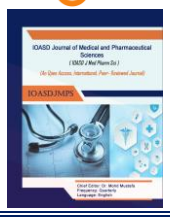
OPEN ACCESS

IOASD Journal of Medical and Pharmaceutical Sciences

IOASD J Med Pharm Sci, Vol-3, Iss-3, Jul-Sept., 2026
Frequency: Quarterly
ISSN: 3049-0294 (Online)
ISSN: 3049-3773 (Print)
Homepage: https://ioasdpublisher.com/ioasdjmps



Coagulation Disorders in Early Childhood: Pathophysiology, Diagnosis and Clinical Implications: A Narrative Review

Emmanuel Ifeanyi Obeagu[1,2*]

[1]Division of Haematology, Department of Biomedical and Laboratory Science, Africa University, Zimbabwe
[2]Department of Molecular Medicine and Haematology, School of Pathology, Faculty of Health Sciences, University of the Witwatersrand, Johannesburg, South Africa

Corresponding Author: Emmanuel Ifeanyi Obeagu
Division of Haematology, Department of Biomedical and Laboratory Science, Africa University, Zimbabwe

DOI: 10.67224/ioasdjmps.2026.v03i03.001

ABSTRACT

Coagulation disorders in early childhood represent a critical group of hemostatic abnormalities that can lead to significant bleeding or thrombotic events. These disorders arise from both inherited defects, such as hemophilia and von Willebrand disease, and acquired conditions like vitamin K deficiency and disseminated intravascular coagulation. The unique developmental physiology of the pediatric coagulation system adds complexity to their pathophysiology and clinical presentation, requiring age-specific considerations for accurate diagnosis and management. Diagnosis of coagulation disorders in young children relies on a combination of thorough clinical assessment and targeted laboratory investigations. Screening tests such as prothrombin time and activated partial thromboplastin time must be interpreted within pediatric reference ranges, and confirmatory factor assays and genetic tests are often necessary. Early identification of these disorders is essential to initiate appropriate therapies, prevent complications, and improve quality of life. The clinical implications of coagulation disorders in early childhood are profound, ranging from life-threatening hemorrhages to venous thromboembolism. Management strategies must be tailored to the child's specific disorder, balancing efficacy and safety in a population with unique physiological needs. This review emphasizes the importance of multidisciplinary care, timely diagnosis, and advances in treatment approaches to optimize outcomes in affected children.

Keywords: Coagulation disorders**,** Early childhood**,** Hemostasis**,** Bleeding disorders**,** Pediatric thrombosis.

Review Article

Article History
Received: 10-05-2026
Accepted: 16-06-2026
Published: 01-07-2026

INTRODUCTION

Coagulation disorders in early childhood are a significant cause of morbidity and mortality worldwide. They encompass a wide spectrum of conditions that affect the delicate balance of hemostasis—the physiological process that prevents excessive bleeding while maintaining blood fluidity. Early childhood, spanning from birth to approximately five years of age, represents a critical period during which the hemostatic system is still maturing. This immaturity, combined with potential genetic or acquired abnormalities, predisposes children to bleeding or thrombotic events that can be challenging to diagnose and manage [1-2]. The hemostatic system is an intricate network involving vascular endothelium, platelets, coagulation factors, and fibrinolytic pathways. In neonates and infants, many coagulation factors and inhibitors are present at lower levels compared to adults, a phenomenon known as developmental hemostasis. This physiological difference results in distinct laboratory values and clinical presentations that require age-specific interpretation. Understanding these developmental nuances is fundamental for clinicians to differentiate between normal hemostatic variations and true coagulation disorders in early childhood [3].

