

Original Research Article

Clinical profile of patients with infantile tremor syndrome in a tertiary care center

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ABSTRACT

Background: Infantile tremor syndrome (ITS) is a condition reported from many areas of Indian subcontinent due to lack of proper nutrition, improper weaning or delayed introduction of complementary feeding. There is no proven macro or micro nutrient deficiency responsible for it but relation with vitamin B12 deficiency has been identified in some studies. The aim of this study was to study the clinical profile of patients with ITS.

Methods: It is a prospective observational study including total 30 patients, from 6 months to 3-year age group, admitted to pediatric wards and nutritional rehabilitation centre, civil hospital, Ahmedabad, from June 2018 to December 2019.

Results: Out of 30 patients studied, 69% had pre-ITS and rest had ITS, 61.5% were males and 38.4% were females, 69.2% had severe acute malnutrition, 84.6% had severe anemia and 23% of them presented with CCF, 15.4% patients had microcephaly and 23% had hypotonia. 23% had motor and speech delay. 61.5% belonged to lower socio-economic group. There was delayed introduction of complementary feeding in 63% of patients. 69% patients had severe vitamin B12 deficiency and 21% had moderate vitamin B12 deficiency.

Conclusion: ITS, is commonly seen among male children belonging to lower socio-economic group among age group of 6 months to 24 months, presents with coarse tremors with moderate to severe anemia with moderate to severe acute malnutrition and is associated with deficiency of vitamin B12. Early diagnosis and treatment including nutritional rehabilitation grossly improved the outcome.

Keywords: ITS, Vitamin B12, Malnutrition

INTRODUCTION

ITS is a clinical state characterized by tremors, anemia, pigmentary skin, regression of mental development and hypotonia of muscles.¹ Exact incidence of infantile tremor syndrome in general population is not known, but ITS has accounted for 0.77-2.5% of the pediatric ward admissions. Very likely, clinically encountered ITS cases represent only 'tip-of-the-iceberg', with vast majority of asymptomatic cases remaining under-recognised.² Its cases have been predominantly reported from the Indian subcontinent. Few cases have been reported in Africa and South East Asia.^{2,3} ITS was first described by Dikshit at

Hyderabad, India, in 1957 who named it as 'nutritional dystrophy and anemia'.²

The aim of study was observing the clinical profile of patients having infantile tremor syndrome and its relation to vitamin B12 levels along with response to treatment and final outcome.

METHODS

It is a prospective observational study including total 30 patients, from 6 months to 3 years' age group. Which was carried out at pediatric wards and nutritional

rehabilitation center, civil hospital, Ahmedabad. From June 2018 to December 2019.

Inclusion criteria included children between 6 months to 3 years of age admitted in civil hospital, Ahmedabad and diagnosed as having pre-ITS or ITS were included in the study.

Detailed history of patients was taken with special emphasis on socio-demographic characteristics and socio-economic factors like poverty, literacy, knowledge of nutritive value of food, environmental hygiene, overcrowding and unemployment. Socio-economic status was established on basis of modified Kuppuswamy classification.⁴

Birth history of each patient was inquired including history of NICU admission and its duration.

Nutrition and child rearing practices were inquired for each patient. It included history of giving pre lacteal feeds, duration of exclusive breastfeeding, timing, type and amount of foods introduced for complementary feeding.

Developmental history was taken in detail and development quotient was calculated for patients with delayed development. Developmental assessment was done based on Trivandrum development screening chart.

Immunization history was taken according to national immunization schedule. Infections and childhood illnesses including measles were enquired. Maternal diet and nutrition, especially including exclusively vegetarian mothers, anemia in mothers, extent of birth spacing, any significant obstetric history. Levels of vitamin B12 of the mothers were also tested.

General and systemic examination and complete anthropometry of all the patients was done by proper methods. Neuro pediatrician opinion was taken, if necessary.

Blood investigations included the following: CBC, peripheral smear, serum electrolytes, serum vitamin B12 and serum iron levels in all patients and other investigations like CXR, LFT, vit D3 levels were done, if needed.

