ORIGINAL RESEARCH PAPER
Volume - 10 | Issue - 01 | January - 2021 | PRINT ISSN No. 2277 - 8179 | DOI : 10.36106/ijsr
INTERNATIONAL JOURNAL OF SCIENTIFIC RESEARCH

IRON DEFICIENCY ANEMIA AND ITS EFFECT ON NEURO DEVELOPMENT IN CHILDREN OF AGE GROUP LESS THEN 2 YEARS

Paediatrics

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ABSTRACT

Micronutrient deficiencies are still a major public health problem in the world today with an estimated 2.5 - 5 billion people so affected and specially in developing countries with infants and pregnant women especially at risk.In the milder form anemia is silent without symptoms , while in the severe cases it is associated with fatigue, weakness, dizziness and drowsiness.

Infants wants extra concern as iron is actively transferred from mother to fetus during pregnancy, the maximal time of transfer being during the third trimester. Among the various biological effects of iron, there is considerable evidence that iron is also important for neurological functioning and development.

The biological basis of the behavioural and congnitive developmental delays observed in iron deficient infants is not completely understood, but possibly include (i) abnormalities in neurotransmitters metabolism , (ii) decreased myelin formation (iii) alteration in brain energy metabolism

Aims And Objective-To know the common complications of iron deficiency. To detect the cognitive, motor, and social-emotional function and effect on it due to iron deficiency and to assess them by "TRIVANDRUM DEVELOPMENT SCREENING CHART".

Material And Methods: It will be a prospective hospital based study. All suspected cases of iron deficiency anemia in children less the 2 years admitted in SIMS hospital will be considered for the study The diagnosis of iron deficiency anemia depends upon the clinical examination with subsequent laboratory confirmation.

To examine the effect of iron deficiency on neurodevelopment we will use "TRIVANDRUM DEVELOPMENT SCREENING SCORE"

RESULT AND CONCLUSION: It was found in our study that incidence was more in those children who were delivered pre-maturely.

Correlation of Trivendram development milestone score with blood parameters. Haemoglobin in normal group were 9.83±0.56, whereas in abnormal group it was 6.29±1.63, it was statistically significant, there was significant difference between serum iron TIBC and Transferrin saturation .

KEYWORDS

Iron def. anemia, Trivandrum development screening chart, Neurodevelopment

INTRODUCTION

Iron deficiency affects lives of more than 1.2 billion people worldwide. Most of them involve women, children, and infants. Studies are going on to document the effects of iron-deficiency anemia on developmental delays in young children and infants [1].In most of the studies which are performed across the world with varying degree of success clearly show that in nearly all situations iron deficiency is a preventable disease with preventable consequences. One such consequence is alteration in cognition that occurs in iron-deficient persons at the early parts of their life and perhaps at later times as well. The distribution of iron in the brain is quite heterogeneous, a characteristic of most species in whom region brain iron concentrations have been determined. Iron in brain is found mostly in the nucleus accumbens, substantia nigra, deep cerebellar nuclei, the red nucleus, and portions of the hippocampus. Hill[2] noted great similarity in the brain iron distribution and brain regions that receive input from ° -aminobutyric acid(GABA) fibers and also are predominately dopaminergic brain regions.

There are different types of cells in brain with different activities ,and so it is not surprising that iron distributions are sensitive to stages of neurodevelopment, metabolic activity and neurodegenerative pathologies.

These studies on brain iron function can be divided into those that focus on

(*a*) *oligodendrocyte metabolism* and myelination,
(*b*) *monoamine metabolism, and*
(*c*) *GABA metabolism.*

(*a*) *oligodendrocyte metabolism* and myelination- Iron is important for myelination of the spinal cord. It is also important for white matter of cerebellar folds , it also acts as a cofactor for a number of enzymes involved in neurotransmitter synthesis, namely tryptophan hydroxylase and tyrosine hydroxylase[3].It also has role in catabolism of these neurotransmitters. It also acts as a cofactor for ribonucleotide reductase, the rate-limiting step in DNA synthesis. The predominant cell type containing iron in the human brain is oligodendrocyte[3]. Oligodendrocytes are responsible for the myelination and hence alterations in the function of these cells is associated with hypomyelination.

Monoamine metabolism- Levels of monoamines are sensitive to variations in brain iron status . Dopaminergic tracts appear to be consistently sensitive to regional brain iron deficiency. Earlier studies by Youdim and colleagues demonstrated lower densities of dopamine D2 receptors in the striatum of rats, recent studies demonstrate that nucleus accumbens is also sensitive to the effects of iron deficiency. In addition, the DA transporter density is significantly diminished in striatum and nucleus accumbens, both terminal fields of neurons originating in the substantia nigra and ventral tegmentum . Microdialysis studies demonstrate that extracellular dopamine is elevated in striatum of iron-deficient rats and returns to normal levels when brain iron content and iron status return to normal .

