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EDITORIAL COMMENTARY

Thromboembolism in Children: Unveiling Risk-Factors

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Though infrequent, thromboembolism (TE) in pediatric patients is on the rise, attributed mainly to the increased utilization of central venous catheters (CVCs) [1]. The fraternity of neonatology, cardiology, and hematology-oncology encounter this daunting problem more frequently. Understanding the risk factors of TE in children is pivotal for identifying at-risk patients and optimizing thromboprophylaxis. The retrospective analysis of the risk-factors, clinical profile, and outcome for TE in children by Öncül et al. is a worthy compilation. The study, conducted at the Department of Pediatric Hematology and Oncology in Malatya, Turkey, examined 84 pediatric TE cases over 11 y [2].

As expected, a sizeable (76.1%) proportion of patients had acquired risk factors for TE: infection (20.2%), CVCs (13.1%), and liver disease (11.9%) topped the list. CVC is listed in the literature as the most common provoking factor for TE in children. CVC-related TE represented a large chunk of cases of hospital-associated TE in large multi-institutional studies, including the CHAT Registry (80%) [3] and the Kids-DOTT study (46.4%) [4]. Interestingly, merely 13.1% of episodes of TE were attributed to CVC in the current study. We speculate if the author's center follows a restrictive approach to using CVCs.

The authors evaluated all patients for inherited thrombophilia, even when a provoking factor for TE was obvious. However, the role of routine testing for inherited thrombophilia is questionable. The results of these tests fail to predict the risk of recurrent TE and guide clinical decisions [5]. The fact is reflected in the study under discussion as well: despite a high prevalence of thrombophilic mutation, the rate of recurrent TE was merely 3.6%. Hence, a "choose wisely" approach rather than universal testing for genetic thrombophilia is typically considered appropriate.

The reported prevalence of the common inherited thrombophilic states in consecutive patients with VTE ranges from 1-20% [5]. In the current study, the prevalence of at least one thrombophilic mutation was noticeable in 41.2%, which the authors attribute to a high prevalence of consanguinity in the region. Factor V Leiden (FVL) and prothrombin 20210A mutations are generally reported as the most prevalent inherited thrombophilias [5, 6]. Of note, polymorphisms involving the plasminogen activator inhibitor-1 and methylenetetrahydrofolate reductase constituted the most common thrombophilic mutations in the current study. FVL and prothrombin 20210A mutation carry a milder disease phenotype. Given the study was conducted in a tertiary care setting, plausibly, children with severe forms of TE were overrepresented. The referral bias might explain the lower incidence of FVL and prothrombin 20210A mutation.

The median duration of anticoagulant therapy in the index study was 12 mo. About three-fourths (76.1%) of TE events were provoked. The duration of therapeutic anticoagulation following provoked TE is a bone of contention. It varies widely from 6 wk to 12 mo, depending upon the thrombus location, risk for recurrence, and response to therapy [1]. In the current era, evidence favors a shorter duration (6 to 12 wk) of anticoagulant therapy [4, 7]. However, if the estimated risk of recurrent TE is high, the duration is often prolonged at the physician's discretion. The authors' choice of using warfarin for maintenance anticoagulation is atypical. Most pediatricians would prefer to continue low molecular weight heparin or, more recently, switch to a direct oral anticoagulant.

The study's strengths lie in its robust sample size ($n = 84$) and reasonable follow-up duration (median: 15 mo), enabling assessment for post-thrombotic complications and unveiling local genetic thrombophilia patterns. However, inherent limitations include its retrospective design and single-center data collection, warranting cautious interpretation.

Data on the epidemiology and risk factors of thrombosis amongst Indian children is scarce. Establishing

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a hospital-based thrombosis registry in India would facilitate prospective, multicentric accrual of data on risk factors of pediatric TE. The exercise would help identify the children at risk for TE and formulate a tailored thromboprophylaxis strategy.

Declarations

Conflict of Interest None.

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