Stoencheva, S. (2026). Hypercoagulability and thrombotic risk in beta-thalassemia: Clinical and laboratory insights, *MEDIS - Medical Science and Research, 5*(1), 33-38.
doi: 10.35120/medisij0501033s UDK: 616.155.194.125-092

HYPERCOAGULABILITY AND THROMBOTIC RISK IN BETA-THALASSEMIA: CLINICAL AND LABORATORY INSIGHTS

Snezhana Stoencheva[1*]

[1]Department of Clinical Laboratory, Faculty of Medicine, Medical University of Plovdiv, University Hospital "St. George", Plovdiv, Bulgaria, e-mail: snezhana.stoencheva@mu-plovdiv.bg

Abstract: Beta-thalassemia is increasingly recognized as a multisystem disorder associated with a chronic hypercoagulable state and an elevated risk of thrombotic complications. Beyond ineffective erythropoiesis, chronic anemia, and transfusion-related iron overload, abnormalities in coagulation and vascular function play an important role in long-term morbidity. Accumulating evidence indicates that patients with beta-thalassemia exhibit persistent activation of cellular and plasma components of hemostasis, even in the absence of overt clinical thrombosis. Hypercoagulability in beta-thalassemia is multifactorial, arising from altered red blood cell membrane architecture with phosphatidylserine externalization, chronic platelet activation, endothelial dysfunction driven by hemolysis and nitric oxide depletion, increased circulating procoagulant microparticles and extracellular vesicles, and imbalances in natural anticoagulant pathways. Iron-related oxidative stress and inflammation further amplify vascular activation and thrombin generation. The magnitude and clinical expression of these abnormalities differ substantially across disease phenotypes. Beta-thalassemia trait is generally not associated with clinically significant thrombosis, whereas non-transfusion-dependent thalassemia (NTDT) carries a particularly high thrombotic burden, especially in splenectomized patients. In transfusion-dependent thalassemia (TDT), regular transfusion modifies erythroid-driven procoagulant mechanisms but introduces additional risk modifiers, including iron overload and catheter-related thrombosis. This review summarizes current knowledge on coagulation disturbances and thrombotic complications in beta-thalassemia, integrating pathophysiological mechanisms with clinically relevant laboratory markers. Particular emphasis is placed on global coagulation assays, cellular biomarkers, and phenotype-specific clinical-laboratory patterns, as well as on contemporary monitoring strategies in TDT. A better understanding of these mechanisms is essential for individualized risk stratification and optimization of thrombosis prevention in patients with beta-thalassemia.

Keywords: *Beta-thalassemia, hypercoagulability, thrombotic risk, iron overload*
Field: Medical Sciences and Health

1. INTRODUCTION

Hemostasis represents a balance between procoagulant and anticoagulant mechanisms that maintains vascular integrity. Disruption of this balance may lead to thrombosis, which is a major cause of morbidity and mortality worldwide (Furie et al., 2008). Thrombus formation is a complex process involving platelet activation, thrombin generation, fibrin formation, and changes in the vascular wall (Furie et al., 2008). Beta-thalassemia is an inherited disorder caused by reduced or absent synthesis of β-globin chains, leading to ineffective erythropoiesis, chronic hemolysis, and anemia of varying severity. Advances in transfusion protocols and iron chelation therapy have significantly improved patient survival. As a consequence, long-term complications have become more apparent, including endocrine dysfunction, cardiovascular disease, and thromboembolic events (Cappellini et al., 2015), (Pennell et al., 2005), (Farmakis et al., 2022). In recent years, thrombosis has emerged as an important clinical issue in patients with thalassemia, particularly in those with non–transfusion-dependent thalassemia (NTDT) and in splenectomized patients (Taher et al., 2008), (Eldor et al., 2002), (Cappellini et al., 2012). This review focuses on thrombosis and hypercoagulable state in beta-thalassemia, integrating established pathophysiological mechanisms with clinically relevant laboratory markers. Emphasis is placed on differences between clinical phenotypes and on current monitoring strategies in transfusion-dependent thalassemia (TDT). Particular attention is given to the increasing use of MRI-based assessment of organ iron overload, as well as to dynamic markers of labile plasma iron and oxidative stress (Farmakis et al., 2022), (Kirk et al., 2009), (Pootrakul et al., 2004), (Levi et al., 2018).

