International Journal of Medical Research Professionals
P-ISSN: 2454-6356; E-ISSN: 2454-6364
DOI: 10.21276/ijmrp

IJMRP

Original Research Article.

To Study Clinical, Hematological and Neuroimaging Profile in Patients of Infantile Tremor Syndrome in a Rural Based Tertiary Care Centre

Anuj Kumar[1], (Col) D.Y. Shrikhande[2], Ekta Singh[3*], Neelanjana De[4], Shantanu Verma[3]

[1]Assistant Professor, [2]Professor and HOD, [3]Junior Resident,
Department of Pediatrics, Rural Medical College (PIMS), Loni, Ahmednagar, Maharashtra, India.
[4]Junior Resident,
Department of Pathology, Rural Medical College (PIMS), Loni, Ahmednagar, Maharashtra, India.

ABSTRACT

Background: Vitamin B12 or cobalamin deficiency is a rare and treatable cause of failure to thrive and delayed development in infants. It is especially more common in infants of vegan mothers. There is a report that every 9 out of 13 mothers are vegan. Studies suggest that the most probable etiology of infantile tremor syndrome is nutritional deficiencies including Vit B12 deficiency. The present study was conducted with the aim to study the clinical, haematological and neuro imaging profile in patients with infantile tremor syndrome amongst patients reporting to a tertiary care hospital.

Materials and Methods: The present study was carried in Rural Medical College (PIMS), Loni, Maharashtra. This descriptive cross-sectional study carried out between August 2016 – May 2017. All the patients underwent a complete hematological work-up, prior to the administration of any form of hematinics. Routine hematological tests including hemoglobin estimation, packed cell volume, reticulocyte count, platelet count, total and differential leukocyte count. The peripheral blood film was examined for red cell morphology and neutrophil hypersegmentation. All the results thus obtained were arranged in a tabulated form and analysed using SPSS software.

Results: The present study consisted of 13 subjects, out of these there were 6 males and 7 females showing female predominance. The mean age of the subjects was 11 months, with the range of 3-48 months. There were 10 patients (76.9%) who presented with knuckle pigmentation. The mean Haemoglobin was observed to be 4.6 gm/dl, with the range from 1.7 - 5.9 gm/dl. Mean Vitamin B12 level was 385.84 pg/ml with minimum Vitamin B12 level being 159 pg/ml and maximum Vitamin B12 level being 1000 pg/ml.

Conclusion: From this study we can conclude that there is association of Infantile tremor syndrome with Vitamin B12 deficiency, as more than 50% of patients in this study had features of megaloblastic anemia.

Keywords: Anaemia, Cobalamin, Tremor.

***Correspondence to:**

Dr Ekta Singh,
Junior Resident, Department of Pediatrics,
Rural Medical College (PIMS),
Loni, Ahmednagar, Maharashtra, India.

Article History:

Received: 02-10-2017, **Revised:** 24-10-2017, **Accepted:** 09-11-2017

Access this article online	
Website: www.ijmrp.com	Quick Response code
DOI: 10.21276/ijmrp.2017.3.6.013	

INTRODUCTION

Vitamin B12 or cobalamin deficiency is a rare and treatable cause of failure to thrive and delayed development in infants. It is especially more common in infants of vegan mothers. There is a report that every 9 out of 13 mothers are vegan. This causes low stores of vitamin B12 in the infant at birth and inadequate amounts of the vitamin in breast milk. Since the only food source of infants is breast milk, deficiency occurs easily. Signs and symptoms of vitamin B12 deficiency usually appear between the age of 4 and 12 months and include macrocytic anemia, weakness, fatigue, failure to thrive and irritability.[1,2] Other common findings include glossitis, vomiting, diarrhea etc. Few cases also exhibit Infantile Tremor Syndrome. Favourable response is achieved via vitamin B12 therapy, and particularly neurological symptoms improve in a few days after the treatment. Thus, complete blood count, serum vitamin B12 levels, and imaging should be performed, and vitamin B12 supplementation should be started immediately. But there is variation in response to therapy, some patients still remain mild to moderately retarded.[3,4] Infantile tremor syndrome is a syndrome characterized by megaloblastic anemia, skin pigmentation, tremors, physical and mental regression. It has been reported in children between 5 months and 3 years of age with a male predominance. The exact incidence of ITS is not available. However, in various studies 0.87- 1.55 % hospital admissions were due to ITS.[5] The exact etiopathogenesis of this condition remains obscure. Studies suggest that the most probable etiology of infantile tremor syndrome is nutritional deficiencies including Vit