Inherited coagulation disorders constitute a major subset of pediatric hemostatic abnormalities. Hemophilia A and B, resulting from deficiencies in factors VIII and IX respectively, are the most commonly diagnosed inherited bleeding disorders in children. Additionally, von Willebrand disease (vWD) is prevalent and presents with mucocutaneous bleeding and prolonged bleeding times. Less common, but clinically important, are rare factor deficiencies and platelet function disorders. Genetic mutations underlie these

conditions, often manifesting during early childhood as spontaneous or trauma-related bleeding, thus necessitating early recognition for effective management [4]. Acquired coagulation disorders are also critical in early childhood and may result from diverse etiologies such as vitamin K deficiency, liver dysfunction, disseminated intravascular coagulation (DIC), or autoimmune disorders. Vitamin K deficiency bleeding (VKDB) is of particular concern in neonates due to their limited vitamin K stores and the potential for life-threatening hemorrhage. Moreover, infections, sepsis, and systemic illnesses can precipitate acquired coagulation abnormalities, complicating the clinical picture in hospitalized children [5].

In addition to bleeding disorders, thrombotic conditions, though less frequent in early childhood, have gained attention due to rising incidence linked to improved survival of critically ill infants and children. Pediatric thrombosis often involves complex interactions between genetic thrombophilia, central venous catheters, infections, and inflammatory states. The pathophysiology involves hypercoagulability, endothelial injury, and venous stasis, which together constitute Virchow's triad. Recognizing thrombotic risk factors early is essential to prevent serious complications such as pulmonary embolism or post-thrombotic syndrome. [6] Diagnosing coagulation disorders in early childhood is fraught with challenges. The nonspecific nature of symptoms like bruising, mucosal bleeding, or swelling often leads to delayed or missed diagnoses. Laboratory evaluation requires careful interpretation, as standard coagulation tests have different normal ranges in young children compared to adults. Advanced diagnostic tools, including specific coagulation factor assays, von Willebrand factor testing, and genetic screening, are indispensable in confirming diagnoses and guiding management decisions [7].

AIM

This narrative review aims to provide a comprehensive overview of coagulation disorders in early childhood, emphasizing their underlying pathophysiology, challenges in diagnosis, and clinical implications.

METHODS

This narrative review was conducted to synthesize current evidence on the pathophysiology, diagnosis, and clinical implications of coagulation disorders in early childhood. A structured yet flexible approach was applied to ensure comprehensive coverage of both classical and emerging concepts.

Literature Search Strategy

A comprehensive literature search was performed across major biomedical databases including PubMed, Scopus, Web of Science, and Google Scholar for publications from January 2000 to October 2025. Keywords and Medical Subject Headings (MeSH) terms used in various combinations included: *"coagulation disorders," "bleeding disorders," "pediatric hematology," "developmental hemostasis," "vitamin K deficiency bleeding," "hemophilia," "von Willebrand disease," "disseminated intravascular coagulation,"* and *"childhood thrombosis."* Boolean operators (AND/OR) were employed to refine searches. Reference lists of relevant articles were manually reviewed to identify additional studies.

Inclusion and Exclusion Criteria

Eligible publications included original research articles, clinical trials, case series, systematic reviews, and authoritative guidelines focusing on coagulation disorders in infants and children up to 12 years of age. Articles were included if they provided mechanistic insights, diagnostic advancements, or clinical management perspectives. Excluded were studies not published in English, those focusing exclusively on adult populations, or papers lacking sufficient hematological context or methodological rigor.

Data Extraction and Synthesis

Data were extracted and organized according to three thematic domains:

1. Pathophysiology and developmental hemostasis — mechanisms underlying coagulation abnormalities in early life.
2. Diagnostic approaches — conventional laboratory testing, advanced assays, and molecular tools.
3. Clinical implications — management strategies, outcomes, and emerging therapeutic innovations.

Findings were synthesized narratively, emphasizing consistency, clinical relevance, and gaps in current knowledge. Where available, comparative evidence between inherited and acquired disorders was highlighted to illustrate key diagnostic and therapeutic distinctions.

.

Quality Assessment

Although not a systematic review, attention was paid to methodological soundness and clinical significance of included studies. Priority was given to peer-reviewed publications, guidelines from recognized bodies such as the World Federation of Hemophilia (WFH), American Society of Hematology (ASH), and International Society on Thrombosis and Haemostasis (ISTH), and landmark studies contributing to pediatric hematology practice.

Ethical Considerations

This review involved no direct patient data collection; therefore, ethical approval was not required. All information was obtained from publicly available, peer-reviewed sources, ensuring adherence to academic integrity and proper citation standards.