Hemostasis encompasses three closely related processes: primary hemostasis, secondary hemostasis (coagulation), and fibrinolysis. Primary hemostasis involves the formation of a platelet plug.

*Corresponding author: snezhana.stoencheva@mu-plovdiv.bg

After vascular injury, platelets adhere to the exposed subendothelium through interactions with von Willebrand factor and collagen. This adhesion leads to platelet activation and aggregation, resulting in the formation of an initial hemostatic plug. Secondary hemostasis stabilizes this plug through activation of the coagulation cascade, which generates thrombin. Thrombin converts fibrinogen into fibrin and further amplifies platelet activation as well as the activation of additional coagulation factors (Furie et al., 2008), (Musallam et al., 2011). Physiological regulation of coagulation is maintained by natural anticoagulant systems, including antithrombin, protein C/protein S pathway, and tissue factor pathway inhibitor, together with a tightly controlled fibrinolytic system. Standard laboratory tests such as prothrombin time (PT/INR) and activated partial thromboplastin time (aPTT) assess isolated components of the coagulation cascade but do not reflect the overall balance between procoagulant and anticoagulant systems. This limitation is particularly relevant in chronic hypercoagulable states, including those associated with thalassemia, where routine tests may appear in the reference range despite an increased thrombotic risk (Eldor et al., 2002), (Singer et al. 2006).

2. THROMBOSIS: MECHANISMS AND CHALLENGES IN LABORATORY ASSESSMENT

Thrombosis is traditionally explained by Virchow's triad, which comprises endothelial injury, abnormal blood flow, and hypercoagulability. These components interact dynamically and their relative contribution varies according to the vascular bed and the underlying clinical context. Venous thrombosis is typically fibrin-rich and is commonly associated with blood stasis, reduced venous flow, and systemic hypercoagulable state. In contrast, arterial thrombosis is predominantly platelet-rich and is usually linked to endothelial disruption, plaque rupture, and conditions of high shear stress, where platelet activation plays a central role (Furie et al., 2008). Laboratory assessment of thrombosis relies on indirect markers of coagulation activation and fibrin turnover. D-dimer is widely used as a marker of fibrin formation and degradation and is particularly useful for excluding acute venous thromboembolism in low-risk settings. However, its specificity is limited in chronic inflammatory conditions, liver disease, pregnancy, and other states associated with increased baseline coagulation activation.

In broader systemic coagulopathies, such as disseminated intravascular coagulation (DIC), diagnostic approaches incorporate composite scoring systems that integrate platelet count, prothrombin time, fibrinogen, and D-dimer or fibrin degradation products. These tools aim to reflect the overall disturbance of hemostasis rather than individual laboratory abnormalities. Expert reviews emphasize that management in such settings is largely supportive and should be tailored to the underlying cause and the patient's bleeding or thrombotic risk (Tripodi et al., 2009). In patients with thalassemia, increasing attention has been directed toward global coagulation assays, such as thrombin generation tests, as well as toward cellular and endothelial biomarkers that may better reflect the prothrombotic milieu of the disease. These approaches are particularly relevant for risk stratification and for understanding phenotype-specific patterns of thrombosis.

3. BETA-THALASSEMIA AND MARKERS OF HYPERCOAGULABILITY

Beyond chronic anemia, beta-thalassemia is increasingly recognized as a systemic disorder with significant vascular and thrombotic complications. The interplay between ineffective erythropoiesis, chronic hemolysis, oxidative stress, and inflammation creates a biological milieu that favours endothelial dysfunction, hypercoagulability, and thrombosis.