Grading of anemia was done according to WHO classification.⁵

Grading of vitamin B12 deficiency was done as below: mild: vitamin B12 levels between 200-300 pg/ml, moderate: Vitamin B12 levels between 100-200 pg/ml and severe: vitamin b12 levels below 100 pg/ml.⁶

Treatment was planned as per the presenting condition and institutional standard operating protocols. Nutritional rehabilitation was started after stabilization. Diet rich in

vitamin B12 and Vitamin B12 supplements were given to patients. Moderate and severe vitamin B12 deficiency was corrected by parenteral injections of vitamin B12 followed by oral supplementation.

Informed consent was obtained from parents.

Microsoft excel was used for the statistical analysis of the study.

RESULTS

Out of the total cases, 61.5% patients had ITS and 38.4% had pre-ITS. A 2:1 male to female ratio is seen with majority of children between 6 to 12 months of age. More incidence was seen in patients born out of reduced birth spacing and increasing birth order.

Table 1: Proportion of patients with ITS and pre-ITS.

Condition	Number	Percentage
ITS	11	38.4
Pre-ITS	19	61.5

Table 2: Sex-wise distribution.

Sex	Number	Percentage
Male	19	61.5
Female	11	38.4

Table 3: Sex-wise distribution in ITS and pre-ITS.

Variables	Male		Female	
Condition	N	%	N	%
ITS	8	26.60	3	10
Pre-ITS	11	36.60	8	26.60

Table 4: Age-wise distribution.

Age (years)	Number	Percentage
<6 m	1	3.33
6-12 m	23	84.6
1-2	5	16.6
2-3	1	3.3

Out of total 30 patients, 61.5% were exclusively breast fed for prolonged periods and 63% of them had delayed introduction of complementary feeding. Those in whom complementary feeding had started, the feeding practice was inadequate and inappropriate. Locally available and culturally accepted food items were given in dilutions with water. 77% of patients had mothers who were pure vegetarian. 73.6% mothers were also anaemic and 56% of them had vitamin B12 deficiency.

63.8% patients belonged to lower socio-economic class according to modified Kuppuswamy classification.⁴ 46% patients were immunised appropriately for age.

23% had motor and speech delay, 14.2% had isolated motor delay, 7.7% had developmental regression and 55.1% had normal development. 10% of patients had global developmental delay. Mean development quotient of patients with pre-ITS was 76% and of those with ITS was 58.4%.

Most of the patients presented with respiratory tract illnesses, ranging from mild upper respiratory tract infection to very severe pneumonia and respiratory failure. 7.7% patients had upper respiratory tract infection (URTI), 29% presented with pneumonia including 3.8% with bronchopneumonia and 27% with lobar pneumonia. 23% presented with congestive cardiac failure, 3.8% had post varicella lower respiratory tract infection (LRTI), 3.8% had viral hepatitis A and 7.7% had pyogenic meningitis.

On general examination, pallor was seen in most of all the patients with varying degree of severity, with 11.4% having some pallor and 84.6% having severe pallor. Knuckle pigmentation was seen in all patients. 15% patients had moderate acute malnutrition and 69% had severe acute malnutrition. 15.4% patients had microcephaly and 23% had hypotonia. One of the patients had scurvy, one had rickets and one had sub-acute combined degeneration of spinal cord. Macrocytic anaemia was present in 77.1% and microcytic anaemia in 26.9%. Mild to moderate iron deficiency was seen in 35.4%. All the patients had vitamin B12 deficiency with 69% having severe and 21% having moderate vitamin B12 deficiency respectively.

Neuroimaging in form of MRI of the brain and spine was performed in one patient which suggested sub-acute combined degeneration of spinal cord.

Tremors of 66% of patients subsided with treatment with vitamin B12 while for the rest, carbamazepine and/or phenobarbitone and/or both were needed to suppress tremors.

Nutritional rehabilitation of each patient was done according to standard national guidelines. Folic acid replenishment was done before starting vitamin B12 and deworming of each patient was done before starting iron therapy.