Pathophysiology of Coagulation Disorders in Early Childhood

The pathophysiology of coagulation disorders in early childhood is rooted in the complex and dynamic process of hemostasis, which involves a tightly regulated balance between procoagulant and anticoagulant forces. Hemostasis ensures that blood remains fluid within vessels while promptly forming clots to prevent excessive bleeding following vascular injury. Disruption of this balance can manifest as either bleeding tendencies or thrombotic events, both of which can be life-threatening in young children (Table 1) [8].

Table 1: Pathophysiology of Coagulation Disorders in Early Childhood

Pathophysiological Mechanism	Underlying Basis	Clinical Consequences
Developmental Hemostasis	Immature hepatic synthesis of coagulation proteins; reduced vitamin K–dependent factors (II, VII, IX, X); decreased natural anticoagulants (protein C, S, and antithrombin).	Physiological prolongation of PT/aPTT; increased susceptibility to bleeding in preterm infants.
Platelet Hyporesponsiveness	Reduced thromboxane A_2 production and α-granule release; decreased adhesion to subendothelium.	Mild mucocutaneous bleeding; prolonged bleeding after trauma.
Fibrinolytic Imbalance	Reduced plasminogen concentration with relative increase in tissue plasminogen activator (tPA).	Increased fibrinolysis causing delayed clot stabilization.
Congenital Factor Deficiency	Genetic mutation leading to decreased synthesis or function of specific coagulation factor (e.g., VIII, IX, XI).	Recurrent soft tissue or joint bleeding, prolonged bleeding post-injury or surgery.
Acquired Coagulopathy	Secondary to infection, liver dysfunction, vitamin K deficiency, or systemic inflammation (DIC).	Variable bleeding tendency, from petechiae to life-threatening hemorrhage.

Developmental Hemostasis: The Foundation of Pediatric Coagulation

One of the key distinguishing features of coagulation in early childhood is the phenomenon of developmental hemostasis. Unlike adults, neonates and infants have physiologically lower plasma concentrations of most coagulation factors, including vitamin K–dependent factors (II, VII, IX, and X), contact factors (XI and XII), and natural anticoagulants such as protein C, protein S, and antithrombin. This immature hemostatic system undergoes progressive maturation during the first year of life, leading to gradually increasing factor levels approaching adult values. Importantly, the fibrinolytic system and platelet function also exhibit age-dependent variations [9]. Despite these differences, the neonatal hemostatic system is generally balanced, providing adequate protection against bleeding and thrombosis under normal conditions. However, this fragile equilibrium can be easily disturbed by genetic mutations, environmental insults, or underlying diseases, leading to coagulation disorders [10].

Inherited Coagulation Disorders: Genetic Defects Impacting Hemostasis

Inherited coagulation disorders result from mutations in genes encoding coagulation factors or related proteins, causing quantitative or qualitative deficiencies. The most commonly encountered inherited bleeding disorders in early childhood include hemophilia A and B, which are X-linked recessive conditions caused by deficiencies in factor VIII and IX, respectively. These deficiencies impair the intrinsic coagulation pathway, leading to inadequate thrombin generation and defective fibrin clot formation [11]. Von Willebrand disease (vWD) is another prevalent inherited bleeding disorder characterized by deficiency or dysfunction of von Willebrand factor (vWF), a crucial protein mediating platelet adhesion and stabilization of factor VIII. Mutations in the vWF gene affect either the quantity or quality of vWF, impairing both primary and secondary hemostasis [11]. Less common but clinically relevant are rare factor deficiencies (such as factors II, V, VII, X, XI, and XIII), which disrupt various points in the coagulation cascade. Additionally, inherited platelet function disorders can compromise clot formation despite normal coagulation factor levels (Table 2) [12].