These observations provide some biological clues regarding the causes of poor attention in iron-deficient infants

(c) GABA metabolism- Iron deficiency in utero and postweaning is associated with significant decreases in glutamate decarboxylase, glutamate dehydrogenase, and GABA transaminase activities.

These latter two enzymes are shunt enzymes responsible for the synthesis and degradation of GABA. Concentrations of GABA are elevated in dietary iron deficiency in hippocampus, striatum, and globus pallidus, and may be related to alterations in brain manganese metabolism.

NEURODEVELOPMENT- A study by French scientists working in Niger examined this relationship.Pregnant women in the second

trimester were randomized to receive either 100 mg elemental Fe throughout the remainder of their pregnancies or a placebo. As expected, iron treatment reduced iron deficiency markedly. Importantly, three months after delivery, serum ferritin concentrations were significantly higher in infants of women in the iron-supplemented group and their neurodevelopment was significantly better than the infants of placebo-treated mothers. A longer-term study of the relationship of maternal iron status and infant neuro development and functioning has recently been published.

The authors evaluated the association of fetal iron status (umbilical cord serum ferritin concentrations) with test scores of mental and psychomotor development at two years of age. Those children in the lowest quartile scored lower on tests of cognition and had significantly worse language ability, fine-motor skills, and tractability than infants in the highest two quartiles.

MATERIAL AND METHODS:

It was a prospective hospital based study. All suspected cases of iron deficiency anemia in children less the 2 years admitted in SIMS hospital were considered for the study.

The diagnosis of iron deficiency anemia depends upon the clinical examination with subsequent laboratory confirmation.

To examine the effect of iron deficiency on neurodevelopment we used

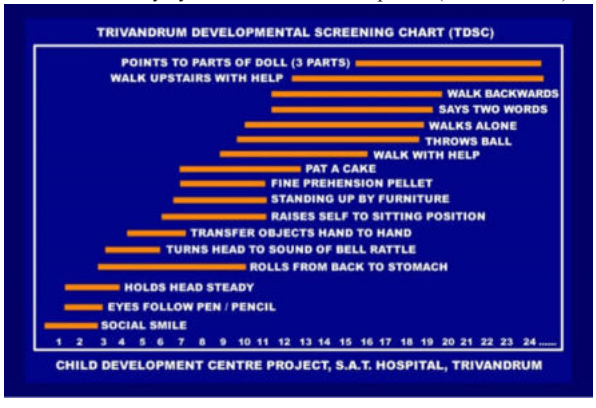
"TRIVANDRUM DEVELOPMENT SCREENING SCORE"

Lab investigations conducted were-
(A) Hemoglobin and hematocrit-
(B) Complete blood count, or CBC –
(C) Peripheral smear-
(D) Iron studies –

TRIVANDRUM DEVELOPMENT SCREENING CHART

It is suitable for development screening of children below 2 years . The range of each test item has been taken from the norms obtained on the Bayley scales of infant development.

It is based on 17 simple test items carefully chosen from among 67 motor items of Bayley scales of infant development.(Baroda norms)



Study Population- A total of 80 children consisiting of term ,preterm babies less then 2 years of age,who were admitted in SIMS Hospital.

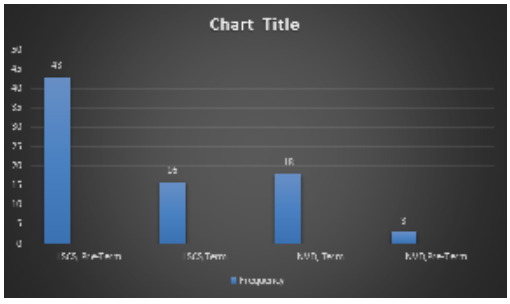
SELECTION OF CASES:

Inclusion Criteria:
All suspected cases of iron deficiency anemia in children less then 02 years of age.

