## **RESEARCH LETTERS**

## Infantile Tremor Syndrome – Down but not Out

Retrospective chart review of 21 infants with infantile tremor syndrome for vitamin B<sub>12</sub> deficiency showed low serum vitamin B<sub>12</sub> levels in 8/16 (50%). Of the eight infants with normal levels, six had received vitamin B<sub>12</sub> before referral. Macrocytosis and low maternal serum B<sub>12</sub> was found in 12 and seven cases each. Treatment with vitamin B<sub>12</sub> alone produced rapid recovery.

Keywords: Movement disorder, Vitamin B<sub>12</sub>,

Infantile tremor syndrome (ITS) is characterized by pallor, developmental regression, tremors, hyperpigmentation of skin, and sparse brown hair. [1]. Though considered to be a vitamin  $B_{12}$  deficiency state by many, opinion has remained divided. We describe some children with ITS to highlight its continued occurrence and also report on its probable etiology.

A retrospective review of the medical records of the children with infantile tremor syndrome attending our center between February 2010 and August 2014 was done. We investigate all infants with ITS and their mothers for vitamin  $B_{12}$  deficiency. All infants are initially treated with intramuscular vitamin  $B_{12}$  alone.

Twenty-one infants, (13 boys) aged 6 to 27 month were studied. Common presenting symptoms were tremors in 12, developmental delay in three, and developmental regression in three. All infants were exclusively breast-fed and their mothers were vegetarians, with little or no milk intake. We found low serum B<sub>12</sub> in 8 of the 16 infants. Six of the 8 infants with normal serum vitamin  $B_{12}$  had received vitamin  $B_{12}$ before referral. Clinical and laboratory parameters are summarized in *Table* I. After treatment with intramuscular vitamin B<sub>12</sub> alone, improvement in general activity, interest in surroundings, and return of social smile was seen within 48-72 hours in all except one. Tremors started to diminish by the end of first week in eight infants. Six infants showed initial worsening of tremors following treatment. Tremors were completely resolved by three to four weeks in all.

There is epidemiological, clinical, laboratory and therapeutic evidence to suggest that vitamin  $B_{12}$  deficiency is causally associated with ITS [2-4].

Epidemiologically, ITS occurs in exclusively breastfed infants of mothers living on diet devoid of animal products, including milk, pointing to vitamin  $B_{12}$ deficiency in infant-mother pairs [3]. All the mothers tested in our series had low serum vitamin  $B_{12}$ . Moreover, the manifestations of ITS are identical to those described with infantile vitamin B<sub>12</sub> deficiency reported from West [4]. Skin hyperpigmentation seen in ITS is also a well-known sign of vitamin  $B_{12}$  deficiency [5]. Infants with normal serum vitamin B<sub>12</sub> levels in this study had other evidence of vitamin B<sub>12</sub> deficiency such as macrocytosis and low maternal serum vitamin B<sub>12</sub>. From therapeutic standpoint, unequivocal improvement in general activity was observed in all the treated infants within 48-72 hours of vitamin  $B_{12}$ . Tremors also improved gradually, all although initial worsening of tremors, a well-documented feature of vitamin  $B_{12}$ deficiency [6], was encountered in six infants

Interestingly enough, first study on ITS by Dikshit [1] had provided initial evidence that the symptoms and signs could be due to vitamin  $B_{12}$  deficiency. Later authors also reported low serum vitamin  $B_{12}$  and good response to vitamin  $B_{12}$  [2,3]. Deshpande and Ingle [7] also concurred with vitamin  $B_{12}$  deficiency in ITS. Elegant study by

**TABLE I** CLINICAL AND LABORATORY FINDINGS IN INFANTS

 WITH INFANTILE TREMOR SYNDROME
 INFANTS

Clinical findings $(n=21)$	Number (%)
Developmental delay and/or regression	21 (100)
Brown scanty hair	21 (100)
Skin hyperpigmentation	21 (100)
Pallor	21 (100)
Lethargy/apathy	21 (100)
Growth retardation*	16 (78)
Hypotonia	15 (75)
Tremors	14 (73)
Laboratory findings (n=18)	Number (%)
Anemia (haemoglobin d" 11g/dl)	15 (83.3)
Macrocytosis (MCV>95)	12 (66.6)
**Low serum $B_{12}(n=16)$	8 (50)
Low maternal serum B <sub>12</sub>	7 (100)
Diffuse cerebral atrophy on neuroimaging	7 (100)

<sup>\*2</sup> infants each also had glossitis, angular cheilitis, edema, and rickets; \*\*of the 8 infants with normal serum vitamin  $B_{12}$ , 6 had received vitamin  $B_{12}$  before referrals.

Garewal, et al. [8] showed unambiguous evidence of vitamin B<sub>12</sub> deficiency in ITS in the form of megaloblastic bone marrow, and low serum vitamin B<sub>12</sub> including cellular evidence of vitamin B12 deficiency was revealed by the dU suppression test. On the other hand, in the studies showing lack of evidence of vitamin B<sub>12</sub> deficiency in ITS, serum vitamin  $B_{12}$  the current gold standard of diagnosis of vitamin B<sub>12</sub> deficiency, was not measured and results were inferred from the mere absence of peripheral blood macrocytosis and megaloblastic bone marrow [9,10]. Occurrence of neurological symptoms of vitamin  $B_{12}$ deficiency in the absence of concomitant hematological changes is well known [8,11]. Interestingly, publication bias also seems to have played a major role in this debate on etiology of ITS. Majority of the studies [2,3,8] reporting vitamin B<sub>12</sub> deficiency in ITS were published in foreign journals and likely to have escaped scrutiny of researchers of the country.

In summary, ITS continues to exist in India in modern times and is causally associated with vitamin  $B_{12}$  deficiency. Since long-term neuro-developmental deficits can occur if treatment is delayed, infants with ITS should be treated early with vitamin  $B_{12}$  for rapid reversal of neurological signs.

*Contributors*: JSG: conceptualized the study, collected the data and wrote the initial and final draft; SK: participated in the data analysis, performed the literature review, and revised the manuscript.

Funding: None; Competing interest: None stated.

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## Impact of House-hold Food Insecurity on Nutritional Status of HIV-infected Children Attending an ART Centre in Tamil Nadu

We studied the level of food insecurity among households with HIV-infected children and its relationship with childhood nutritional indicators. Among the 147 children assessed, food insecurity was present in 59% of households. Majority of children with stunting belonged to-food insecure families. Stunting and Underweight were more prevalent among children >5 years of age.

Keywords: AIDS, Children living with HIV, Stunting, Underweight.

Human Immunodeficiency Virus (HIV) infection has been shown to lead to food insecurity and severe malnutrition, as it hits the productive age groups the most, thereby causing a fall in the family income, and reduced food availability for the entire household. [1]. This malnutrition in early childhood affects the cognitive, psychosocial and physical development, and also affects academic performance of the child [2]. A cross-sectional study was conducted in the Anti-retroviral Treatment (ART) Center of a government tertiary-care hospital in Chennai between August and December 2012, to evaluate the status of food security among households with HIVinfected children, and to correlate it with the nutritional status and growth of the child. Households were eligible to participate if they had at least one child aged between 1

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