, with inflammation, endotheliopathy, and thrombosis tightly interwoven. In the post-acute setting, many individuals experience prolonged or relapsing symptoms—fatigue, dyspnea, chest discomfort, cognitive complaints, exercise intolerance, and dysautonomia—whose biological basis is likely multifactorial. A central, unifying hypothesis is that a subset of patients develops a persistent thromboinflammatory state in which vascular injury, immune dysregulation, and hemostatic imbalance fail to fully resolve. Within this framework, platelets are not passive bystanders: they are immune-responsive effector cells that integrate inflammatory cues, interact with leukocytes and endothelium, and amplify coagulation through procoagulant surface exposure and mediator release. Platelet hemostasis in post-COVID syndrome is therefore increasingly studied as both a potential driver of symptoms and a determinant of longer-term vascular risk. Yet the literature is not uniform: different cohorts, viral variants, vaccination histories, comorbidities, and assay platforms can yield apparently conflicting results. Reviews emphasize that platelet “activation” and “reactivity” are distinct concepts and that methodology (whole blood vs platelet-rich plasma, flow cytometry vs aggregometry, soluble markers vs functional assays) strongly shapes conclusions.

MATERIALS AND METHODS

A useful starting point is the biological logic of persistence. During acute infection, platelet activation can be triggered by systemic inflammation, endothelial injury, complement activity, neutrophil extracellular trap (NET) formation, and circulating prothrombotic mediators. If these triggers diminish slowly—or if a low-grade inflammatory program remains active—platelet function may remain shifted toward hyperreactivity even after clinical recovery. A prominent thromboinflammation review describes post-acute signatures consistent with sustained endothelial dysfunction, heightened thrombin generation capacity, and platelet-neutrophil aggregate formation, linking these processes to microvascular thrombosis and perfusion abnormalities reported in long COVID [1].

RESULTS AND DISCUSSION

From the platelet perspective, several recurring alterations have been reported in post-COVID cohorts. First, markers of basal platelet activation can remain elevated in some patients, including surface expression changes (e.g., P-selectin/CD62P) and increased circulating platelet-derived

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extracellular vesicles or microparticles. Second, platelets may demonstrate exaggerated responsiveness to agonists such as collagen, thrombin, or ADP in functional testing, suggesting a "primed" state that can more readily propagate thrombus formation under physiological stress. Third, platelet–leukocyte aggregates, particularly platelet–neutrophil and platelet–monocyte interactions, appear as a functional readout of thromboinflammatory coupling, facilitating leukocyte recruitment, NET-related immunothrombosis, and tissue factor–associated coagulation amplification. The methodological review by Luzak and colleagues highlights both the reported signals (soluble markers such as P-selectin and PF4; aggregates; microparticles) and the reasons results vary across studies, underscoring the need to interpret platelet findings in the context of assay design and sample handling.

Endothelial dysfunction is a major bridge between symptoms and hemostasis. The endothelium regulates vascular tone, barrier function, and antithrombotic homeostasis; when it is activated or injured, it can promote platelet adhesion (via von Willebrand factor release), increase leukocyte recruitment, and shift the local environment toward coagulation. In post-COVID syndrome, persistent endothelial activation markers and vascular dysregulation are frequently invoked to explain exertional intolerance and microcirculatory symptoms. Platelets, in turn, can worsen this loop by releasing vasoactive and pro-inflammatory mediators, supporting leukocyte transmigration, and contributing to microthrombus formation at sites of endothelial disturbance.

Another angle is the broader coagulation system, where platelet changes coexist with plasma-based hypercoagulability. A prospective study of post-COVID patients assessed standard coagulation parameters and viscoelastic testing and reported that a procoagulant pattern may persist for months, declining over time but still present in a subset at 12–18 months. The study also reported an association between persistent symptoms and a procoagulant state, supporting the hypothesis that ongoing microthrombosis or thrombi formation could contribute to physical symptom burden in some individuals. While such findings do not prove causation, they strengthen the rationale for investigating platelet–coagulation interactions as part of a multi-component post-COVID pathophysiology [2].