Table 2: Inherited Coagulation Disorders — Genetic Defects Impacting Hemostasis

Disorder	Genetic Defect / Affected Factor	Inheritance Pattern	Key Laboratory Findings	Clinical Manifestations
Hemophilia A	Factor VIII deficiency (F8 gene mutation)	X-linked recessive	Prolonged aPTT; normal PT; low FVIII activity	Hemarthrosis, muscle hematomas, prolonged

Disorder	Genetic Defect / Affected Factor	Inheritance Pattern	Key Laboratory Findings	Clinical Manifestations
				bleeding after minor trauma
Hemophilia B	Factor IX deficiency (F9 gene mutation)	X-linked recessive	Prolonged aPTT; normal PT; low FIX activity	Similar to Hemophilia A; deep tissue bleeding
Von Willebrand Disease (vWD)	Deficiency or dysfunction of von Willebrand factor (VWF gene)	Autosomal dominant/recessive (type-dependent)	Prolonged bleeding time; normal or slightly prolonged aPTT; low vWF antigen/activity	Epistaxis, easy bruising, mucosal bleeding, menorrhagia
Factor XI Deficiency	Deficiency of FXI (F11 gene)	Autosomal recessive	Prolonged aPTT; normal PT; low FXI activity	Variable bleeding, often after surgery or trauma
Factor XIII Deficiency	FXIII (F13A1 or F13B gene mutation)	Autosomal recessive	Normal PT/aPTT; abnormal clot solubility test	Umbilical stump bleeding, poor wound healing, intracranial hemorrhage
Afibrinogenemia/Hypofibrinogenemia	FGA, FGB, or FGG gene mutation affecting fibrinogen synthesis	Autosomal recessive	Prolonged PT, aPTT, and TT; low fibrinogen	Umbilical bleeding, mucosal hemorrhage, spontaneous abortion (in females)

Acquired Coagulation Disorders: Secondary Disruptions to Hemostasis

Acquired coagulation disorders in early childhood occur due to external factors or systemic conditions that alter hemostatic balance. Vitamin K deficiency bleeding (VKDB) is a notable example, especially in neonates with limited vitamin K stores and inadequate supplementation. Vitamin K is essential for the post-translational gamma-carboxylation of factors II, VII, IX, and X; its deficiency leads to production of inactive clotting factors and bleeding risk [12]. Other causes of acquired coagulation disorders include liver disease, which impairs synthesis of multiple coagulation factors, and disseminated intravascular coagulation (DIC), a severe systemic process characterized by widespread activation of coagulation, consumption of clotting factors and platelets, and secondary fibrinolysis. Autoimmune conditions such as antiphospholipid syndrome can also provoke coagulation abnormalities via autoantibody-mediated interference with clotting regulation (Table 3) [11].

Table 3: Acquired Coagulation Disorders — Secondary Disruptions to Hemostasis

Disorder	Etiology/Pathophysiology	Key Laboratory Findings	Clinical Features	Management Approach
Vitamin K Deficiency Bleeding (VKDB)	Inadequate vitamin K for synthesis of factors II, VII, IX, and X; often due to lack of prophylaxis or antibiotic use	Prolonged PT and aPTT; normal platelets	Umbilical, gastrointestinal, or intracranial bleeding in neonates	Intramuscular or intravenous vitamin K; prevention by prophylaxis at birth
Liver Disease–Related Coagulopathy	Impaired synthesis of most clotting factors due to hepatic dysfunction	Prolonged PT, aPTT; low fibrinogen; thrombocytopenia	Easy bruising, epistaxis, mucosal bleeding	Treat underlying liver disease; plasma or factor replacement as needed

Disorder	Etiology/Pathophysiology	Key Laboratory Findings	Clinical Features	Management Approach
Disseminated Intravascular Coagulation (DIC)	Systemic activation of coagulation leading to consumption of platelets and clotting factors	Prolonged PT/aPTT; elevated D-dimer; low fibrinogen	Bleeding with microvascular thrombosis; organ dysfunction	Treat underlying cause; supportive care with plasma and platelets
Drug-Induced Coagulopathy	Anticoagulant therapy (heparin, warfarin) or chemotherapeutic agents interfering with coagulation	Variable depending on drug; prolonged PT/aPTT	Easy bruising, bleeding tendency	Dose adjustment, vitamin K, or protamine sulfate as reversal agent
Infection-Related Coagulopathy	Sepsis and severe inflammation triggering cytokine-mediated coagulation cascade	Elevated D-dimer; variable PT/aPTT	Bleeding, petechiae, purpura fulminans	Antibiotics, plasma, and supportive therapy
Thrombosis of Childhood	Imbalance between procoagulant and anticoagulant systems, often with catheter use or congenital thrombophilia	Elevated D-dimer; imaging confirms thrombosis	Limb swelling, pain, venous obstruction	Anticoagulation (LMWH), remove provoking factors

