



Clinico-Investigative Profile of Infantile Tremor Syndrome

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Developmental regression in a young child is always a challenge to investigate and treat [1]. Before we consider inherited metabolic conditions it is always important to rule out acquired conditions that are mostly treatable such as nutritional deficiencies like vitamin-B12 presenting as infantile tremor syndrome (ITS) and protein energy malnutrition; infections like human immunodeficiency virus and slow viral infections and environmental toxins like lead exposure *etc.*

Infantile tremor syndrome has been reported from India in the last six decades but the exact cause and treatment of this condition is not clear from the published literature [2]. Many studies done in the past have implicated many etiological factors like deficiency of zinc, vitamin-B12, iron, magnesium *etc* [3]. Role of vitamin-B12 deficiency in the causation of ITS is also not clear with many patients of ITS having normal vitamin-B12 levels. Is ITS really due to vitamin-B12 deficiency in these cases and if yes, how do work up these cases further is always a difficult task.

Many of us depend on the tremors to suspect and diagnose babies with ITS but it may not always be there in a given case and just regression of milestones with skin color change could be the only manifestations. Though previously termed as pre-ITS in literature this has not been correctly characterized. Sankhyan and colleagues have done a detailed evaluation of 92 children and their mothers with ITS and pre-ITS using detailed clinical examination, standard psychometric tests, hematological tests and extensive biochemical tests to study the role of vitamin-B12 in the causation and treatment of ITS [4]. As presented in the study by Chaudhary et al., the tremors were seen only in 21.7% (20 out of 92) children and almost all of them had skin changes in the form of pallor and hyperpigmentation of skin. The absence of tremors in a given case

may dissuade a physician from considering ITS in an infant with neuro-regression. The term Neurocutaneous infantile B-12 (NIB) aptly describes the key clinical features, provides clue to the underlying cause and can lead to prompt treatment of this condition and there is a need to change from ITS/ pre-ITS to neurocutaneous infantile vitamin B12 to label these children.

Serum vitamin-B12 levels were less than the normal cut off (211 pg/ml) in only 42% children in the current study which is similar to that reported by Goraya et al. [5]. The practice of many medical professionals prescribing multivitamin syrups as appetite stimulants could be one of the main reasons for getting normal vitamin-B12 levels in most of the cases. However other evidence of vitamin-B12 deficiency in the form of increased homocysteine levels in 96.5% cases, elevated C3:C2 ratio in 79.5% cases and increased urine methylmalonic acid in urine was seen in 70.1% cases. Only 3 out of the total 92 did not have any biochemical evidence of vitamin B-12 deficiency [4]. If we combine hematological findings, all children with ITS had some evidence of vitamin-B12 deficiency and none of them had folate deficiency in the study population.

As only 42% of cases had low serum vitamin-B12 levels, it would be a wise decision to do serum homocysteine levels in the baby if he has received vitamin-B12 supplementation in last few days. Estimating vitamin-B12 and homocysteine in the mother also is a good option if there is history of receiving oral vitamin-B12 for long time or if injectable vitamin-B12 was given to the baby in the past. As most of the babies are exclusively or predominantly breastfed, a low vitamin B12 in the mother would be a surrogate marker for vitamin-B12 levels in the child.

Majority of the children with ITS, are borne to exclusively breast-fed mostly vegan mothers who themselves are vitamin-B12 deficient and because of delayed weaning the vitamin-B12 deficiency in the baby gets exaggerated. Presentation with developmental delay and/or regression and response to vitamin-B12 supplementation confirms the role of vitamin-B12 in the causation of ITS. If vitamin-B12 levels are normal in a given case of ITS, then other tests should be done.

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Compliance with Ethical Standards

Conflict of Interest None.

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