Clinically, beta-thalassemia presents with a wide range of phenotypes. Beta-thalassemia minor (trait) is typically associated with mild microcytic anemia, elevated HbA2 levels, and a relatively preserved or increased red blood cell count, and is generally not linked to clinically significant thrombotic risk. At the other end of the spectrum, TDT requires regular lifelong red blood cell transfusions to maintain adequate hemoglobin levels and suppress ineffective erythropoiesis. While transfusion therapy mitigates some disease-related prothrombotic drivers, it introduces additional factors such as iron overload, chronic inflammation, and exposure to central venous catheters, all of which may influence thrombotic risk. NTDT includes intermediate phenotypes characterized by chronic anemia, persistent ineffective erythropoiesis, and intermittent transfusion requirements. This group carries the highest burden of thrombotic complications. Persistent hemolysis, increased intestinal iron absorption driven by hepcidin suppression, and the high prevalence of splenectomy contribute to a vascular risk profile that differs from that observed in TDT patients. Clinical observations consistently demonstrate a higher incidence of both venous and arterial thrombotic events in NTDT, particularly following splenectomy (Taher et al., 2008), (Eldor et al., 2002), (Cappellini et al., 2012).

Hypercoagulability in beta-thalassemia is multifactorial and reflects the interaction of cellular, endothelial, and plasma abnormalities. Accumulating evidence supports the presence of a lifelong prothrombotic state driven by red blood cell membrane damage, chronic platelet activation, endothelial dysfunction, and alterations in natural anticoagulant and fibrinolytic pathways (Eldor et al., 2002)

Red blood cell membrane injury represents a central pathogenic mechanism. Oxidative stress and membrane remodeling lead to externalization of phosphatidylserine (PS) on the erythrocyte surface, providing a catalytic platform for the assembly of coagulation complexes and enhanced thrombin generation (Eldor et al., 2002), (Cappellini et al., 2012). In parallel, chronic hemolysis releases free hemoglobin and heme into the circulation, resulting in nitric oxide scavenging, endothelial dysfunction, and progressive vasculopathy (Taher et al., 2008), (Cappellini et al., 2012). Platelet activation is another consistent feature of beta-thalassemia and is particularly pronounced in splenectomized patients, in whom clearance of activated platelets and circulating cellular fragments is impaired. Associations between platelet activation, pulmonary vascular disease, and hypercoagulability have been reported, supporting a contributory role of platelets in both microvascular and macrovascular complications (Kheansaard et al., 2018). More recently, extracellular vesicles (EVs), including circulating microparticles (MPs) derived from red blood cells, platelets, and endothelial cells, have emerged as important amplifiers of coagulation. Experimental data from β-thalassemia/HbE models indicate that circulating MPs directly promote endothelial dysfunction, supporting a pathophysiological link between EV burden and vascular complications (Klaihmon et al., 2024). In addition, whole-blood viscoelastic assays, such as thromboelastometry, have demonstrated a hypercoagulable profile in splenectomized patients, underscoring the importance of cellular elements that are not captured by conventional platelet-poor plasma assays (Vehapoglu et al, 2014). These observations highlight that thrombotic risk in beta-thalassemia is closely linked to disease pathogenesis and is modulated by clinical phenotype, splenic status, transfusion exposure, and iron burden.

Laboratory assessment of hypercoagulability in beta-thalassemia remains challenging. No single laboratory parameter reliably reflects the overall balance between procoagulant and anticoagulant forces in this condition. Assessment therefore requires a phenotype-oriented approach that combines routine laboratory data with more specialized tests in selected high-risk patient populations. Routine laboratory markers provide indirect but clinically relevant information. Platelet count is often increased, particularly after splenectomy, reflecting both thrombocytosis and heightened platelet activation. Markers of hemolysis, including lactate dehydrogenase and indirect bilirubin, reflect the degree of red blood cell destruction and are closely linked to endothelial dysfunction and nitric oxide depletion. D-dimer levels may be elevated in some patients, but their interpretation is limited by confounding factors including chronic hemolysis, ongoing inflammation, and liver involvement. Global coagulation assays allow for a more integrated evaluation of coagulation potential. Thrombin generation testing reflects the combined contribution of cellular and plasma-based procoagulant mechanisms and has demonstrated increased endogenous thrombin potential in patients with more severe thalassemia phenotypes. Whole-blood viscoelastic assays provide complementary insights and are particularly informative in splenectomized patients, in whom cellular elements play a dominant role in driving hypercoagulability that may not be apparent in platelet-poor plasma based assays (Eldor et al., 2002), (Cappellini et al., 2012), (Vehapoglu et al, 2014). Circulating MPs and other EVs expand the laboratory framework for assessing thrombotic risk. Both experimental and clinical studies in β-thalassemia/HbE have shown that patient-derived microparticles induce endothelial dysfunction, supporting their role not only as biomarkers but also as active mediators to the prothrombotic vascular milieu (Klaihmon et al., 2024).