Pathophysiology of Pediatric Thrombosis

While bleeding disorders are more common, thrombotic disorders are increasingly recognized in pediatric populations. Pediatric thrombosis results from an imbalance favoring coagulation, often precipitated by the classic Virchow's triad: endothelial injury, venous stasis, and hypercoagulability. Central venous catheters, infections, surgery, and inflammatory states frequently contribute to endothelial damage and local stasis in young children [13]. Inherited thrombophilias, including Factor V Leiden mutation, prothrombin G20210A mutation, and deficiencies of natural anticoagulants (protein C, protein S, and antithrombin), heighten the risk of pathologic clot formation. In neonates and infants, the immature anticoagulant systems combined with these prothrombotic conditions can lead to deep vein thrombosis, pulmonary embolism, or cerebral sinovenous thrombosis (Figure 1) [6].

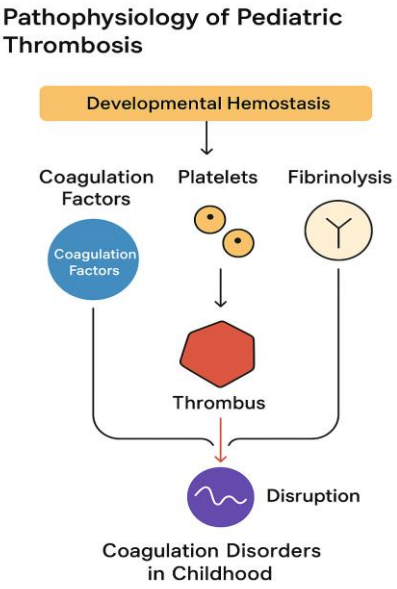


Figure 1: Pathophysiology of Pediatric Thrombosis

Diagnosis of Coagulation Disorders in Early Childhood

Diagnosing coagulation disorders in early childhood presents unique challenges due to the developmental variations in the hemostatic system, the nonspecific nature of clinical presentations, and limitations in laboratory testing. A high index of suspicion combined with careful clinical evaluation and age-appropriate laboratory investigations is essential for accurate diagnosis and effective management [14].

Clinical Assessment

The initial evaluation begins with a thorough clinical history and physical examination. Key features suggestive of coagulation disorders include unexplained or excessive bleeding following minor trauma, surgery, or dental procedures, spontaneous bruising, mucocutaneous bleeding (such as epistaxis, gum bleeding), hemarthrosis, or prolonged bleeding from vaccination or heel prick sites in neonates. A detailed family history of bleeding or thrombosis is crucial, as many coagulation disorders are inherited [15]. In contrast, thrombotic events in young children may present with limb swelling, pain, discoloration, or organ-specific symptoms such as respiratory distress (pulmonary embolism) or neurologic deficits (cerebral venous thrombosis). Recognizing these clinical signs promptly is vital, given the potential severity of thrombosis.

Laboratory Screening Tests

Laboratory evaluation typically starts with screening tests to assess the overall coagulation status. These include:

- **Prothrombin Time (PT):** Evaluates the extrinsic and common coagulation pathways, primarily factors I (fibrinogen), II, V, VII, and X.
- **Activated Partial Thromboplastin Time (aPTT):** Assesses the intrinsic and common pathways, including factors VIII, IX, XI, and XII.
- **Platelet Count:** Detects thrombocytopenia or platelet abnormalities.

- **Bleeding Time or Platelet Function Analysis:** Evaluates primary hemostasis, though bleeding time is less commonly used due to variability.
- **Fibrinogen Levels and D-dimer:** Useful in evaluating consumptive coagulopathies like disseminated intravascular coagulation.

Importantly, reference ranges for these tests vary with age, especially in neonates and infants, due to developmental hemostasis. Interpretation must consider these age-specific norms to avoid misdiagnosis [6].