B12 deficiency. Despite predominance of neurological symptoms, very few studies have documented neuroanatomical and/ or neurophysiological changes in infantile tremor syndrome.[6] Reduced brain substance has been documented in children with infantile tremor syndrome. Improvement in nutritional status, living condition and better weaning practices could explain the reducing incidence rates over the years. It has been primarily reported from India and South East Asia countries in Asia and Africa.[7] The present study was conducted with the aim to study the clinical, haematological and neuro imaging profile in patients with infantile tremor syndrome amongst patients reporting to a tertiary care hospital.

MATERIALS AND METHODS

The present study was carried in Rural Medical College (PIMS), Loni, Maharashtra. This descriptive cross-sectional study carried out between August 2016 – May 2017. The study included total of 13 subjects. The study was approved by the Institutional ethical committee and all the subjects were informed about the study and a written consent was obtained from all in their vernacular language. In this study the type of anaemia and levels of folic acid and cobalamine was given special emphasis. Patients aged between 6 months to 5 years with infantile tremor syndrome were included in the study. All the patients with any other chronic illness like tuberculosis were excluded from the study. Patients with malaria were also excluded from the study. The diagnosis of megaloblastic anaemia was obtained by both clinical and laboratory findings. A complete detail of clinical presentations of all the patients was obtained. All the patients underwent a complete hematological work-up, prior to the administration of any form of hematinics. Routine hematological tests including hemoglobin estimation, packed cell volume, reticulocyte count, platelet count, total and differential leukocyte count. The peripheral blood film was examined for red cell morphology and neutrophil hypersegmentation by methods recommended by Dacie and Lewis. Folate was estimated by a microbiological assay using L. casei. Vitamin B12 was also determined by a microbiological assay using Euglena gracilis. All the results thus obtained were arranged in a tabulated form and analysed using SPSS software.

RESULTS

The present study consisted of 13 subjects, out of these there were 6 males and 7 females showing female predominance. The mean age of the subjects was 11 months, with the range of 3-48 months. There were 10 patients (76.9%) who presented with knuckle pigmentation. All the patients had pallor. Regression of milestones was seen in 3 patients (23%). Table 1 shows the aggregate results of the study.

The mean Haemoglobin was observed to be 4.6 gm/dl, with the range from 1.7 - 5.9 gm/dl. Severe anemia (Hb < 6gm/dl) was seen in all 13 patients. The mean MCV was observed to be 88.4 fl. Above normal MCV (normal MCV= 76-90fl) was seen in 7 patients (53.8%). In PBS picture, hypersegmented neutrophils were seen in 2 patients (15.3) and macrocytes were seen in 9 patients (69%). In 2 patients (15.3%), dimorphic PBS picture was seen.

Mean serum folic acid level was 12.7 ng/ml with minimum folic acid level being 2.2 ng/ml and maximum folic acid level being 20 ng/ml. Below normal levels (normal range=5-21ng/ml) seen in 3 patients (23.07%).

Mean Vitamin B12 level was 385.84 pg/ml with minimum Vitamin B12 level being 159 pg/ml and maximum Vitamin B12 level being 1000 pg/ml. Patients with levels 1000pg and above were already on B12 supplementation before admission to our centre. Below normal Vitamin B12 level (normal range=200-500 pg/ml) was seen in 7 patients (53.85%)

CT scan study showed cerebral atrophy in 7 patients (53.8%), subdural hygroma in 2 patients and rest of the 4 patients were normal.