Available evidence indicates that hypercoagulability in beta-thalassemia is best characterized through a combined assessment of conventional laboratory parameters, global coagulation assays, and cellular biomarkers, interpreted within the appropriate clinical and phenotypic context. Laboratory markers of hypercoagulability exhibit phenotype-specific patterns across the spectrum of β-thalassemia. Conventional coagulation screening tests, including PT and aPTT, are typically within the reference range across all phenotypes (thalassemia minor, NTDT, and TDT), despite well-documented clinical evidence of a prothrombotic state, highlighting their limited sensitivity for detecting chronic hypercoagulability (Al-Sanabra et al., 2025), (Lecut et al., 2015). Exposure of PS on red blood cell (RBC) membranes, reflecting the presence of procoagulant RBCs, is minimal in thalassemia minor, markedly increased in NTDT, and generally moderate in TDT. The higher burden observed in NTDT has been attributed to persistent hemolysis and ineffective erythropoiesis, whereas regular transfusions in TDT partially dilute the population of damaged erythrocytes (Kuypers et al., 2007), (Ibrahim et al., 2014). Markers of platelet activation follow a similar phenotype-dependent gradient. They are usually low in thalassemia minor, significantly increased in NTDT, particularly after splenectomy, and moderate to high in TDT, especially in splenectomized individuals (Cappellini et al., 2012), (Eldor et al., 2002). Splenectomy consistently

emerges as an important modifier, amplifying platelet count, platelet activation, and circulating procoagulant elements. Circulating MPs and EVs, particularly PS-positive microparticles derived from RBCs, platelets, and endothelial cells are increased in both NTDT and TDT compared with minor forms. Levels tend to be especially elevated in splenectomized patients, supporting their contribution to thrombin generation and endothelial dysfunction (Abdel et al., 2022), (Ammar et al., 2014), (Kheansaardet al., 2018). Global coagulation assays provide a more integrated evaluation of thrombotic potential. Thrombin generation testing often demonstrates increased endogenous thrombin potential in NTDT and in high-risk TDT subsets, while whole-blood viscoelastic assays may reveal enhanced clot strength in splenectomized patients (Tripodi et al., 2009). In contrast, signal intensity is usually low or unremarkable in thalassemia minor. Natural anticoagulant (protein C, protein S, and antithrombin) are generally preserved in minor forms but may be reduced in NTDT and TDT. These reductions are often context-dependent and influenced by liver dysfunction, chronic hemolysis, or splenectomy (Ahmadi et al., 2024), (Ali et al., 2024)

Interpretation of thrombotic risk in thalassemia must be phenotype-specific, as hypercoagulability is not a single measurable abnormality but rather the result of interacting cellular, vascular, and treatment-related factors. In beta-thalassemia minor, a consistent laboratory pattern suggestive of hypercoagulability is generally lacking, and clinically relevant thrombotic events are uncommon. Laboratory evaluation in this setting is therefore primarily diagnostic rather than prognostic. In contrast, NTDT is associated with a clearly increased prothrombotic tendency. Clinical studies and large reviews consistently report a higher incidence of thromboembolic events in NTDT, particularly in splenectomized patients. As a result, NTDT represents a clinical setting in which closer surveillance, individualized risk assessment, and consideration of thromboprophylaxis in selected high-risk situations are warranted (Taher et al., 2008), (Eldor et al., 2002), (Cappellini et al., 2012), (Tanno et al., 2007).