Specific Coagulation Factor Assays and Functional Tests

If screening tests suggest a coagulation disorder, targeted assays measuring individual coagulation factors are performed to identify specific deficiencies. For example, prolonged aPTT with normal PT often prompts factor VIII and IX assays to diagnose hemophilia A or B. Similarly, factor VII deficiency is suspected with isolated prolonged PT. For von Willebrand disease (vWD), specialized tests include measurement of von Willebrand factor antigen (vWF:Ag), ristocetin cofactor activity (vWF:RCo), and factor VIII activity. Multimer analysis of vWF may be required to classify vWD subtypes. Platelet function disorders require platelet aggregation studies, flow cytometry for platelet glycoproteins, or genetic testing in selected cases [15].

Thrombophilia Screening

In cases of suspected thrombotic disorders, evaluation for inherited and acquired thrombophilias is necessary. Tests may include:

- Genetic analysis for Factor V Leiden and prothrombin gene mutations.
- Measurement of natural anticoagulant levels: protein C, protein S, and antithrombin.
- Screening for antiphospholipid antibodies (lupus anticoagulant, anticardiolipin antibodies).

Given the dynamic nature of coagulation proteins in early childhood and during acute illness, timing of testing and repeat evaluations are important considerations [16].

Additional Diagnostic Considerations

Imaging studies, such as Doppler ultrasonography, magnetic resonance imaging (MRI), or computed tomography (CT), play an adjunctive role in diagnosing thrombosis and assessing organ involvement. Genetic counseling and family studies are recommended for inherited conditions to guide prognosis and family planning [17-18].

Clinical Implications and Management

Coagulation disorders in early childhood carry significant clinical implications that affect morbidity, mortality, and quality of life. The manifestations range from mild bleeding episodes to life-threatening hemorrhages or thrombotic events. Early recognition and tailored management strategies are essential to minimize complications, optimize growth and development, and improve long-term outcomes for affected children [19].

Clinical Implications

Bleeding disorders such as hemophilia and von Willebrand disease often present with spontaneous or trauma-related bleeding, including hemarthrosis, muscle hematomas, mucosal bleeding, and prolonged bleeding after medical procedures. Recurrent bleeding into joints and muscles can lead to chronic pain, deformities, and disability if left untreated. In neonates, severe vitamin K deficiency bleeding may cause intracranial hemorrhage, resulting in neurological deficits or death [19]. Thrombotic disorders, although less common, are increasingly recognized in pediatric populations, especially in critically ill infants and children with central venous catheters or underlying thrombophilic conditions. Venous thromboembolism can lead to acute complications such as pulmonary embolism and long-term sequelae including post-thrombotic syndrome. Both bleeding and thrombotic disorders can impose psychological stress on children and families, necessitating psychosocial support alongside medical care [6].

Management Strategies

Management of coagulation disorders in early childhood must be individualized, considering the specific disorder, severity, age of the child, and potential complications. A multidisciplinary approach involving pediatric hematologists, nurses, physiotherapists, and social workers is often required [6].

Treatment of Bleeding Disorders

For inherited bleeding disorders, replacement therapy with clotting factor concentrates remains the cornerstone of management. In hemophilia A and B, prophylactic or on-demand intravenous administration of factor VIII or IX concentrates reduces bleeding frequency and prevents joint damage. Recombinant and plasma-derived products are available, and newer extended half-life factors and gene therapy approaches are under development [20-21]. Von Willebrand disease treatment depends on subtype and severity; desmopressin (DDAVP) can be used to release endogenous vWF in mild to moderate cases, while replacement with vWF-containing concentrates is necessary in severe disease or when DDAVP is ineffective [22]. In acquired disorders such as vitamin K deficiency, prompt administration of vitamin K1 (phytonadione) is essential to restore functional coagulation factor synthesis. Management of DIC involves treating the underlying cause alongside supportive measures such as blood product transfusions [23].