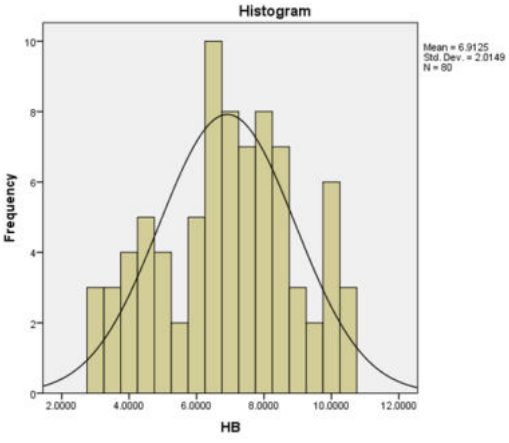
Exclusion Criteria:
Cases presented with other types of anemia like megaloblastic, hemolytic,sickle cell anemia or thallassemias. Children with other syndromes or CNS abnormality

Stastical Analysis
All data was collected and verified. Collected data was subjected to EPINFO 7.0 and Microsoft excel for analysis. Data was expressed as frequencies and mean the parameters, Chi-square and t test was performed to visualize the difference .P value<0.05 was considered significant

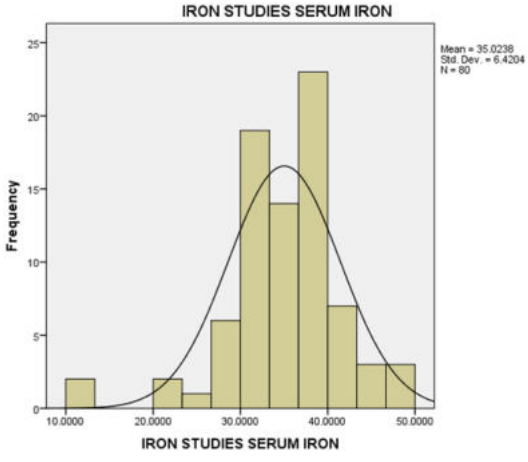
RESULT-



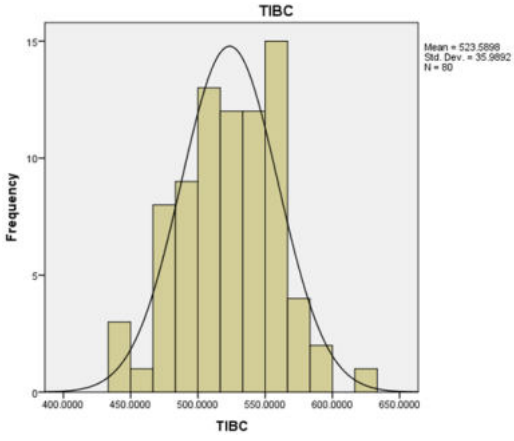
MODE OF BIRTH

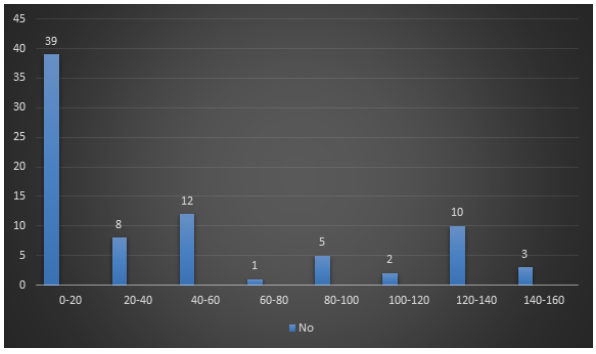


HAEMOGLBIN CONCENTRATION

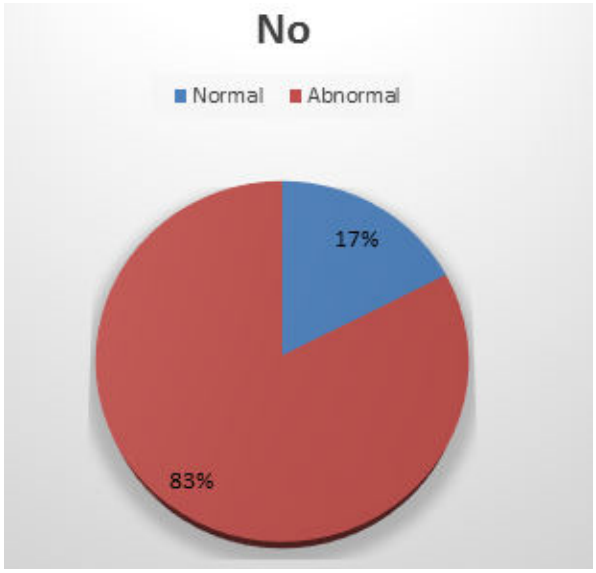


SERUM IRON





Distribution Of Study Subjects As Per Serum Ferritin



Distribution Of Study Subjects As Per Trivandrum Development Milestone Score

Blood Parameter	Trivandrum Development Score		P value
	Normal	Abnormal	
Haemoglobin	9.83±0.56	6.29±1.63	<0.001
Serum Iron	39.33±5.52	34.11±6.26	0.005
TIBC	496.57±23.71	529.32±35.65	0.001
Transferrin saturation	16.54±3.26	14.23±3.48	0.02

DISCUSSION-

Worldwide iron deficiency is a very common nutritional disorder and is known to affect almost one third of the global population. The iron deficiency alters a number of biochemical and physiological processes, of particular importance is the effect on central nervous system which leads to the defect in the cognition and learning process in humans.

