

Clinical Insights into Blood Coagulation and Viscosity: An Observational Study

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Abstract: The correlation between blood coagulation and viscosity plays a crucial role in understanding the dynamics of hemostasis and the risk of thromboembolic events. This study aims to examine the relationship between key components of the blood coagulation profile (such as fibrinogen levels, clotting factors, and prothrombin time) and blood viscosity in a clinical laboratory setting. A cohort of 150 patients was analyzed, with data collected on their coagulation profiles, including prothrombin time (PT), international normalized ratio (INR), activated partial thromboplastin time (aPTT), fibrinogen levels, and hematocrit. Blood viscosity was measured using a viscometer under standard laboratory conditions. The study found a statistically significant correlation between elevated fibrinogen levels and increased blood viscosity, as well as between hematocrit levels and viscosity. The findings suggest that changes in the coagulation profile, particularly fibrinogen and hematocrit, may directly influence blood viscosity, contributing to an increased risk of thromboembolic events. This study highlights the clinical importance of monitoring both coagulation and viscosity in patients with clotting disorders or a history of thromboembolic disease.

Keywords: Blood coagulation, blood viscosity, clinical laboratory study, fibrinogen, prothrombin time, clotting factors, hematocrit, thromboembolic events, viscosity measurement, hemostasis.

Introduction: Blood viscosity refers to the thickness and stickiness of blood, which is influenced by various factors such as hematocrit (red blood cell concentration), plasma proteins, and the elasticity of blood cells. Blood viscosity plays a vital role in the circulatory system as it affects blood flow and microvascular resistance. The hemodynamic properties of blood, including viscosity, are influenced by numerous physiological and pathological conditions. One such condition is the blood coagulation profile, which involves a series of complex processes that ensure proper clotting of blood in response to injury, thus preventing excessive bleeding.

Blood coagulation is typically assessed through laboratory tests that measure the levels of clotting factors, prothrombin time (PT), activated partial thromboplastin time (aPTT), fibrinogen, and platelet

function. These parameters provide insights into the ability of the blood to form a clot and stop bleeding. However, it is less understood how blood coagulation relates to blood viscosity, and whether changes in coagulation factors can directly affect the viscosity of blood.

Viscosity is influenced by multiple factors, with fibrinogen and hematocrit being particularly important. Fibrinogen, a plasma protein, plays a central role in blood clotting by promoting the aggregation of platelets and the formation of a clot. Elevated levels of fibrinogen are commonly observed in conditions like inflammation, atherosclerosis, and hypercoagulable states. Similarly, hematocrit, which represents the proportion of red blood cells in blood, has a direct impact on viscosity—higher hematocrit levels typically lead to increased blood viscosity, which can hinder

blood flow and promote thrombosis.

Understanding the correlation between coagulation factors and viscosity may have important clinical implications, especially in patients with conditions such as hypercoagulability, thrombophilia, or cardiovascular disease, where blood viscosity can influence the risk of thromboembolic events such as deep vein thrombosis, pulmonary embolism, and stroke. This study aims to explore the relationship between these two variables and how they might influence clinical outcomes in patients with altered coagulation profiles.

METHODS

Study Design

This is a prospective observational study conducted at a tertiary care hospital's clinical laboratory. The study was designed to investigate the correlation between blood coagulation profile parameters and blood viscosity in a cohort of 150 adult patients. The study included patients who presented with a range of conditions that might influence coagulation, including cardiovascular disease, diabetes, hypertension, inflammatory disorders, and clotting disorders.

Inclusion and Exclusion Criteria

- Inclusion Criteria:
 - o Patients aged 18-80 years.
 - o Patients with clinical indications for coagulation tests (e.g., history of thromboembolism, cardiovascular disease, etc.).
 - o No history of severe liver disease or acute infection that might significantly alter coagulation.
- Exclusion Criteria:
 - o Patients who were on anticoagulant therapy (e.g., warfarin, heparin, direct oral anticoagulants).
 - o Pregnant women.
 - o Patients with known bleeding disorders such as hemophilia or von Willebrand disease.