DISCUSSION

The current study reveals that vitamin B12 deficiency was present in 7 out of 13 infantile tremor syndrome cases. Two out of the cases had normal levels of Vit B12 as they were already under treatment by private practitioners which could explain the normal levels obtained. Majority of the infantile tremor syndrome cases had manifestations of megaloblastic anemia with subnormal levels of vitamin B12. Some had neutrophilic hypersegmentation in the peripheral blood smear. A classical picture of infantile tremor syndrome (ITS) is an infant between 6 to 18 months with presence of malnutrition. Usually these children are listless, apathetic and disinterested in surroundings. Scalp hair is sparse and light colored. Dark pigmentation is present over dorsal aspects of hands, nail folds, feet, knees, ankles, buttocks and axilla. There is regression of milestones in the recent past. Tremors have an acute onset following an acute infection or stress.[8] Initially they are intermittent but become continuous in a few days. They are more prominent in distal parts of the limbs, head, face and tongue. These tremors disappear during sleep. There is presence of anemia, which is usually macrocytic, but maybe dimorphic, microcytic or normocytic.[9,10] The etiology of ITS is still elusive. Vit. B12 deficiency has been found to be associated in many studies. It is usually seen in children who are exclusively breast-fed for prolonged periods by vegan mothers. The low levels of vitamin B12 and its transport protein Transcobalamine II (TC II) in the cerebrospinal fluid (CSF) may be responsible for the neurological features of this syndrome.[11] Iron, Magnesium and zinc deficiency have also been postulated to cause ITS. It is usual to find direct or indirect evidence of associated other nutritional deficiencies like protein, vitamin A, D, K and other micronutrients. Other speculations for its etiology include viral encephalitis and degenerative processes.[12] Vitamin B12 levels in mother may also be low suggesting low levels in the breast milk. Serum levels of zinc, ascorbic acid and magnesium may be low.[13] Cortical atrophy and prominence of subarachnoid space and ventricular system are the commonest findings in CT/ MRI of brain, and were seen in our cases.[14,15] Treatment consist of therapy for anemia and nutritional deficiency. Vitamin B12 in high doses may be required if B12 levels are low. Multivitamins, Vitamin C, iron may be necessary. For severe tremors phenobarbitone (3-5 mg/kg/day) may be required to decrease the intensity.[16,17] The tremors subside slowly. Initially there is gradual reduction in the amplitude and severity, then the tremors become intermittent and finally stop. Propanolol and chlorpromazine are other drugs which can be used to control tremors.[18,19] In a case study by Kocaoglu C et al, they concluded that deficiency of vitamin B12 should be considered as an etiological factor for neurological syndromes.[20]

Table 1: Showing the compiled data of the study.

Name	Age	Sex	C/F	Hb gm%	MCV 76-90 fl	PBS	Sr.folic acid 5-21ng/ml	Sr. B12 200-500pg/ml	CT Scan
Case 1	4m	F	Pallor, Knuckle Pigmentation	3.0	111.76	Macrocytic Hypochromic	20	159	Cerebral atrophy
Case 2	8m	M	Pallor, Knuckle Pigmentation	5.9	91.8	Macrocytic, Anisocytosis, Poikilocytosis, Severe thrombocytopenia, leukopenia	13.4	185	Subdural Hygroma
Case 3	3m	M	Pallor, knuckle pigmentation	3.2	96.5	Macrocytic Hypochromic	4.3	159	Cerebral atrophy
Case 4	5m	M	Pallor, Knuckle Pigmentation, Tremor	4.3	91.8	Macrocytes, few Schistocytes present, few microcytes	13.6	210	Normal
Case 5	8m	F	Knuckle pigmentation, Pallor, Delayed Milestones	1.7	74.5	Microcytic Hypochromic, Tear drop cells	16.5	159.0	Subdural hygroma in fronto-parieto temporal region on both sides
Case 6	10m	F	Pallor, Knuckle pigmentation	4.4	88.2	Macrocytic Hypochromic, Hyper segmented neutrophils	10.1	235	Cerebral atrophy
Case 7	8m	M	Pallor, Knuckle pigmentation, Tremors, Milestone Regression	5.2	96	Macrocytic Hypocromic, thrombocytopenia	20	1000	Cerebral atrophy
Case 8	11m	F	Knuckle pigmentation, Pallor	4.7	69.4	Macrocytic Hypochromic	15.5	1000	Normal
Case 9	11m	F	Knuckle pigmentation, Pallor	4.4	107	Macrocytic Hypochromic	2.2	162	Cerebral atrophy
Case 10	8m	F	Pallor, Delayed milestones	9.7	91.7	Normocytic, Hypochromic	3.6	170	Normal
Case 11	8m	F	Knuckle pigmentation, Severe Pallor	3.6	86.5	Macrocytic hypochromic , Hypersegmented neutrophils	20	159	Cerebral atrophy
Case 12	15m	M	Pallor	5.0	52.2	Diamorphic picture	9.13	675	Cerebral atrophy
Case 13	4yrs	M	Severe pallor	5.0	51.8	Diamorphic picture	9.4	743	Cerebral atrophy

CONCLUSION

From this study we can conclude that there is association of infantile tremor syndrome with Vitamin B12 deficiency, as more than 50% of patients in this study had features of megaloblastic anemia. Cerebral atrophy was the common CT-scan finding in majority of the cases.

