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A comprehensive review on the epidemiology and clinical characteristics of thrombophilia in children

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Abstract
Thrombophilia, a predisposition to abnormal blood clotting, is a condition that has gained increasing recognition in the pediatric population. This research paper provides a thorough review of the epidemiology and clinical characteristics of thrombophilia in children. The aim is to enhance our understanding of this condition in the pediatric age group, with a focus on prevalence, risk factors, diagnostic methods, and the diverse clinical manifestations associated with thrombophilia in children.

Keywords: Thrombophilia, clinical, children, VTE, pediatric, RVT

Introduction
Thrombophilia refers to a group of disorders that increase the propensity for abnormal blood clotting. While it is commonly studied in adults, its occurrence in children has been gaining attention due to its potential impact on morbidity and mortality [3, 4]. Understanding the epidemiology and clinical characteristics of thrombophilia in children is crucial for early detection, appropriate management, and improved outcomes.
Thrombotic events, such as venous thromboembolism (VTE) and stroke, are being more frequently identified in hospitalized pediatric patients, but remain uncommon in healthy children. Most occurrences of juvenile VTE are associated with underlying risk factors, with the presence of an indwelling central venous catheter being the most prevalent. Inherited thrombophilias (IT) also increase the risk of VTE, but the prevalence of IT varies significantly depending on the specific patient group [1, 2]. Patients with spontaneous VTE are more likely to have an underlying thrombophilia compared to those with provoked VTE, such as catheter-related cases. Venous thromboembolic disorder (VTE) is uncommon in children. The annual incidence varies from 0.07 to 0.14 per 10,000 children and is expected to be 5.3 per 10,000 hospital admissions. The occurrence appears to be rising in the last few decades. Raffini *et al.* [8] documented a 70% increase in the yearly occurrence of VTE, from 34 to 58 instances per 10,000 hospital admissions. Boulet *et al.* [9], this increase is probably due to heightened disease awareness, advancements in radiologic imaging, and enhanced survival rates for children with previously untreatable conditions as a result of medical and surgical progress. A 2008 systematic review and meta-analysis on pediatric VTE and inherited thrombophilia found increased thrombotic risks in children with deficiencies of antithrombin, protein C, protein S, factor V Leiden mutation, and prothrombin mutation [7]. This paper aims to consolidate existing knowledge and identify gaps in our understanding of pediatric thrombophilia.

Epidemiology of Pediatric Thrombophilia
This section explores the prevalence of thrombophilia in children, considering variations across different age groups, ethnicities, and geographical regions. Examining the risk factors associated with pediatric thrombophilia, including genetic predispositions, acquired conditions, and environmental factors.

Clinical Characteristics
Young *et al.* demonstrated that thrombophilia has a role in newborn VTE development, noting that neonates were not well-represented in their meta-analysis. Approximately 5.1 out

of 100,000 babies experience symptomatic VTE in neonates, with almost 95% of cases being linked to at least one clinical risk factor, typically a CVC. There is a limited amount of research on thrombophilia in newborns with central venous catheter-related blood clots [6]. Renal vein thrombosis (RVT) is the most common noncatheter-related venous thromboembolism (VTE) in neonates, with an incidence of 2.2 per 100,000 births in Germany. Studies before 2008 suggest that hereditary thrombophilia is more common in newborns with RVT compared to those with catheter-related VTE, but there is limited research on this topic [5]. Kosch *et al.* [10] case-control study found a greater prevalence of thrombophilia in neonates compared to controls, with 67.8% of neonates having at least 1 thrombophilia compared to 11.9% of controls. The odds ratio was 15.6 with a 95% confidence interval of 7.2-34.2. This study verified that infant RVT is a complex condition with multiple contributing causes including hypoxia, sepsis, diabetic fetopathy, and CVCs.

- **Thrombotic Events:** An analysis of the various thrombotic events observed in children with thrombophilia, such as deep vein thrombosis, pulmonary embolism, and cerebral venous sinus thrombosis.
- **Non-thrombotic Manifestations:** Exploring the non-thrombotic clinical features of pediatric thrombophilia, including skin manifestations, neurological abnormalities, and other organ system involvement.

