

## Immature Platelet Fraction – A Simple and Useful Novel Marker in Dengue Hemorrhagic Fever

In dengue fever, thrombocytopenia is ascribed to destruction of platelets by antiplatelet antibodies, disseminated intravascular coagulation, marrow suppression and peripheral sequestration of platelets. Platelet counts vary considerably during the course of illness, and patients may require platelet transfusion when the counts are  $<10000/\text{mm}^3$  [1]. Platelet count is expected to rise in the late critical or the recovery phase of the infection. Immature platelet fraction (IPFL, the percentage of immature platelets) can be used to fairly predict the rise or fall of platelet count during the course of dengue fever [2]. IPF defines the immature and larger platelets that have been recently released from the marrow, and have much larger RNA content than the mature platelets. A high IPF is usually found in either consumptive or recovering thrombocytopenic disorders, while a low IPF is characteristic of bone marrow suppression [2]. IPF is identified by simple flow cytometry technique and the use of a nucleic acid specific dye (e.g., oxazine dye 0.0003%) in the optical platelet channel which is available in most hematology laboratories. The test is simple, inexpensive and reproducible [3]. An IPF reference range in healthy

neonates is  $4.1 \pm 1.8$ , and in children is  $2.7 \pm 1.3$  [4]. IPF has been shown to have a strong correlation with the recovery of platelet counts in patients with dengue fever [5]. Patients with no warning signs or symptoms but with NS1 positive and borderline platelet count keep the treating pediatrician under dilemma – whether to admit the patient or to observe. Performing IPF in dengue patients may help in decision for admitting or monitoring during recovery in dengue fever.

\*D SHIVSHANKAR AND #KARTHIK NAGESH  
*Manipal Advanced Child Centre,  
 Manipal hospitals, Bengaluru, India.  
 \*ShivI.diggikar@gmail.com.*

### REFERENCES

1. WHO. National Guidelines for Clinical Management of Dengue Fever 2015.
2. Sehgal KK, Dadu T, Choksey U, Dalal RJ, Khodaiji JS. Reference range evaluation of complete blood count parameters with emphasis on newer research parameters on the complete blood count analyser sysmex-XE-2100. *Indian J Pathol Microbiol.* 2013;56:120-4.
3. Briggs C, Kunka S, Hart D, Oguni S, Machin SJ. Assessment of an immature platelet fraction (IPF) in peripheral thrombocytopenia. *Br J Hematol.* 2004;126:93-99.
4. Diagnostic Perspectives – The Sysmex Europe eJournal for Clinical Laboratory Medicine. Published 2011 by Sysmex.
5. Dadu T, Sehgal K, Joshi M, Khodaiji S. Evaluation of the immature platelet fraction as an indicator of platelet recovery in dengue patients. *Int J Lab Hematol.* 2014;36:499-504.

## Infantile Tremor Syndrome: A Syndrome in Search of its Etiology

Indian Pediatrics has done a great service by revisiting 'Infantile Tremor Syndrome' (ITS) [1]. Even though, ITS has existed for almost 60 years, it continues to be perceived as a syndrome of unknown etiology. However, there is now enough epidemiological, clinical, laboratory and therapeutic evidence in the literature to support vitamin B<sub>12</sub> deficiency as the cause of ITS.

Epidemiologically, ITS occurs in exclusively breastfed infants of strictly vegetarian mothers. As a

result, these infants are predisposed to develop vitamin B<sub>12</sub> deficiency. Clinically, symptoms and signs of ITS are similar to those of vitamin B<sub>12</sub> deficiency in infants. Many studies in the past excluded vitamin B<sub>12</sub> deficiency in ITS on the basis of mere absence of macrocytosis or megaloblastic bone marrow. Absence of these features does not exclude the diagnosis of vitamin B<sub>12</sub> deficiency which requires serum vitamin B<sub>12</sub> measurement. Several studies [2-4] have consistently demonstrated low serum vitamin B<sub>12</sub> in these infants. Study by Bajpai, *et al.* [5] is the only report to have found normal serum vitamin B<sub>12</sub>, but only 20 (15%) of 134 infants were tested in this series. Additionally, in some studies from India, infants with megaloblastic anemia due to vitamin B<sub>12</sub> deficiency

displayed symptoms and signs consistent with ITS [5]. In one such study [9] of 52 infants with megaloblastic anemia, pallor was present in 96%, skin hyperpigmentation in 77%, developmental delay in 67%, and 43% had hypotonia.