Management of Pediatric Thrombosis

Treatment of thrombosis in children includes anticoagulation therapy with agents such as low molecular weight heparin (LMWH) or unfractionated heparin, followed by oral anticoagulants when appropriate. Duration and intensity depend on the thrombus location, underlying risk factors, and bleeding risk. Novel oral anticoagulants (NOACs) are being studied in pediatric populations but require careful monitoring [24]. Preventive strategies include minimizing invasive catheter use, early mobilization, and addressing modifiable risk factors such as infection and inflammation. In inherited thrombophilia, long-term anticoagulation may be indicated in recurrent or severe thrombosis [25].

Supportive Care and Monitoring

Supportive care includes physical therapy to preserve joint function in bleeding disorders, psychosocial support for patients and families, and education on bleeding prevention and injury avoidance. Regular monitoring of factor levels, inhibitor development, and treatment side effects is critical for optimizing therapy.

CONCLUSION

Coagulation disorders in early childhood represent a complex group of conditions arising from both inherited and acquired abnormalities in the delicate balance of hemostasis. Understanding the unique aspects of developmental hemostasis is essential for accurate diagnosis and effective management. Early recognition through comprehensive clinical evaluation and age-appropriate laboratory investigations enables timely intervention, which is crucial to preventing severe bleeding complications or thrombotic events that can adversely affect growth, development, and long-term quality of life. Advances in diagnostic techniques and therapeutic options, including factor replacement therapies, anticoagulants, and emerging gene therapies, have significantly improved outcomes for affected children. Nonetheless, challenges remain in optimizing individualized care, especially in resource-limited settings. Continued research and multidisciplinary collaboration are vital to expanding our understanding of the pathophysiology, refining diagnostic algorithms, and developing innovative treatment modalities tailored to pediatric needs.

Conflicts of Interest

The authors declare no conflict of interest

Sources of Funding

No fund was received to write this review paper

Ethical Approval

Not applicable

Consent

Not applicable

REFERENCES

1. Moiseiwitsch, N., & Brown, A. C. (2021). Neonatal coagulopathies: a review of established and emerging treatments. *Experimental Biology and Medicine*, *246*(12), 1447-1457. doi: 10.1177/15353702211006046.
2. Davenport, P., & Sola-Visner, M. (2021). Hemostatic challenges in neonates. *Frontiers in pediatrics*, *9*, 627715. doi: 10.3389/fped.2021.627715.
3. Abdulsalam, A. H., Al-Rahal, N. K., & Ghiath, Y. (2021). Inherited Bleeding Disorders in Pediatric Patients; experience of the national referral center in Iraq. *Indian Journal of Hematology and Blood Transfusion*, *37*(1), 96-100. doi: 10.1007/s12288-020-01306-8.
4. McMillan, C. W., Weiss, A. E., & Johnson, A. M. (1972). Acquired coagulation disorders in children. *Pediatric Clinics of North America*, *19*(4), 1029-1045. doi: 10.1016/s0031-3955(16)32780-8.
5. Obeagu, E. I. (2025). Pediatric thrombosis: Risk factors, diagnosis, and prevention strategies. *Medicine*, *104*(29), e43370. doi: 10.1097/MD.0000000000043370.
6. Sarnaik, A., Kamat, D., & Kannikeswaran, N. (2010). Diagnosis and management of bleeding disorder in a child. *Clinical pediatrics*, *49*(5), 422-431. doi: 10.1177/0009922809351090.
7. Gong, F., Zheng, X., Zhao, S., Liu, H., Chen, E., Xie, R., ... & Chen, Y. (2025). Disseminated intravascular coagulation: cause, molecular mechanism, diagnosis, and therapy. *MedComm*, *6*(2), e70058. doi: 10.1002/mco2.70058.
8. Gorio, C., Molinari, A. C., Martini, T., Ferretti, A., Albrici, G., Carracchia, G., ... & Santoro, R. C. (2025). Hemostasis Laboratory Diagnostics in Newborns. *Journal of Clinical Medicine*, *14*(14), 5068. doi: 10.3390/jcm14145068.
9. Khizroeva, J., Makatsariya, A., Vorobev, A., Bitsadze, V., Elalamy, I., Lazarchuk, A., ... & Blbulyan, D. (2023). The hemostatic system in newborns and the risk of neonatal thrombosis. *International Journal of Molecular Sciences*, *24*(18), 13864. doi: 10.3390/ijms241813864.
10. Hoang, T., & Dowdy, R. A. (2024). Review of inherited coagulation disorders. *Anesthesia Progress*, *71*(2), 87-95. doi: 10.2344/anpr-71-2_continuing_edu.
11. Tourbih, H., Harrach, A., Bencharef, H., Dehbi, H., Oukkache, B., & TOURBIH, H. (2025). Molecular Aspects of Rare Coagulation Factor Deficiencies. *Cureus*, *17*(7) e89102. doi: 10.7759/cureus.89102.
12. O'Brien, S. H., & Zia, A. (2022). Hemostatic and thrombotic disorders in the pediatric patient. *Blood, The Journal of the American Society of Hematology*, *140*(6), 533-541.doi: 10.1182/blood.2020006477.