Laboratory Testing

- Coagulation Profile: Blood samples were collected into citrate tubes, and prothrombin time (PT), international normalized ratio (INR), activated partial thromboplastin time (aPTT), and fibrinogen levels were measured using standard laboratory techniques.
- Blood Viscosity: Blood viscosity was measured using a rotational viscometer (Brookfield DV3T), which provided precise measurements of blood's apparent viscosity at different shear rates. The viscosity values were recorded at a temperature of 37°C, which is close to normal body temperature.
- Hematocrit Measurement: Hematocrit levels were measured using automated hematology analyzers

as part of routine clinical blood tests.

Data Collection

Demographic data (age, sex, comorbidities) and clinical characteristics were recorded for each participant. Additionally, laboratory results were compiled, including values for PT, INR, aPTT, fibrinogen, hematocrit, and blood viscosity. All measurements were performed under standardized conditions by experienced laboratory personnel to ensure consistency and reliability.

Statistical Analysis

Descriptive statistics (mean, median, and standard deviation) were used to summarize the clinical and laboratory data. The correlation between blood viscosity and coagulation profile components (fibrinogen, PT, INR, aPTT, and hematocrit) was analyzed using Pearson's correlation coefficient for normally distributed data and Spearman's rank correlation for non-normally distributed variables. Multiple linear regression was used to examine the independent effects of coagulation factors and hematocrit on blood viscosity. Statistical significance was set at $p < 0.05$.

RESULTS

Patient Demographics

A total of 150 patients were included in the study, with a mean age of 56.4 years (range: 18-80 years). The cohort consisted of 60% males and 40% females. Common comorbidities included hypertension (52%), diabetes mellitus (34%), and cardiovascular disease (45%). The median fibrinogen level was 350 mg/dL (range: 180-600 mg/dL), and the mean hematocrit was 42.3% (range: 30-50%).

Correlation Between Coagulation Profile and Blood Viscosity

- Fibrinogen: A strong positive correlation was found between fibrinogen levels and blood viscosity ($r = 0.62$, $p < 0.001$). Higher fibrinogen levels were associated with increased blood viscosity, supporting the role of fibrinogen in enhancing blood's resistance to flow.
- Hematocrit: There was also a significant positive correlation between hematocrit levels and blood viscosity ($r = 0.55$, $p < 0.001$). As hematocrit increased, blood viscosity increased, reflecting the impact of red blood cell concentration on blood thickness.
- PT, INR, and aPTT: No significant correlations were found between prothrombin time (PT), INR, or aPTT and blood viscosity ($p > 0.05$). This suggests that these clotting time parameters may not have as direct

an influence on viscosity as fibrinogen and hematocrit.

Multivariate Analysis

In a multivariate regression model, fibrinogen levels ($\beta = 0.58$, $p < 0.001$) and hematocrit ($\beta = 0.33$, $p < 0.01$) were identified as independent predictors of blood viscosity. The model explained 46% of the variability in blood viscosity.

DISCUSSION

This study examined the relationship between key components of the blood coagulation profile and blood viscosity, with a focus on fibrinogen and hematocrit levels. The findings revealed significant correlations between elevated fibrinogen levels, increased hematocrit, and higher blood viscosity, suggesting that both these factors play an important role in altering blood flow dynamics and may contribute to thromboembolic events. The clinical implications of these results are crucial for understanding how coagulation and viscosity interact in patients at risk for vascular complications.

Fibrinogen and Blood Viscosity

Fibrinogen is a plasma protein essential for blood clot formation, but it also plays a significant role in increasing blood viscosity, especially when its levels are elevated. In this study, we found a strong positive correlation ($r = 0.62$, $p < 0.001$) between fibrinogen levels and blood viscosity. Fibrinogen is known to enhance the aggregation of platelets and the formation of the fibrin clot, both of which increase the blood's resistance to flow. When fibrinogen is elevated, it increases the thickness of blood, which can be particularly problematic in high-risk patients, such as those with atherosclerosis, inflammatory disorders, or chronic diseases.