Parenteral injection of vitamin B12 was given for 5 days and then patients were discharged on oral supplements containing vitamin B12. Massive parenteral supplementation of vitamin B12 was done. Mothers were given multi-vitamin supplements containing vitamin B12. Response of patients to vitamin B12 supplementation was observed in form of improvement in appetite, increased interest in surroundings and improvement in complete blood counts. 38.4% patients required transfusion of blood. 50% patients were admitted for ≥ 14 days while 15.4% for 7 days and remaining for 7-14 days.

Improvement was noted in neurological parameters on follow up. There were total 3 expiries within first 48 hours of admission wherein very severe pneumonia and septic shock were causes of death.

DISCUSSION

ITS is a clinical state which is characterized by tremors in form of rhythmic, coarse, twitching of the angles of eye, mouth, eyelids and tongue with a tremulous cry resembling bleating of a goat, tossing movement of the head, wriggling movements of the trunk and coarse rhythmic continuous rapid movements of varying but usually of low amplitude in the extremities, most marked in the distal parts especially the fingers along with anemia, dull apathetic look, sparse scalp hair, expressionless face with drooling of saliva, pigmentation over extremities, mild hepatomegaly with or without splenomegaly, regression of mental development and hypotonia of muscles.³

It is prevalent in age group of 6 months to 3 years, with maximum number of patients belonging to age range of 6 months to 24 months, similar to our study. Males are more affected than females, with increase in incidence with increasing birth order, as was seen in our study.² It is seen mainly among children belonging to lower socio-economic group, with majority of them being malnourished and having moderate to severe anemia, correlating with this study.

Children with ITS are likely to be on breast feeding alone for prolonged periods or delayed introduction of complementary feeding or poor complementary feeding practices. It is noted that those breast fed by strict vegetarian mothers have more propensity to develop ITS.³ It is combined result of poverty, ignorance and lack of nutritional advice which was also noted in our study.²

Anemia is a prominent feature in ITS and was present in all patients of our study. Infants have also been reported with glossitis, angular cheilitis, oedema, rickets and scurvy.

ITS mainly gets precipitated by inter-current illnesses involving the respiratory system and gastrointestinal system. Majority of children with ITS are severely malnourished and have additional symptoms of anorexia, refusal to feed solid foods and spitting of food which further lead to difficult weaning.² There is no proven macro or micro nutrient causing ITS, but most studies favour role of vitamin B12 deficiency and such was also observed in our study.⁷ Corresponding with our study, low maternal serum vitamin B12 levels act as surrogate marker of infantile vitamin B12 deficiency.^{1,7} Inconclusive data are also favouring deficiencies of zinc, magnesium and calcium.^{1,8}

There are three stages of ITS on the basis of history, physical examination and follow up.

Pre-tremor stage: neuro motor regression, pallor, sometimes tremulous voice, tremor stage: sudden onset of tremors and post tremor stage: resolution of tremors.³

Tremors in ITS involve various parts of the body, mainly extremities of hands and feet. Tremors are coarse in character, decreased or disappeared in sleep. Limb muscles are usually flabby to feel, however, there is presence of extrapyramidal type of rigidity on passive movements.¹

Neuroimaging in ITS shows non-specific cerebral atrophy, dilatation of ventricles and prominence of extra cerebral spaces.² There is a possibility that these scans can revert back to normal on follow up after proper nutritional rehabilitation.^{2,3}

Treatment involves treatment of the precipitating infectious illness, nutritional rehabilitation, treatment of tremors by propranolol, carbamazepine, phenytoin, phenobarbitone. Treatment of mothers with vitamin B12 is equally important.²

Prognosis

ITS, in majority of cases, resolves within 4 to 6 weeks of its natural course.⁹ Response to treatment is seen within 48-72 hours of vitamin B12 administration. However, defects in cognitive and language skills may persist in long term with children showing catch up in neurodevelopment over several years.^{2,8}

CONCLUSION

ITS is commonly seen among infants between 6 months to 18 months of age who are exclusively breast fed for prolonged periods or not given proper complementary feeding practice. It was related with deficiency of vitamin B12 causing moderate to severe anemia. If diagnosed in early pre tremor stage, early nutritional rehabilitation gives excellent results. There is no direct evidence of specific micro or macro nutrient deficiency causing ITS hence supplementation of all essential nutrients is necessary.

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Ethical approval: The study was approved by the Institutional Ethics Committee

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