Infants have high risk of developing iron deficiency anemia due to their rapid growth and limited dietary sources of iron. With this background the present study was undertaken. In this study we have summarized differences in mental, motor social/emotional and neuro-physiological functioning while infants are iron deficient to lay groundwork for considering long term effects and explanatory mechanisms.

MODE OF DELIVERY:

Pre term infants are prone to develop iron deficiency anemia in the early months of life as compared to term infants because of lower iron stores at birth in preterm infants.

This is firstly because most of the iron is transferred from mother to fetus during the third trimester of gestation and secondly preterm infants have higher requirement of iron at birth because of growth velocity of premature infants is maximal at postmenstrual age of 28-38 weak reflecting particularly high iron need.

Our study was in compliance with **Grantham-McGregor et al.**[4]

They also proved that preterm infants are more prone to develop iron deficiency anemia.

HEMOGLOBIN:

Hb is one of the method to define the severity of anemia, W.H.O classify anemia on the basis of Hb concentration as mild, moderate, severe, as 10-10.9gm/dl, 7-9.9gm/dl, <7gm/dl respectively.[107,108]

Our study showed most of the children with neurological abnormality having iron deficiency anemia were present in severe to moderate category which was contra-indicatory to the study conducted by **Collard et al**[5].where all the children had Hb level in severe deficiency category.

The p value came to be significant (p<0.001) as it is less then 0.05 as proposed before in the methodology.

Serum Iron Level:

The most common causes of IDA observed in children include inadequate intake together with rapid growth, low birth weight and gastrointestinal losses due to excessive consumption of cow's milk.

In developing country low iron bio-avability of the diet is the primary cause of iron deficiency anemia.

In our study we found lower then normal level of serum iron in children which was in accordance with the previous studies.

TIBC and TRANSFERRIN saturation:

In our study we observed lower value of transeferrin saturation and higher value of TIBC in children having neuro-developmental abnormality due to iron deficiency anemia.

Transferrin is a protein which transports iron in our blood.

Severe anemia leads to increase in TIBC due to decreases in iron load in our body also the p value of TIBC and transferring saturation in our study was significant ie p=0.001 and p=0.02 respectively which was less then 0.05 as discussed in methodology.

Multiple studies conducted in past showed the similar result like those done by **Ortiz E et al, Van Rheenen et al**[6].

TRIVANDRUM DEVELOPMENT SCORE(TDS):

The term development delay is used when a child's development lags behind established normal ranges (norms) for his or her age in areas of motor, cognitive, language, behavioral, emotional, or social development delay among children of less than 2years of age is often identified only by professionals, when they are brought for medical advice for other reasons. At the community level, these children are usually not identified due to the lack of a simple tool that can be used by community health worker. Early detection of development delay is important for instituting community based intervention program as possible in an effort to prevent onward progression to disability.In our study we have studied the effect of iron deficiency on neurodevelopment using TDS score.

A consistent finding in different countries is that severe, chronic iron deficiency in infancy identifies children with poorer cognitive function and lower scores in school achievement tests, suggesting that irreversible abnormalities result from a deficiency at a critical period of growth and differentiation of the brain. Poorer function, however, may also result from psychosocial and economic disadvantage.

The paper by **Chauhan VH et al**[7] is an important contribution. Their finding of significant improvements in motor and language development after 12 months of supplemental iron is strong evidence that iron deficiency has an effect on neurodevelopment of children. Our study was in accordance with their study as in our study we also found around 82.5 percent children with iron deficiency had delay in development of milestone on the basis of TDS.

CONCLUSION

It was found in our study that incidence was more in those children who were deliver pre-maturely then those children who were delivered at term.

Correlation of Trivandrum development milestone score with blood parameters. Hemoglobin in normal group were 9.83±0.56, whereas in

abnormal group it was 6.29±1.63, it was statistically significant, there was significant difference between serum iron TIBC and Transferrin saturation with p value <0.001, 0.005, 0.001 and 0.02.

Through our study we concluded that there was significant relationship between neurological abnormality in form of delayed milestones in any of the social motor or cognitive parameters as described in TDSS with lower values of serum iron, serum ferritin and transferrin saturation and higher values of TIBC in the study subjects.

Further high-quality studies on the impact of iron deficiency on developmental outcomes are needed.

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