REFERENCES

1. Sachdev HPS, Shah D. Vitamin B12 (Cobalamin)... In: Kliegman RM, Stanton BF, St. Geme JW, 3rd, Schor NF, Behrman RE, editors. Nelson textbook of pediatrics. 19th ed. Philadelphia, PA: Saunders, 2011:197-8.

2. Chalouhi C, Faesch S, Anthoine-Milhomme M-C, Fulla Y, Dulac O, Cheron G. Neurological consequences of vitamin B12 deficiency and its treatment. Pediatr Emerg Care 2008;24:538-41.

3. Graham SM, Arvela OM, Wise GA. Long-term neurologic consequences of nutritional vitamin B12 deficiency in infants. J Pediatr 1992;121(Pt 1):710-4.

4. von Schenck U, Bender-Götze C, Koletzko B. Persistence of neurological damage induced by dietary vitamin B-12 deficiency in infancy. Arch Dis Child 1997;77:137-9.

5. Gupte S, Pal M, Gupta SK, Sangra KR. Infantile tremor syndrome (ITS). In Gupte S, ed. Textbook of Paediatric Nutrition. New Delhi. Peepee 2006; 255-65.

6. Ghai OP, Gupta P. Infantile tremor syndrome. In: Ghai OP, Gupta P, Paul VK, eds. Ghai Essential Paediatrics 6th edn. New Delhi Dr. Ghai 2005; 539-40.
7. Grattan-Smith PJ, Wilcken B, Procops PG, Wise GA. The neurological syndrome of infantile cobalamin deficiency: developmental regression and involuntary movements. Mov Disord 1997;12: 39–46.
8. Rasmussen AS, Fernhoff PM, Scanlon KS... Vitamin B12 deficiency in children and adolescents. J Pediatr 2001;138:10–17.
9. Graham SM, Arvela OM, Wise GA. Long-term neurologic consequences of nutritional vitamin B 12 deficiency in infants. J Pediatr 1992;121:710–4.
10. Emery ES, Homans AC, Colleti RB. Vitamin B 12 deficiency: a cause of abnormal movements in infants. Pediatrics 1997; 99: 255–6.
11. Ozer EA, Turker M, Bakiler AR, Yaprak I, Ozturk C. Involuntary movements in infantile cobalamin deficiency appearing after treatment. Pediatr Neurol2001;25:81–3.
12. Pohowalla JN, Kaul KK, Bhandari NR, Singh SD. Infantile meningoencephalitic syndrome. Ind J Pediat 1960:27:49-54.
13. Jadhav M, Webb JKB, Vaishnava S, Baker SJ. Vitamin B, deficiency in Indian Infants: a clinical syndrome. Lancet 1962; ii: 903-8.
14. Sachdeva KK, Manchanda SS, Lai H. The syndrome of tremors, mental regression and anaemia in infants and young children: A study of 102 cases. Ind Pediat 1965; 2: 239-51.
15. Bajpai PC, Misra PK, Tandon PN. Further observations on infantile tremor syndrome. Ind Pediat 1968; 5: 297-307.
16. Desphande TV, Ingle VN. Tremor syndrome in children. Ind Pediat 1969; 6: 550-6.
17. Ramakumar L, Pandava SP. Infantile tremor syndrome. Ind J Pediat 1975; 42: 215-25.
18. Frader J. Reibman B, Turkewitz D. Vitamin B12 deficiency in strict vegetarians. N Engl J Mcd 1978; 299: 1319.
19. Davis JR, Goldenring J, Lubin BH. Nutritional vitamin B12 deficiency in infants. Am J Dis Childh 1981; 135: 566-7.
20. Kocaoglu C, Akin F, Çaksen H, Böke SB, Arslan Ş, Aygün S. Cerebral atrophy in a vitamin B12-deficient infant of a vegetarian mother. Journal of health, population, and nutrition. 2014 Jun;32(2):367.

Source of Support: Nil.

Conflict of Interest: None Declared.

Cite this article as: Anuj Kumar, (Col) D.Y. Shrikhande, Ekta Singh, Neelanjana De, Shantanu Verma. To Study Clinical, Hematological and Neuroimaging Profile in Patients of Infantile Tremor Syndrome in a Rural Based Tertiary Care Centre. Int J Med Res Prof. 2017 Nov; 3(6):63-66.
DOI:10.21276/ijmrp.2017.3.6.013