Journal of Cardiovascular Disease Research

ISSN:0975 -3583,0976-2833 VOL 15, ISSUE 08, 2024

Original research article

Infantile tremor syndrome: Serum vitamin b12, magnesium and zinc levels

[1]Dr. Shridhar Shellikeri, [2]Dr. Lakshmi K, [3]Dr. Md. Altaf Attar, [4]Dr. Shivakumar Indi

[1]Pediatrician, Ovum Hospital, Banashankari, Bengaluru, Karnataka, India

[2]Senior Resident, Department of Pediatrics, BMC & RI, Bellary, Karnataka, India

[3]Senior Resident, Department of Pediatrics, YIMS, Yadgir, Karnataka, India

[4]Senior Resident, Department of Pediatrics, Al-Ameen Medical College, Vijayapur, Karnataka, India

Corresponding Author:
Dr. Md. Altaf Attar

Abstract

An obscure entity, characterized by anemia, developmental delay or regression, skin pigmentation, hair changes with or without tremors in infants and young children, was termed infantile tremor syndrome (ITS). This disorder is seen among exclusively breast-fed infants among the mothers who are vegetarian. In the scenario of limited resources to access advanced biomarkers of B12 deficiency a profile of the trace elements and haematological indices to conclusively diagnose this syndrome. This study was planned to determine the proportion of patients with infantile tremor syndrome having low serum levels of trace elements (Vitamin B12, Magnesium, Zinc) in conjunction with hematological indices compared to that of healthy children. This was an Analytical cross-sectional study involving Children admitted pediatric ward. Serum vitamin B12 levels of baby, serum homocysteine and Zinc & Magnesium levels of the baby had been estimated in this current study. Mean vit. B12 levels was (155.48±121.38) significantly lower in babies of ITS group than that of controls (354.04±37.03) (0.014), mean homocysteine levels was (52.56±17.75) significantly higher in babies of ITS group than that of controls (29.19±18.81) (<0.0001).

Keywords: Vitamin B12, magnesium, zinc

Introduction

During current beyond, it has been located that not all toddlers with ITS be afflicted by megaloblastic anaemia fact, a few do no longer have it at all even as others show dimorphic anaemia. There are cases who have purely iron-deficiency anaemia. Moreover, even those suffering from megaloblastic anaemia may need folic acid alone or in combination with vitamin B12 for adequate response. At the same time, babies without megaloblastic anaemia, won't need vitamin B12 and folic acid and yet evince therapy with correction of iron deficiency anaemia and improvement within the universal nutritional fame [1].

Even magnesium deficiency has been blamed as every other viable etiologic thing. It has been found that reduced magnesium in chronic fatigue syndrome (CFS) of infants suffering from ITS. Tremors and rigidity, among other neurologic manifestations, are known to result from such deficiency. How a ways magnesium lack contributes to the development of ITS is difficult to mention. Zinc deficiency in body tissues and fluids is also documented. In view of presence of anaemia, pigmentation, hair changes, tremors and mental lethargy, role of zinc deficiency in its etiology appears quite probable [2].

The presence of pallor, skin and hair modifications, and dull apathetic look that the infants with ITS exhibit is quite reminiscent of kwashiorkor. In an ordinary scenario, affected infants' appearance plump with preserved subcutaneous fats. Others have pronounced failure to thrive and wasted or marasmic appearance [3].

In any case, growth parameters are normal at birth and for the first 5-6 months of age. Later growth faltering takes place due to insufficient feeding caused by endured exclusive breastfeeding. Refusal to solid ingredients, anorexia, and intercurrent infections further aggravate the dietary imbalance. In addition to anemia, toddlers with ITS frequently happen to have more than one micronutrient deficiencies in the form of angular cheilitis, stomatitis, and glossitis. Rickets, scurvy and edema have additionally been suggested as Vitamin A deficiency [4].

