

# Leading Article

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## Riddles of Lupus Anticoagulant in children

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Ever so often we get confused with the term Lupus anticoagulant (LA). Some of us might even consider this anticoagulant as the sole association of Systemic Lupus erythematosus. In reality it is not that simple; particularly in accordance to its detection and interpretation in childhood as its presence sometimes is merely transient and bears no clinical importance.

Lupus anticoagulant is really a misnomer as it is an acquired immunoglobulin G or immunoglobulin M antibody that inhibits the phosphorous dependent reaction and associated with certain autoimmune conditions like drugs, infections, pregnancy loss, bleeding disorders and malignancies.<sup>1</sup>The discovery of Lupus anticoagulant is mainly credited to Conley and Hartman, who, for their patients with SLE that had prolonged aPTT, mixed normal plasma with the patient's blood to correct the aPTT. The unknown compound was named LA. It was hypothesized to act against negatively charged phospholipids presents on the surface of platelets.<sup>2</sup>These phospholipids are an integral part of Vitamin K dependent clotting factor homeostatic arcade. Lupus anticoagulant belongs to the antiphospholipid antibodies that also includes the anti cardiolipin antibody and anti Beta 2 glycoprotein 1 antibody.<sup>3</sup>

Incidence and clinical importance of Lupus anticoagulant in children: Lupus anticoagulant is one of the antiphospholipid antibodies reacting with phosphorous protein complex and can arise after events triggering immune system. The presence of LA is an important cause for prolonged aPTT test in children.<sup>4,5,6</sup> The presence of which in turn is usually transient without causing any damage. However, children may rarely develop complications such as stroke and it does not increase the risk of bleeding. Diagnosis of LA in asymptomatic children is usually incidental.<sup>7</sup> This gets determined when aPTT

is prolonged after an upper respiratory tract infection (URTI) or during screening tests before surgical intervention. The presence of this antibody is generally temporary and is not corroborating with clinical status. Erdel Peker et al in 2011 studied 165 patients in Turkey where 77 were female, 88 male and median age of the patients 5.0 yrs with a range of 1.5 to 11 yrs. The presence of LA was positive in 8 (4.8%) but the mean age was found to be lower in LA positive patients. Activated partial thromboplastin time was prolonged in six patients and 2 of the six patients were positive for LA. The presence of LA disappeared in 7 patients.<sup>7</sup> Kalanagowder et al in another retrospective study in 112 children in new Orleans US found 18 patients to be LA positive. These patients were referred to the paediatric Haematology/Oncology department who had prolonged aPTT and came for minor surgical procedure. Sixty Seven percent of these positive patients (12) were female and the mean age was 6.05 years. Eighty nine percent (16) of LA positive patients were clinically asymptomatic. Two symptomatic patients had epistaxis and one had concomitant thrombo-cytopenia. Ten of 18 patients became LA negative.<sup>3</sup>

Two major subsets of LA in children could be seen.

1. The childhood type -It is frequently benign, transient and possibly post infectious.
2. An auto immune type similar to the adult type and starting in adolescents and persist with associated Thromboembolic manifestations.<sup>6,8</sup>

The childhood type when associated with hypoprothrombinemia or thrombocytopenia can manifest with bleeding.<sup>9,10,11</sup> Presence of LA in a child with SLE enhances the risk of Thromboembolism.<sup>12,13</sup> P Venugopalan et al in 2001 had found 2 patients with accidental detection of LA and both had undergone successful cardiac surgery.<sup>8</sup> Male et al in 1999 in a retrospective study of 95 children had their median age to be 5.3 yrs (1.7-17yrs). At diagnosis 80 of the 95 (84 percent) children were free of symptoms and LA was found incidentally. Of the remaining 15, nine

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children had bleeding symptoms, 5 had thrombosis and one patient had SLE. Among the patients with bleeding, 5 had transient severe thrombocytopenia after adenovirus infection and three had thrombocytopenia.<sup>6</sup> Association of anti phospholipid antibodies had earlier been seen in infections including Mycoplasma pneumonia as well as viruses, particularly adenovirus and other viruses like measles, mumps, chicken pox etc.<sup>9,10</sup>

Diagnosis of LA: Lupus anticoagulant is a laboratory phenomenon that results from autoantibodies inhibiting varieties of in vitro phosphorous dependent coagulation tests.<sup>8</sup> No specific tests are available for conclusively diagnosing LA and it is diagnosed indirectly. Phospholipid dependent test such as aPTT and dRVVT (DiLutedRusselViper Venom test) are used as screening test.<sup>3</sup> The patient's plasma is mixed with normal plasma (mixing study) and normalization of the clotting time solicits confirmatory testing. Nowadays Phospholipid is added to the patient's plasma and if this addition brings the clotting time to the reference range, the patient is said to be positive for LA.<sup>5</sup> Assay for LA is not the measurement of antibody titre rather it is a functional test. Although a single test could sometimes be sufficient, two or more tests are recommended for LA positivity because no single test is 100 percent sensitive for LA.<sup>14,15,16,17,18,19,20</sup>

So in conclusion it can be said that as per our common understanding Lupus anticoagulant (LA) is not though common could be a consideration in childhood. It is definitely not a sine qua non finding in SLE and is often found incidentally before screening for Surgery or after an attack of Respiratory tract infections, particularly with adenovirus. The most common laboratory abnormality is a prolonged aPTT. They are mostly transient and generally disappears after 12 weeks. As because LA detection is an indirect functional test rather than an assay of antibodies. The interpretation should be carefully done in reference laboratory as sensitivity wise it greatly varies.

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