Response to treatment with vitamin B<sub>12</sub> in ITS is rapid with improvement in general activity and responsiveness within 48-72 hours. This is followed by the return of social smile and improved appetite. Lost developmental milestones are gradually regained. The tremors begin to subside by the end of first week and disappear completely by 3-4 weeks [2,3]. It follows that infants with vitamin B<sub>12</sub> deficiency can present with predominantly hematological (megaloblastic anemia) or predominantly neurological (infantile tremor syndrome) manifestations. Some infants may have purely neurological or purely hematological presentations. Most importantly, evidence of vitamin B<sub>12</sub> deficiency has been found wherever it has been adequately looked for. It is, therefore, time to discard the syndrome status for this

disorder, and rename it as 'nutritional vitamin B<sub>12</sub> deficiency in infants' as it is known elsewhere in the world.

\*JATINDER S GORAYA AND #SUKHJOT KAUR

From Departments of Pediatrics and

#Dermatology, Dayanand Medical College and Hospital,

Ludhiana, Punjab, India.

\*gorayajs@gmail.com

## REFERENCES

1. Mukherjee SB. Infantile tremor syndrome – A tale of 50 years. *Indian Pediatr.* 2015;52: 599-600.
2. Goraya JS, Kaur S. Infantile tremor syndrome: Down but not out. *Indian Pediatr.* 2015;52:249-50.
3. Jain R, Singh A, Mittal M, Talukdar B. Vitamin B<sub>12</sub> deficiency in children: A treatable cause of neurodevelopmental delay. *J Child Neurol.* 2015;30:641-3.
4. Bajpai PC, Misra PK, Tandon PN. Further observations on infantile tremor syndrome. *Indian Pediatr.* 1968;5: 297-307.
5. Mittal VS, Agarwal KN. Observations on nutritional megaloblastic anemia of early infancy. *Indian J Med Res.* 1969;57:730-8.

## Hypervitaminosis D with Dyslipidemia: An Unusual Scenario

Vitamin D plays an important role in calcium homeostasis, and for skeletal growth and bone strength. Vitamin D toxicity may occur at excessively high doses. For many people, the word 'vitamin' implies something that is beneficial and essential, not potentially harmful [1]. We recently encountered an infant with iatrogenic hypervitaminosis D associated with asymptomatic dyslipidemia.

A six-month-old girl was brought to us with fever for one day and one episode of generalized seizure. There was no history of cough, rash, ear discharge, polyuria, polydipsia, constipation, nausea, vomiting or similar such episode. She received two mega doses (600,000 IU each) of oral vitamin D in last two months. Blood counts, kidney function tests, urine examination, blood culture, CSF examination and ultrasonography of the abdomen were normal. Serum levels of 25-OH Vitamin D<sup>3</sup> were high (>160 ng/mL) with a normal serum calcium (10.1 mg/dL) and normal serum parathyroid hormone (46 pg/mL). We incidentally sent her serum lipid profile, which revealed high

TABLE I LIPID PROFILE OF THE PATIENT

Parameter	Results	Reference range [2]
Total Cholesterol	123 mg/dL	106-186
Triglycerides	403 mg/dL	65-234
HDL Cholesterol	27 mg/dL	24-84
VLDL Cholesterol	81 mg/dL	0-30
LDL Cholesterol	15 mg/dL	34-111

triglycerides (403 mg/dL), normal total cholesterol (123 mg/dL), and high VLDL cholesterol (81 mg/dL). The lipid profile of parents and other siblings were within normal limits. Secondary causes of hyperlipidemia were ruled out.

Vitamin D receptors are found ubiquitously, including in adipose tissue, and 25(OH)D plays an important role in lipid metabolism via several mechanisms, including induction of an increase in lipoprotein lipase activity [3], increased lipogenesis and lipolysis, and enhanced intestinal calcium absorption, which could reduce the formation of calcium fatty soaps in the gut and increase the absorption of fat. In a recent report [4], cholesterol and triglyceride levels were found to be increased in an adolescent following vitamin D treatment. Similar findings in adults have been reported earlier [5].