The relationship between fibrinogen and viscosity is crucial because elevated fibrinogen levels have been associated with an increased risk of thrombosis. In conditions such as cardiovascular disease, stroke, or deep vein thrombosis, higher blood viscosity could impair the flow of blood in microcirculation, increase vascular resistance, and promote clot formation, ultimately raising the likelihood of severe thromboembolic events.

Furthermore, the results support earlier studies which have suggested that fibrinogen is an independent risk factor for cardiovascular complications, with increased viscosity acting as a potential contributing mechanism. It is important to note that fibrinogen levels are often elevated in acute-phase reactions or inflammatory conditions, meaning that monitoring and managing fibrinogen levels may help mitigate risks in patients with systemic inflammation or chronic diseases

associated with higher clotting risks.

Hematocrit and Blood Viscosity

The study also found a significant positive correlation ($r = 0.55$, $p < 0.001$) between hematocrit and blood viscosity. Hematocrit represents the percentage of red blood cells in blood, and its levels directly impact the fluidity of blood. As hematocrit increases, so does the viscosity, since red blood cells are the largest contributors to blood's resistance to flow. Higher hematocrit means that there are more red blood cells in circulation, leading to thicker blood, which can hinder blood flow, particularly in smaller vessels and capillaries. This can result in an increased workload on the heart and may also raise the risk of clot formation due to impaired flow dynamics.

In clinical practice, increased hematocrit levels are often seen in patients with polycythemia vera or dehydration, and in individuals living at high altitudes. These conditions are known to elevate blood viscosity, which, as shown in this study, could have significant clinical consequences for patients. For example, high blood viscosity is known to increase the risk of deep vein thrombosis (DVT), pulmonary embolism (PE), and stroke, particularly in patients with other vascular risk factors.

Furthermore, elevated hematocrit levels may also lead to reduced microcirculatory blood flow, which could promote ischemic conditions in peripheral organs. As such, managing hematocrit levels could be essential in preventing complications in patients who are at risk for thromboembolic events. Clinicians may benefit from monitoring hematocrit levels alongside viscosity measurements to better predict and manage vascular risk in at-risk populations.

Prothrombin Time, INR, aPTT, and Blood Viscosity

Interestingly, no significant correlations were observed between prothrombin time (PT), international normalized ratio (INR), or activated partial thromboplastin time (aPTT) and blood viscosity. These clotting time parameters are widely used to assess the functionality of clotting factors in the blood and help monitor the effectiveness of anticoagulant therapies. While these parameters are crucial for determining a patient's risk for bleeding or clotting, they did not directly correlate with viscosity in this study.

One possible explanation for this finding is that clotting time parameters assess the rate at which blood clots, rather than the physical characteristics of the blood that affect its flow, such as fibrinogen concentration and hematocrit. Therefore, while prothrombin time, INR, and aPTT are vital for determining clotting potential, they do not necessarily correlate with blood

viscosity, which is more closely influenced by plasma proteins like fibrinogen and the concentration of red blood cells.

This distinction highlights the importance of evaluating multiple factors when assessing a patient's vascular health and emphasizes that blood viscosity may offer valuable insights into conditions where thromboembolic events are a concern, even in patients with normal clotting times.

Clinical Implications and Recommendations

The findings of this study have several clinical implications. Given the positive correlation between fibrinogen levels and viscosity, clinicians should consider monitoring fibrinogen in patients who are at risk for thromboembolic events. This is particularly relevant for patients with cardiovascular disease, diabetes, or hypercoagulable states. Monitoring blood viscosity could serve as a complementary diagnostic tool alongside traditional coagulation tests in these populations.

Furthermore, hematocrit levels should be considered when evaluating the viscosity of blood. Elevated hematocrit, particularly in conditions like polycythemia vera or dehydration, may increase blood viscosity, contributing to vascular complications. Reducing hematocrit levels, when appropriate, could reduce viscosity and improve microvascular circulation.

Clinicians should also be aware that even in patients with normal PT, INR, and aPTT values, abnormal blood viscosity might still be present, indicating that these conventional tests alone may not fully capture the risks associated with elevated viscosity. Thus, viscosity measurement could be particularly useful in patients with unexplained thromboembolic events or those who are not responding well to conventional anticoagulation therapy.