In TDT, regular transfusions suppress ineffective erythropoiesis and reduce the proportion of abnormal endogenous red blood cells, potentially mitigating some red cell-driven procoagulant mechanisms. However, this benefit is counterbalanced by a distinct set of modifiers, including transfusional iron overload, chronic low-grade inflammation, and an increased risk of catheter-related thrombosis. Current management increasingly relies on MRI-based quantification of organ iron burden. In particular, cardiac T2* imaging has emerged as a robust predictor of cardiac complications, outperforming serum ferritin and liver iron concentration in stratifying myocardial risk (Kirk et al., 2009), (Levi et al., 2018), (Cappellini et al., 2020). In addition, dynamic iron parameters such as labile plasma iron (LPI) provide insight into short-term chelation effectiveness and exposure to redox-active iron, with potential implications for endothelial dysfunction and hypercoagulability (Pootrakul et al., 2004).

4. MANAGEMENT OF THROMBOSIS IN BETA-THALASSEMIA

Thrombotic complications in beta-thalassemia include venous thromboembolism, such as deep vein thrombosis and pulmonary embolism, as well as cerebrovascular events and pulmonary vascular disease. The clinical presentation and overall thrombotic risk are influenced by several modifiers, including splenectomy, thrombocytosis, severity of hemolysis, transfusion exposure, and the presence of additional acquired risk factors (Eldor et al., 2002), (Cappellini et al., 2012), (Kheansaard et al., 2018). Splenectomy represents one of the most important risk modifiers. Its prothrombotic effect is thought to be mediated by persistent platelet activation, increased levels of circulating MPs and EVs, and alterations in whole-blood rheology. Data from whole-blood viscoelastic testing support the concept that cellular components play a central role in driving hypercoagulability after splenectomy, a phenomenon that is not adequately captured by conventional plasma-based assays (Vehapoglu et al., 2014).

Management of thrombosis in beta-thalassemia should be individualized and based on overall risk assessment. Routine long-term anticoagulation is not universally recommended. However, risk-adapted thromboprophylaxis may be appropriate in selected high-risk situations, including the perioperative period, pregnancy, prolonged immobilization, prior thrombotic events, and the presence of central venous catheters. Decisions regarding anticoagulation should carefully balance thrombotic risk against bleeding risk and consider disease phenotype and comorbidities. In TDT, contemporary management increasingly emphasizes systematic monitoring of iron-related toxicity. Current guideline-based approaches, including those outlined by the Thalassaemia International Federation, recommend defined transfusion targets, individualized chelation strategies, and regular organ surveillance, with particular emphasis on MRI-based assessment of iron burden (Farmakis et al., 2022). Optimized iron control may have indirect but clinically relevant effects on vascular function and thrombotic risk.

Disease-modifying therapies in beta-thalassemia have the potential to influence hypercoagulability indirectly by reducing ineffective erythropoiesis, hemolysis, and transfusion requirements. In a phase

3 clinical trial, luspatercept significantly reduced transfusion burden in patients with TDT (Cappellini et al., 2020). By improving erythroid maturation and reducing red blood cell turnover, such therapies may alter key upstream drivers of the prothrombotic state over time. Advances in the understanding of iron regulation have also highlighted the importance of the erythropoiesis–hepcidin axis. Experimental models have demonstrated that erythroferrone contributes to hepcidin suppression and iron overload in beta-thalassemia, while elevated levels of growth differentiation factor 15 (GDF15) have been shown to further inhibit hepcidin expression (Kautz et al., 2015), (Tanno et al., 2007). These pathways are being recognized as potential therapeutic targets, with possible downstream implications for oxidative stress, endothelial dysfunction and hypercoagulability.

Despite these advances, data specifically addressing thrombosis-related outcomes and longitudinal changes in coagulation biomarkers remain scarce. Further prospective studies are warranted to determine how emerging therapies affect thrombotic risk and whether laboratory markers of hypercoagulability parallel clinical improvement.