Tremors are the one of the most characteristic features of ITS allowing instant recognition of the syndrome by the experienced clinicians. Tremors are generally absent early in the course of illness, the pre-ITS stage. The onset of tremors is preceded or accompanied by some stress in the form of acute

ISSN:0975 -3583,0976-2833 VOL 15, ISSUE 08, 2024

lower respiratory infection (ALRI) or gastroenteritis. Tremors tend to be coarse and have jerky (myoclonus-like) character. Onset is usually focal from one of the upper extremities with rapid progression to generalized involvement. Sudden onset of generalized tremors is not uncommon. Even when generalized, tremors have asymmetric and multifocal appearance. Involvement of facial, labial, lingual, and laryngeal musculature is an unmistakable sign of ITS [5, 6].

Methodology

Inclusion Criteria

Children aged 6 months to 3 years clinically diagnosed as having infantile tremor syndrome, defined as having

1. Pallor.
2. Developmental delay/Regression.
3. Skin Hyperpigmentation.
4. Scanty depigmented scalp hair.
5. With/without tremors.

Exclusion Criteria

1. If an alternative diagnosis was confirmed.
2. Children who had received a blood transfusion in the previous one month Children who had received nutritional supplements in the previous one month.

After application of inclusion and exclusion criteria to the study population, Data will be collected in predesigned pre-structured proforma, later correlated with clinical, laboratory parameters.

Detailed history was elicited where Mothers were asked about the complaints with which child was brought to the hospital with special emphasis given on diet history of the child. If the child was exclusively breast fed diet history of the mother was asked and looked upon for calorie and protein deficit. Detailed developmental history of the child was elicited so as to label the child of having either normal, delayed or regression of milestones. Also the socioeconomic status, maternal educational status was also documented as it will help in assessing the level of nutrition the child was provided and the level of care that the child received.

Child was mainly examined for signs of Vitamin B12 deficiency like hyper pigmentation of skin, sparse hairs and presence of any involuntary movements after noting down all the VITALS. Anthropometry measurements were noted and child nourishment status was categorized based on WHO classification. Also standard deviation of head circumference was also noted. Detailed neurological examination was done to assess for tone, power, reflexes. Normal development of these children will be assessed using a screening tool (Trivandrum Developmental Screening Chart). Other system pertaining to the child's chief complaints was also examined in detail.

Results

Figure 1 shows age distribution, in our study 92% of children were 6-12 months of age & 8% were 13-24 months of age.

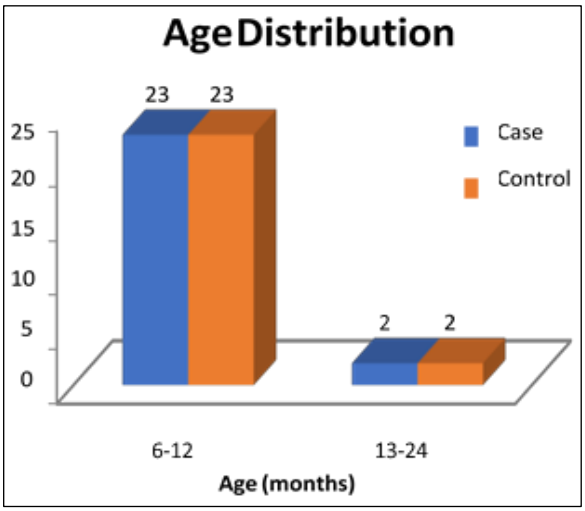

Fig 1: Age Distribution

ISSN:0975 -3583,0976-2833 VOL 15, ISSUE 08, 2024

Table 1: Education Status Distribution

Education	Case		Control	
	N	%	N	%
Illiterate	2	8.00	1	4.00
Primary	13	52.00	7	28.00
High school	9	36.00	10	40.00
PUC	1	4.00	4	16.00
Degree	0	0.00	3	12.00
Total	25	100.00	25	100.00

Table 3 & figure 20 shows education distribution, 52%, 36%, 4% were studied till primary school, high school, PUC, degree respectively in our study group.