Diagnostic Approaches

- **Laboratory Tests:** A review of laboratory tests commonly used for diagnosing thrombophilia in children, such as clotting factor assays, genetic testing, and biomarkers.
- **Imaging Modalities:** An overview of imaging techniques employed in the diagnosis and monitoring of thrombophilia-related complications in children, with a focus on ultrasound, magnetic resonance imaging, and computed tomography.

Management and Treatment

- **Anticoagulation Therapy:** An assessment of the current recommendations and challenges associated with anticoagulation therapy in pediatric patients with thrombophilia.
- **Long-term Care and Follow-up:** Addressing the importance of long-term care, monitoring, and the prevention of recurrent thrombotic events in children with thrombophilia.

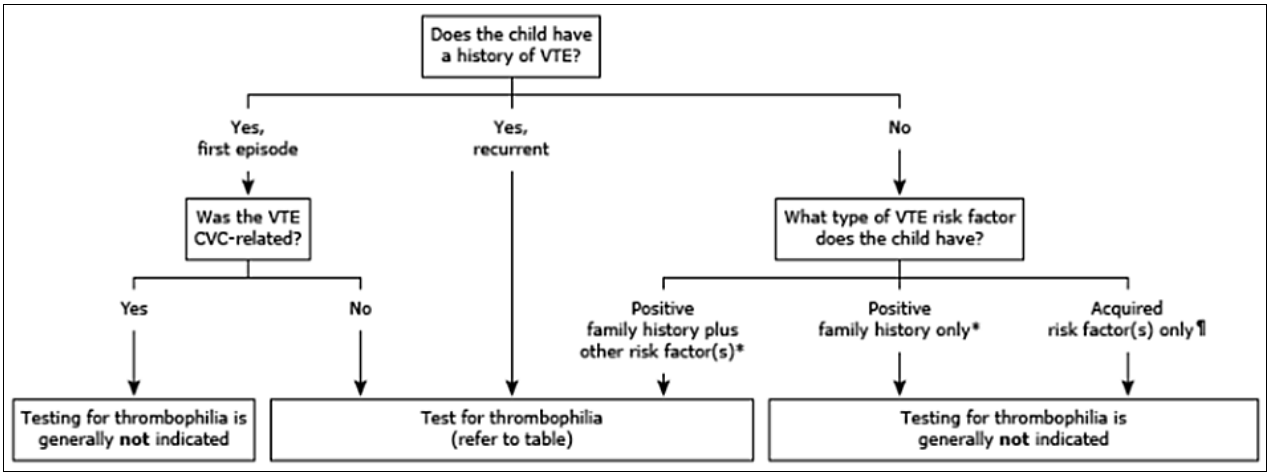

Fig 1: Approach to thrombophilia testing in children

Genetic Factors in Pediatric Thrombophilia

- **Inherited Thrombophilias:** Exploring the role of inherited genetic mutations in pediatric thrombophilia, such as deficiencies in antithrombin, protein C, and protein S, as well as the impact of factor V Leiden and prothrombin gene mutations.
- **Acquired Thrombophilias:** Examining acquired conditions that may contribute to thrombophilia in children, including systemic illnesses, infections, and autoimmune disorders, shedding light on the complex interplay between genetics and environmental factors.

Complications and Comorbidities

- **Neurological Complications:** A detailed analysis of neurological complications associated with pediatric thrombophilia, including ischemic stroke, transient ischemic attacks, and cognitive impairments.
- **Cardiovascular and Renal Complications:** Exploring potential cardiovascular and renal manifestations in children with thrombophilia, emphasizing the need for comprehensive screening and management strategies.

Conclusion

This research paper provides a comprehensive overview of the epidemiology and clinical characteristics of thrombophilia in children, emphasizing the importance of early detection, appropriate management, and ongoing research to advance our understanding of this condition in the pediatric population. Continued efforts in research and clinical practice are essential to refine diagnostic approaches, optimize treatment strategies, and improve outcomes for children with thrombophilia. Summarizing the key findings and insights presented in this review, emphasizing the multifaceted nature of pediatric thrombophilia, and calling for continued collaboration between researchers, clinicians, and policymakers to improve outcomes for affected children. Additionally, acknowledging the need for ongoing research to unravel the complexities of thrombophilia in the pediatric population

and enhance our ability to provide targeted and effective care.

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