5. CONCLUSIONS

Beta-thalassemia is a systemic disorder in which disturbances of coagulation and vascular biology contribute substantially to long-term morbidity. Hypercoagulability results from the interplay of procoagulant red blood cell surfaces, chronic platelet activation, endothelial dysfunction, circulating MPs and EVs, and context-dependent alterations in natural anticoagulant pathways. Differences in clinical presentation and laboratory profiles across beta-thalassemia minor, NTDT, and TDT support a phenotype-adapted approach to thrombosis risk assessment. In modern care, particularly for transfusion-dependent patients, MRI-based quantification of organ iron burden and monitoring of dynamic iron species such as labile plasma iron are increasingly integrated into routine practice and may have important implications for vascular risk and hypercoagulability. A deeper understanding of disease-specific mechanisms, integrated with individualized clinical and laboratory assessment, is essential for optimizing thrombosis prevention and management in β-thalassemia.

REFERENCES

Abdel Aziz, Hanan M.,El-Beih, Esam A.S., Sayed, Doua M., Afifi, Ola A., Thabet, Ahmad F., Elgammal, Sahar, Mansor, Shima G., Moeen, & Sawsan M.(2022). Increased levels of circulating platelet microparticles as a risk of hypercoagulable state in β-thalassemia intermedia patients. Egyptian Journal of Haematology, 47(3), 187–193

Ahmadi, A., Hosseini, S., Dorgalaleh, A., Hassani, S., Tabibian, S., Tavasoli, B., Shabannezhad, A., Taheri, M., & Shams, M. (2024). Natural anticoagulant protein levels in patients with beta-thalassemia major: A case-control study. Journal of Hematology, 13(1–2), 23–28.

Ali, A., & Kashmoola, M. (2024). EVALUATION OF PROTEIN C AND S IN B-THALASSEMIA MAJOR. Georgian medical news, (352-353), 155–160.

Al-Sanabra, O. M., Abbas, M. A., Hazà, W. J., Hazàa, A. A., & Al Tibi, A. K. (2025). Coagulation and Fibrinolysis Dysregulation in β-Thalassemia Major: Potential Impact of Splenectomy and Medications on Thrombotic Risk. Clinical and applied thrombosis/hemostasis, 31, 10760296251359291.

Ammar, S., Elsayh, K. I., Zahran, A. M., & Embaby, M. M. (2014). Splenectomy for patients with β-thalassemia major: Long-term outcomes. Egyptian Journal of Surgery, 33, 232–236.

Cappellini, M. D., & Motta, I. (2015). Anemia in Clinical Practice-Definition and Classification: Does Hemoglobin Change With Aging? Seminars in hematology, 52(4), 261–269.

Cappellini, M. D., Musallam, K. M., Poggiali, E., & Taher, A. T. (2012). Hypercoagulability in non-transfusion-dependent thalassemia. Blood reviews, 26 Suppl 1, S20–S23.

Cappellini, M. D., Poggiali, E., Taher, A. T., & Musallam, K. M. (2012). Hypercoagulability in β-thalassemia: a status quo. Expert review of hematology, 5(5), 505–512.

Cappellini, M. D., Viprakasit, V., Taher, A. T., Georgiev, P., Kuo, K. H. M., Coates, T., Voskaridou, E., Liew, H. K., Pazgal-Kobrowski, I., Forni, G. L., Perrotta, S., Khelif, A., Lal, A., Kattamis, A., Vlachaki, E., Origa, R., Aydinok, Y., Bejaoui, M., Ho, P. J., Chew, L. P., … BELIEVE Investigators (2020). A Phase 3 Trial of Luspatercept in Patients with Transfusion-Dependent β-Thalassemia. The New England journal of medicine, 382(13), 1219–1231.

Eldor, A., & Rachmilewitz, E. A. (2002). The hypercoagulable state in thalassemia. Blood, 99(1), 36–43.

Farmakis, D., Porter, J., Taher, A., Domenica Cappellini, M., Angastiniotis, M., & Eleftheriou, A. (2022). 2021 Thalassaemia International Federation Guidelines for the Management of Transfusion-dependent Thalassemia. HemaSphere, 6(8), e732.

Furie, B., & Furie, B. C. (2008). Mechanisms of thrombus formation. The New England journal of medicine, 359(9), 938–949.

Ibrahim, H. A., Fouda, M. I., Yahya, R. S., Abousamra, N. K., & Abd Elazim, R. A. (2014). Erythrocyte phosphatidylserine exposure in β-thalassemia. Laboratory hematology, 20(2), 9–14.