The concept of "microclots" has attracted attention as a potential explanatory model for symptom persistence, especially when classical thrombosis is not evident. One highly discussed study in Cardiovascular Diabetology reported associations between long-COVID symptoms and findings described as fibrin amyloid microclots together with platelet hyperactivation, proposing that microvascular obstruction and impaired oxygen delivery could contribute to fatigue and cognitive symptoms. At the same time, this area remains debated: definitions, detection methods, and clinical endpoints vary, and controlled interventional evidence is limited. A balanced interpretation is that microclot-related hypotheses are biologically plausible and testable, but they require standardized assays, blinded analyses, and prospective correlation with validated clinical outcomes before they can guide routine clinical care [3].

A practical challenge is heterogeneity—both of the syndrome and of the data. Post-COVID syndrome is not a single disease entity; it is an umbrella for multiple trajectories that may include persistent viral antigen reservoirs, autoimmunity, dysautonomia, deconditioning, organ-specific sequelae, and psychological stress responses, often overlapping. Platelet phenotypes likely differ across these trajectories. Moreover, platelet testing is unusually sensitive to pre-analytical variation: delays to processing, centrifugation protocols, temperature, anticoagulants used in collection tubes, and the choice of agonists can all shift results. The Luzak review explicitly cautions that diversity of methods

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and plasma components can drive divergent conclusions, which helps explain why one study may observe hyperreactivity while another reports reduced activation markers in whole blood. This does not invalidate the field; it signals that the next stage must be standardization and harmonized reporting.

Clinically, the key question is how platelet hemostasis changes translate into outcomes that matter: thrombotic events, organ function, symptom severity, and response to therapy. Evidence suggests that some survivors have elevated thrombotic risk up to a year after infection, and mechanistic reviews connect this to sustained thromboinflammation, endothelial dysfunction, and hemostatic imbalance. However, for many long-COVID patients the dominant issue may not be overt thrombosis but microvascular and inflammatory sequelae that reduce functional capacity. In that context, platelet hyperreactivity could contribute through repeated micro-scale clotting and inflammatory signaling rather than large-vessel occlusion [4]. The distinction matters because preventive anticoagulation and antiplatelet therapy carry bleeding risk, and the risk-benefit profile is not established for symptom-driven use without conventional thrombotic indications.

CONCLUSION

Changes in platelet hemostasis are increasingly recognized as part of the biological landscape of post-COVID syndrome, especially within the broader concept of persistent thromboinflammation. Across studies, a subset of patients demonstrates signals consistent with sustained platelet activation or hyperreactivity, increased platelet–leukocyte aggregate formation, and coexistence of a procoagulant, fibrinolysis-resistant milieu that may persist for months after acute infection.

REFERENCES

1. Nicolai L., Kaiser R., Stark K. Thromboinflammation in long COVID—the elusive key to postinfection sequelae? // Journal of Thrombosis and Haemostasis. – 2023. – Vol. 21. – P. 2020–2031. – DOI: 10.1016/j.jtha.2023.04.039. PubMed

2. Luzak B. Complex Pattern of Platelet Activation/Reactivity After SARS-CoV-2 Infection // International Journal of Molecular Sciences. – 2024. – Vol. 26, No. 1. – Art. 49. – DOI: 10.3390/ijms26010049. PubMed+1

3. Ranucci M., Baryshnikova E., Anguissola M., et al. The Long Term Residual Effects of COVID-Associated Coagulopathy // International Journal of Molecular Sciences. – 2023. – Vol. 24, No. 6. – Art. 5514. – DOI: 10.3390/ijms24065514. MDPI

4. Pretorius E., et al. Prevalence of symptoms, comorbidities, fibrin amyloid microclots and platelet pathology in individuals with Long COVID/Post-Acute Sequelae of COVID-19 (PASC) // Cardiovascular Diabetology. – 2022. – Vol. 21, No. 1. – Art. 148. – DOI: 10.1186/s12933-022-01579-5.