Table 2: Socioeconomic Status

SES	Case		Control	
	N	%	N	%
Lower	19	76.00	4	16.00
Lower upper	4	16.00	6	24.00
Lower middle	0	0.00	6	24.00
Upper middle	2	8.00	7	28.00
Upper	1	4.00	2	8.00
Total	25	100.00	25	100.00

Table 2 shows socio economic status distribution, in our study 76% were lower class, 16% were lower upper, 4% were upper middle class.

Table 3: Serum Homocystiene Levels

S. Homocysteine	Case		Control	
	N	%	N	%
<30 (Normal)	3	12.00	14	56.00
≥30	21	84.00	11	44.00
Total	24	96.00	25	100.00

Chi square 10.22, P value 0.001 (S)

Table 4: S. Zinc level levels

S. Zinc (52-286mcg/dl)	Case		Control	
	N	%	N	%
<52	3	12.00	3	12.00
52-286	21	84.00	22	88.00
>286	1	4.00	0	0.00
Total	25	100.00	25	100.00

Chi square 1.023, P value 0.599 (NS)

Table 5: S. Magnesium Level Levels

S. Magnesium (1.90-3.10)	Case		Control	
	N	%	N	%
<1.90	8	32.00	0	0.00
1.90-3.10	16	64.00	23	92.00
>3.10	1	4.00	2	8.00
Total	25	100.00	25	100.00

Chi square 9.590, P value 0.008 (S)

Table 6: S. Vitamin B12 Value Levels

Vit. B12 (211-911pg/dl)	Case		Control	
	N	%	N	%
<211	19	76.00	7	28.00
211-911	6	24.00	17	68.00
>911	0	0.00	1	4.00
Total	25	100.00	25	100.00

Chi square 11.79, P value 0.002 (S)

Discussion

Our study was conducted on 25 infants of which males were 13(52%) and females were 12(48%) which

ISSN:0975 -3583,0976-2833 VOL 15, ISSUE 08, 2024

shows slight male predominance comparable with studies conducted by Sachdev *et al*. shows male to female ratio of 3:2. Sharda *et al*. showed 75% male and 25% were female children. Deeksha *et al*. showed female predominance. Some studies showed equal incidence among male and female children. The possible reason for male predominance is prolonged breastfeeding beyond 6 months as compared to female child in Indian scenario.

Also the mean age of presentation of ITS has been noted to be 11.4+_4.1 months which is almost similar to the other studies compared with. Vykuntraju *et al*. [7], found 82.8%, Bajpai *et al*. found 94.1% and Sachdev *et al*. found 89.2% children between 6 and 18 months. All the studies included for the comparison in the above table are prospective studies. The reason for this age of presentation may be improper introduction of complementary food and predominant breastfeeding; large number of malnourished individuals were also seen in this age group.

In our study 80% of affected children belongs to lower class SES compared to control group were they majority belongs to upper and lower middle class comparable with study done by vykuntraju *et al*. 70% of cases belongs to lower SES class. Bajpai *et al*. showed all seventy nine cases (100%) belongs to lower SES. However L.S Arya *et al*. showed that out of nine cases only two belongs to lower SES. Lower SES will directly impact nutritional status of the family hence the child [8].

According to a similar study done by savage *et al*. noted that there was high sensitivity of serum Mma and Hcy in diagnosisng vitamin B12 deficiency. The combined sensitivity of Hcyand Mma in diagnosing Vitamin B12 deficiency was noted to be 99.8% [9].