Kautz, L., Jung, G., Du, X., Gabayan, V., Chapman, J., Nasoff, M., Nemeth, E., & Ganz, T. (2015). Erythroferrone contributes to hepcidin suppression and iron overload in a mouse model of β-thalassemia. Blood, 126(17), 2031–2037.

Kheansaard, W., Phongpao, K., Paiboonsukwong, K., Pattanapanyasat, K., Chaichompoo, P., & Svasti, S. (2018). Microparticles from β-thalassaemia/HbE patients induce endothelial cell dysfunction. Scientific reports, 8(1), 13033.

Kirk, P., Roughton, M., Porter, J. B., Walker, J. M., Tanner, M. A., Patel, J., Wu, D., Taylor, J., Westwood, M. A., Anderson, L. J., & Pennell, D. J. (2009). Cardiac T2* magnetic resonance for prediction of cardiac complications in thalassemia major. Circulation, 120(20), 1961–1968.

Klaihmon, P., Khuhapinant, A., Kheansaard, W., & Pattanapanyasat, K. (2024). Internalization of cell-derived microparticles triggers endothelial pro-inflammatory responses. Asian Pacific journal of allergy and immunology, 42(4), 420–428.

Kuypers F. A. (2007). Membrane lipid alterations in hemoglobinopathies. Hematology. American Society of Hematology. Education Program, 68–73.

Lecut, C., Peters, P., Massion, P. B., & Gothot, A. (2015). Quelle place pour le test de génération de thrombine au sein du laboratoire de biologie clinique? [Is there a place for thrombin generation assay in routine clinical laboratory?]. Annales de biologie clinique, 73(2), 137–149.

Levi, M., & Scully, M. (2018). How I treat disseminated intravascular coagulation. Blood, 131(8), 845–854.

Musallam, K. M., & Taher, A. T. (2011). Thrombosis in thalassemia: why are we so concerned? Hemoglobin, 35(5-6), 503–510.

Pennell D. J. (2005). T2* magnetic resonance and myocardial iron in thalassemia. Annals of the New York Academy of Sciences, 1054, 373–378.

Pootrakul, P., Breuer, W., Sametband, M., Sirankapracha, P., Hershko, C., & Cabantchik, Z. I. (2004). Labile plasma iron (LPI) as an indicator of chelatable plasma redox activity in iron-overloaded beta-thalassemia/HbE patients treated with an oral chelator. Blood, 104(5), 1504–1510.

Singer, S. T., Kuypers, F. A., Styles, L., Vichinsky, E. P., Foote, D., & Rosenfeld, H. (2006). Pulmonary hypertension in thalassemia: association with platelet activation and hypercoagulable state. American journal of hematology, 81(9), 670–675.

Taher, A. T., Otrock, Z. K., Uthman, I., & Cappellini, M. D. (2008). Thalassemia and hypercoagulability. Blood reviews, 22(5), 283–292.

Tanno, T., Bhanu, N. V., Oneal, P. A., Goh, S. H., Staker, P., Lee, Y. T., Moroney, J. W., Reed, C. H., Luban, N. L., Wang, R. H., Eling, T. E., Childs, R., Ganz, T., Leitman, S. F., Fucharoen, S., & Miller, J. L. (2007). High levels of GDF15 in thalassemia suppress expression of the iron regulatory protein hepcidin. Nature medicine, 13(9), 1096–1101

Tripodi, A., Cappellini, M. D., Chantarangkul, V., Padovan, L., Fasulo, M. R., Marcon, A., & Mannucci, P. M. (2009). Hypercoagulability in splenectomized thalassemic patients detected by whole-blood thromboelastometry, but not by thrombin generation in platelet-poor plasma. Haematologica, 94(11), 1520–1527.

Vehapoglu, A., Ozgurhan, G., Demir, A. D., Uzuner, S., Nursoy, M. A., Turkmen, S., & Kacan, A. (2014). Hematological indices for differential diagnosis of beta thalassemia trait and iron deficiency anemia. Anemia, 576738.