Limitations and Future Directions

This study has certain limitations that must be considered. First, it was conducted at a single center, and the sample size was limited to 150 patients. Future studies with larger and more diverse patient populations could help validate these findings and explore whether the correlations between fibrinogen, hematocrit, and viscosity hold true in different clinical settings. Additionally, this study did not explore the direct clinical outcomes related to blood viscosity, such as the incidence of thromboembolic events. Future research could examine how changes in blood viscosity, in conjunction with coagulation parameters, impact long-term patient outcomes, especially in populations at high risk for stroke, heart attacks, and DVT.

Furthermore, while viscosity was measured using a

rotational viscometer, more advanced methods, such as shear rate-dependent measurements or in vivo imaging techniques, could provide a more detailed understanding of the interaction between blood flow and coagulation parameters.

In conclusion, the present study highlights the significant correlation between fibrinogen levels, hematocrit, and blood viscosity, and emphasizes the importance of these factors in assessing the risk of thromboembolic events. While coagulation profile parameters like PT, INR, and aPTT provide valuable insights into clotting function, they do not directly influence blood viscosity. Given the findings, future clinical practice may benefit from monitoring blood viscosity alongside traditional coagulation tests to better assess and manage patients at risk for thrombosis. Managing fibrinogen levels and hematocrit may be critical in reducing the incidence of thromboembolic complications in high-risk populations.

This study demonstrates a significant correlation between fibrinogen levels and blood viscosity, supporting the hypothesis that increased fibrinogen contributes to thicker blood and potentially greater resistance to blood flow. Elevated fibrinogen levels have been associated with several pathological conditions, including inflammation and cardiovascular disease, which could further exacerbate the risk of thromboembolic events.

Additionally, the study found that hematocrit levels, which reflect red blood cell concentration, are also positively correlated with viscosity. As expected, higher hematocrit levels contribute to an increase in blood thickness, which can impair microcirculatory flow and promote clot formation.

Interestingly, clotting time parameters such as PT, INR, and aPTT did not show a direct relationship with blood viscosity. This suggests that while these measures are critical for assessing clotting function, they may not have as direct an effect on blood flow dynamics as other factors like fibrinogen and hematocrit.

These findings suggest that fibrinogen and hematocrit should be considered as potential clinical markers of blood viscosity, which may provide valuable insight into the risk of thromboembolic events, especially in patients with a hypercoagulable state. Monitoring and managing elevated fibrinogen levels and hematocrit could play a role in improving patient outcomes, particularly in those at risk for stroke, deep vein thrombosis, or pulmonary embolism.

CONCLUSION

This observational study provides significant evidence

of the relationship between blood coagulation profile components and blood viscosity, highlighting the critical roles of fibrinogen and hematocrit in influencing blood flow. The study underscores the importance of considering both coagulation parameters and viscosity measurements when assessing thrombotic risk in clinical practice. Future studies are needed to further investigate the clinical implications of these findings and explore how viscosity management might reduce the incidence of thromboembolic events in at-risk populations.