Ueland *et al*. in his study noted that newborns and infants there was elevated levels of Mma and or Hcy levels who were born to cobalamin deficient mothers and were exclusively breastfed. The increase in these metabolites indicate low cobalamin stores and impaired function of cobalamin in the tissues. Few studies also have mentioned that elevation of these above mentioned metabolites in infants may be an innocuous process which may not be related to cobalamin deficiency but may be due to the enhanced production of Mma by intestinal microorganisms and formation of Mma from odd chain fatty acids present in human breast milk. These elevated levels once formed may be slowly cleared from the infant's body due to immature enzymes or the organ systems.

Styler *et al*. mentioned that measurement of Mma, Hcy or both of them are very useful in making diagnosis of vitamin B12 deficiency who have not received treatment. Both these metabolites are widely elevated in majority of the cases >98% with clinical Vitamin B12 deficiency which includes those who have only neurological manifestations of deficiency (But no anaemia). Elevated levels of these metabolites will decrease once started on treatment with Vitamin B12 which can be documented by remeasuring the levels of these metabolites. In 50% of cases these metabolites levels may be normal even if the vitamin B12 levels are low indicating that these low values are false positive results. The elevations of Hcy levels are comparatively less sensitive when used alone since its levels tends to be elevated in folate deficiency, classic homocystinuria and renal failure [10].

In a study showed that Vitamin B12 deficiency was more prudent than folate deficiency in case of ITS. Chhabra *et al*. in 2012 concluded that nutritional deficiency of vitamin B12 occurs commonly in malnourished children with common age group being 3-18 months. These children are exclusively breast fed by mothers who also have poor nutritional intake. Yakhouba *et al*. On assessment of iron, folate and vitamin B12 concluded that prevalence of Vitamin B12 deficiency was more among children with SAM.

Conclusion

1. In children Serum Vitamin B12 levels were lower among 76% of cases with 84% cases having elevated serum homocysteine levels.
2. S. Zinc level found low in 12% cases and magnesium level in 32% cases. There was no significant correlation found between these levels with causation of ITS.

References

1. Mohammad Amin NM, Mohammad Zeki J. Infantile tremor syndrome in Iraqi Kurdistan. Indian Journal of Pediatrics. 2005;72(10):839-42.
2. Gupta R, Rawat AK, Singh P, Gupta J, Pathak A. Infantile tremor syndrome: current perspectives. Research and reports in tropical medicine; 2019 Jul. p. 103-8.
3. Kumar S, Sah S, Ray P, Bhattacharya P, Chatterjee N. Infantile Tremor Syndrome with Movement Disorder: Current Perspective. Cureus; 2022 Dec, 14(12).
4. Chopra D, Aulakh S, Garg A, Garg A. Infantile tremor syndrome, often overlooked diagnosis in dermatology. Indian Journal of Pediatric Dermatology. 2022 Apr;23(2):156-8.
5. Cyr A, Frehlick R, Stammers D, Crone M. Case Report: Propranolol Therapy for Infantile Tremor Syndrome in a Child With Vitamin B12 Deficiency. Frontiers in Pediatrics; 2021. p. 1321.
6. Mahajan CM, Walia BN, Dutta BN. Infantile tremor syndrome-some aspects of serum biochemistry and liver histology. Indian Pediatrics. 1971 Dec;8(12):831-3.
7. Gowda VK, Kolli V, Benakappa A, Srinivasan VM, Shivappa SK, Benakappa N. Case series of infantile tremor syndrome in tertiary care paediatric centre from southern India. Journal of Tropical

ISSN:0975 -3583,0976-2833 VOL 15, ISSUE 08, 2024

Pediatrics. 2018;64(4):284-8.
8. Bajpai PC, Tandon PN, Sharma NL, Misra PK. Infantile tremor syndrome. Acta Neurol Scand. 1965;41:473-86.
9. Amin NM, Zeki JM. Infantile tremor syndrome in Iraqi Kurdistan. The Indian Journal of Pediatrics. 2005 Oct;72:839-42.
10. Bhagwat C, Sankhyan N. Vitamin responsive conditions in pediatric neurology. Karnataka Paediatric Journal. 2021 Jun;36(1):42-8.