13. Gorio, C., Molinari, A. C., Martini, T., Ferretti, A., Albrici, G., Carracchia, G., ... & Santoro, R. C. (2025). Hemostasis Laboratory Diagnostics in Newborns. *Journal of Clinical Medicine*, *14*(14), 5068. doi: 10.3390/jcm14145068.
14. Neutze, D., & Roque, J. (2016). Clinical evaluation of bleeding and bruising in primary care. *American family physician*, *93*(4), 279-286.
15. Merriman, L., & Greaves, M. (2006). Testing for thrombophilia: an evidence-based approach. *Postgraduate medical journal*, *82*(973), 699-704.doi: 10.1136/pgmj.2006.048090.
16. Kanne, J. P., & Lalani, T. A. (2004). Role of computed tomography and magnetic resonance imaging for deep venous thrombosis and pulmonary embolism. *Circulation*, *109*(12_suppl_1), I-15-21.doi: 10.1161/01.CIR.0000122871.86662.72.
17. Rahaghi, F. N., Minhas, J. K., & Heresi, G. A. (2018). Diagnosis of deep venous thrombosis and pulmonary embolism: new imaging tools and modalities. *Clinics in chest medicine*, *39*(3), 493-504. doi: 10.1016/j.ccm.2018.04.003.
18. Santhosh, V. C., Mahajan, A., Manas, A., Pawar, M., & Gupta, S. (2025). Oral health and quality of life in children with blood coagulation disorders and hemoglobinopathies. A cross-sectional study. *Journal of Family Medicine and Primary Care*, *14*(6), 2497-2501. doi: 10.4103/jfmpc.jfmpc_1911_24.
19. Morfini, M., Coppola, A., Franchini, M., & Di Minno, G. (2013). Clinical use of factor VIII and factor IX concentrates. *Blood Transfusion*, *11*(Suppl 4), s55-63. doi: 10.2450/2013.010s.
20. Lim, M. Y. (2021). How do we optimally utilize factor concentrates in persons with hemophilia?. *Hematology*, *2021*(1), 206-214. doi: 10.1182/hematology.2021000310.
21. Tuohy, E., Litt, E., & Alikhan, R. (2011). Treatment of patients with von Willebrand disease. *Journal of blood medicine*, 49-57. doi: 10.2147/JBM.S9890.
22. Stephens, K., Miller, J. L., Harkin, M., Neely, S. B., Haws, L., & Johnson, P. N. (2023). Effect of phytonadione on correction of coagulopathy in pediatric patients with septic shock. *The Journal of Pediatric Pharmacology and Therapeutics*, *28*(5), 423-429. doi: 10.5863/1551-6776-28.5.423.
23. Monagle, P., & Newall, F. (2018). Management of thrombosis in children and neonates: practical use of anticoagulants in children. *Hematology 2014, the American Society of Hematology Education Program Book*, *2018*(1), 399-404. doi: 10.1182/asheducation-2018.1.399.
24. Onwuzo, C., Olukorode, J., Sange, W., Tanna, S. J., Osaghae, O. W., Hassan, A., ... & Fayemi, T. (2023). A review of the preventive strategies for venous thromboembolism in hospitalized patients. *Cureus*, *15*(11): e48421. doi: 10.7759/cureus.48421.