REFERENCES

- Bateman, R.M.; Sharpe, M.D.; Jagger, J.E.; Ellis, C.G.; Solé-Violán, J.; López-Rodríguez, M.; Herrera-Ramos, E.; Ruíz-Hernández, J.; Borderías, L.; Horcajada, J.; et al. 36th International Symposium on Intensive Care and Emergency Medicine: Brussels, Belgium, 15–18 March 2016. *Crit. Care* 2016, 20 (Suppl. S2), 94. [Google Scholar] [PubMed]
- Forsyth, A.L.; Giangrande, P.; Hay, C.R.; Kenet, G.; Kessler, C.M.; Knöbl, P.N.; Llinás, A.; Santagostino, E.; Young, G. Difficult clinical challenges in haemophilia: International experiential perspectives. *Haemophilia* 2012, 18 (Suppl. S5), 39–45. [Google Scholar] [CrossRef] [PubMed]
- Briane, A.; Horvais, V.; Sigaud, M.; Trossaert, M.; Drillaud, N.; Ternisien, C.; Fouassier, M.; Babuty, A. Bleeding management in type 3 von Willebrand disease with anti-von Willebrand factor inhibitor: A literature review and case report. *EJHaem* 2024, 5, 964–970. [Google Scholar] [CrossRef]
- Ambrosi, P.; Juhan-Vague, I. Dyslipidemia, lipid lowering drugs and thrombosis. *Arch. Mal. Coeur Vaiss.* 1995, 88, 1641–1645. [Google Scholar]
- Sonksen, J.R.; Kong, K.L.; Holder, R. Magnitude and time course of impaired primary haemostasis after stopping chronic low and medium dose aspirin in healthy volunteers. *Br. J. Anaesth.* 1999, 82, 360–365. [Google Scholar] [CrossRef]
- Rosenson, R.S.; Wolff, D.; Green, D.; Boss, A.H.; Kensey, K.R. Aspirin. Aspirin does not alter native blood viscosity. *J. Thromb. Haemost.* 2004, 2, 340–341. [Google Scholar] [PubMed]
- Cattaneo, M. Response variability to clopidogrel: Is tailored treatment, based on laboratory testing, the right solution? *J. Thromb. Haemost.* 2012, 10, 327–336. [Google Scholar] [CrossRef]
- Bhatt, D.L.; Eikelboom, J.W.; Connolly, S.J.; Steg, P.G.; Anand, S.S.; Verma, S.; Branch, K.R.H.; Probstfield, J.; Bosch, J.; Shestakovska, O.; et al. Role of combination antiplatelet and anticoagulation therapy in diabetes mellitus and cardiovascular disease. *Circulation* 2020, 141, 1841–1854. [Google Scholar] [CrossRef] [PubMed]
- Lowe, G.D. Virchow's triad revisited: Abnormal flow. *Pathophysiol. Haemost. Thromb.* 2003, 33, 455–457. [Google Scholar] [CrossRef] [PubMed]
- Roldan, V.; Marin, F.; Manzano-Fernandez, S.; Gallego, P.; Vilchez, J.A.; Valdes, M.; Vicente, V.; Lip, G.Y. The HAS-BLED score has better prediction accuracy for major bleeding than CHADS2 or CHA2DS2-VASc scores in anticoagulated patients with atrial fibrillation. *J. Am. Coll. Cardiol.* 2013, 62, 2199–2204. [Google Scholar] [CrossRef]
- Fan, K.; Xiao, Y.; Xue, A.; Zhou, J. Clinical outcomes, management, healthcare resource utilization, and cost according to the CHA(2)DS(2)-VASc scores in Asian patients with nonvalvular atrial fibrillation. *Int. J. Cardiol.* 2024, 417, 132496. [Google Scholar] [CrossRef]
- Nwose, E.U.; Richards, R.S.; Jelinek, H.F.; Kerr, P.G. D-dimer identifies stages in the progression of diabetes mellitus from family history of diabetes to cardiovascular complications. *Pathology* 2007, 39, 252–257. [Google Scholar] [CrossRef] [PubMed]
- Belkhir, D.; Blibech, H.; Kaabi, L.; Miladi, S.; Jebali, M.A.; Daghfous, J.; Mehiri, N.; Laatar, A.; Ben Salah, N.; Snene, H.; et al. Laboratory findings predictive of critical illness in hospitalized COVID-19 patients in Tunisia. *F1000Research* 2024, 13, 918. [Google Scholar] [CrossRef]
- Corrêa, H.L.; Deus, L.A.; Nascimento, D.D.C.; Rolnick, N.; Neves, R.V.P.; Reis, A.L.; de Araújo, T.B.; Tzanno-Martins, C.; Tavares, F.S.; Neto, L.S.S.; et al. Concerns about the application of resistance exercise with blood-flow restriction and thrombosis risk in hemodialysis patients. *J. Sport Health Sci.* 2024, 13, 548–558. [Google Scholar] [CrossRef] [PubMed]
- Piech, P.; Haratym, M.; Borowski, B.; Węglowski, R.; Staśkiewicz, G. Beyond the fractures: A comprehensive Comparative analysis of Affordable and Accessible laboratory parameters and their coefficients for prediction and Swift confirmation of pulmonary embolism in high-risk orthopedic patients. *Pract. Lab. Med.* 2024, 40, e00397. [Google Scholar] [CrossRef] [PubMed]
- Nwose, E.U. Whole blood viscosity assessment issues II: Prevalence in endothelial dysfunction and hypercoagulation. *N. Am. J. Med. Sci.* 2010, 2, 252–257. [Google Scholar]
- Wi, M.; Kim, Y.; Kim, C.H.; Lee, S.; Bae, G.S.; Leem, J.; Chu, H. Effectiveness and safety of Fufang Danshen Dripping Pill (Cardiotonic Pill) on blood viscosity and hemorheological factors for cardiovascular event prevention in patients with type 2 diabetes mellitus: Systematic review and meta-analysis. *Medicina* 2023,

59, 1730. [Google Scholar] [CrossRef] [PubMed]

Tamariz, L.J.; Young, J.H.; Pankow, J.S.; Yeh, H.-C.; Schmidt, M.I.; Astor, B.; Brancati, F.L. Blood viscosity and hematocrit as risk factors for type 2 diabetes mellitus: The atherosclerosis risk in communities (ARIC) study. *Am. J. Epidemiol.* 2008, 168, 1153–1160. [Google Scholar] [CrossRef]

Muldoon, M.F.; Herbert, T.B.; Patterson, S.M.; Kameneva, M.; Raible, R.; Manuck, S.B. Effects of acute psychological stress on serum lipid levels, hemoconcentration, and blood viscosity. *Arch. Intern. Med.* 1995, 155, 615–620. [Google Scholar] [CrossRef] [PubMed]

Nwose, E.U.; Richards, R.S.; McDonald, S.; Jelinek, H.F.; Kerr, P.G.; Tinley, P. Assessment of diabetic macrovascular complications: A prediabetes model. *Br. J. Biomed. Sci.* 2010, 67, 59–66. [Google Scholar] [CrossRef] [PubMed]

Nwose, E.U.; Butkowski, E.G. Algorithm for whole blood viscosity: Implication for antiplatelet bleeding risk assessment. *Aust. J. Med. Sci.* 2013, 34, 50–55. [Google Scholar]

Nwose, E.U.; Bwititi, P.T. Whole blood viscosity: Affordances and re-evaluation of sensitivity and specificity for clinical use. *Int. J. Biol. Lab. Sci.* 2022, 11, 96–103. [Google Scholar]

Cakmak, G.; Alkan, F.A.; Korkmaz, K.; Saglam, Z.A.; Karis, D.; Yenigun, M.; Ercan, M. Blood viscosity as a forgotten factor and its effect on pulmonary flow. *Transl. Respir. Med.* 2013, 1, 3. [Google Scholar] [CrossRef] [PubMed]

Ozcan Cetin, E.H.; Cetin, M.S.; Canpolat, U.; Kalender, E.; Topaloglu, S.; Aras, D.; Aydogdu, S. The forgotten variable of shear stress in mitral annular calcification: Whole blood viscosity. *Med. Princ. Pract.* 2015, 24, 444–450. [Google Scholar] [CrossRef] [PubMed]

Celik, T.; Balta, S.; Ozturk, C.; Iyiso, A. Whole blood viscosity and cardiovascular diseases: A forgotten old player of the game. *Med. Princ. Pract.* 2016, 25, 499–500. [Google Scholar] [CrossRef]

Paisey, R.B.; Harkness, J.; Hartog, M.; Chadwick, T. The effect of improvement in diabetic control on plasma and whole blood viscosity. *Diabetologia* 1980, 19, 345–349. [Google Scholar] [CrossRef]

Zarkovic, M.; Kwaan, H.C. Correction of hyperviscosity by apheresis. *Semin. Thromb. Hemost.* 2003, 29, 535–542. [Google Scholar] [PubMed]

Perez Rogers, A.; Estes, M. Hyperviscosity syndrome. In *StatPearls* [Internet]; StatPearls Publishing: Treasure Island, FL, USA, 2023. [Google Scholar]