A Clinical Study Of Cognitive Function In Children With Iron Deficiency Status Aged 6months To 2 Years

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ABSTRACT

Background: Iron deficiency is the most prevalent nutritional disorder in the world. The most worrying consequences of it is the alteration of behaviour and cognitive performance such as reduced attention span, reduced emotional responsiveness and low scores on tests of intelligence. There is a wealth of research that shows that iron deficiency anaemia can exert a direct deleterious effect on the brain but does this also happen with iron deficiency status. **Objective**: To assess the role of iron deficiency status and iron deficiency anaemia on cognitive function in children aged 6 months to 2 years.The Case control prospective study from the Tertiary care hospital in Bangalore, Karnataka. **Participants**: Total of 150 children between age of 6 months and 2 years who fulfilled the inclusion criteria. **Intervention**: Clinical history was taken, physical examination and assessment of the cognitive function was done following which they were all subjected to blood investigations. The cognitive function was assessed using Vineland social maturity scale. 50 children diagnosed with iron deficiency anaemia and 50 children with iron deficiency status constituted the case group and 50 children who did not have anaemia constituted the control group. **Results**: There were significant differences in the intellectual level in the three groups. It showed that iron deficiency anaemia group had lower mean intellectual score when compared to iron deficiency status ($p=0.002$) and control groups ($p<0.001$) and similarly, the mean intellectual score was lower for iron deficiency status group when compared to control group ($p=0.001$). **Conclusion**: Cognitive dysfunction in iron deficient children starts at the period of iron deficiency status itself making early recognition and intervention of paramount importance before these effects become irreversible.

INTRODUCTION

Iron deficiency (ID) remains the most prevalent single-nutrient deficiency in developing and developed countries. The World Health Organisation[1] estimates that, worldwide, 1.6 billion to 2 billion people are anaemic. It is estimated that 24.8% of the world's population have anaemia, highest prevalence is in preschool children (39.8%) and approximately 50% of cases are due to iron deficiency. Other possible causes of anaemia include genetic, infectious, and other nutritional deficiencies. Infants, children, and women of reproductive age are at highest risk of developing ID and ID

anaemia (IDA), largely because of their high physiologic requirements associated with growth combined with greater losses and poor dietary intake**.** Globally, almost half of preschool-aged children and pregnant women and close to one-third of non-pregnant women have anaemia[1,2].
However, despite recent economic development[3] and the existence of a national anaemia-control program[4] the prevalence of anaemia in India is still very high. Alleviating childhood iron-deficiency anaemia is a public-health priority, because anaemia is associated with impaired cognitive and psychomotor development.[3,4] Anaemia has been shown to weaken immune status and resistance to infections[3] to lower work capacity[5], and to possibly repress child growth.[6]Some studies have found that IDA affected the development of children, motor skills, memory, fine motor skills, language and personal/social skills.[7,8,9] Early stages of IDA, termed as Non-anaemic Iron deficiency (NAID) provides an opportunity for early detection and treatment before progression of these impairments.

METHODS

It was a single centre, case control prospective study conducted from February 2021 to May 2022 at a tertiary care teaching hospital in Bangalore, Karnataka. Approval was obtained from the institutional ethics committee. Informed and written consent was obtained from the parents of the children. Purposive sampling technique was employed and children between the age groups of 6 months to 2 years who were attending paediatricOPD / admitted to the paediatric ward were included after excluding those who had perinatal complications, known haemoglobinopathies, known disorders causing psychomotor deficit and those who were on drugs interfering with cognition. A relevant clinical history of these children was taken. Physical examination was done. These children were then subjected to cognitive function assessment by Vineland social maturity scale and the following lab investigations were done, namely

1. Haemoglobin
2. Mean corpuscular volume
3. Peripheral smear and
4. Serum ferritin.

Three groups were made amongst the participants.

Children were included in the iron deficiency anaemia group if their blood investigations were as follows:

1. Haemoglobin<11 g%
2. Mean corpuscular volume <74 fl
3. Serum ferritin <12 microgram/dl and
4. Microcytic Hypo-chromic anaemia on peripheral smear.

Children were included in the iron deficiency status group if their blood investigations were as follows:

1. Haemoglobin>11 g%
2. Mean corpuscular volume >74 fl
3. Serum ferritin < 12 microgram/dl and
4. Normocytic Normochromic blood picture on peripheral smear.

A total of 50 children were included in the iron deficiency anaemia group and 50 were included in the iron deficiency status group. The control group included 50 children without iron deficiency admitted/visiting for other illnesses making it a total of 150 participants. While using the Vineland scale for social maturity, the number of tasks from the list the child performed/would be able to perform were counted and scored from 0 to 1. Final score was calculated and with the help of the reference sheets, social age was calculated corresponding to the social score attained.

The social age obtained was converted into a social quotient by the formula

Social Quotient = Social age *100
Chronological age

and based on the social quotient, children were graded as follows:

Very superior (>130)
Superior (120-129)
Bright normal (110-119)
Average (90-109)
Dull normal (80-89)
Borderline (71-79)
Mild Mental retardation (MR) (50-70)
Moderate MR (35-49)
Severe MR (21-34)
Profound MR (<20)

RESULTS

Out of the total 150 children, majority i.e. 92 (61.3%) were male children and 58(38.7%) were female children. As seen in **table 1,** in iron deficiency anaemia group it is seen that 78% were male children and 22% were female children when compared to control group where 52% were males and 48% were females. In IDS group 54% were males and 46% were female. Out of the 150 mothers of the children, 48% of had antenatal anaemia and 52% had no antenatal anaemia. Distribution of antenatal anaemia within groups as seen in **table 1** shows that iron deficiency anaemia group children showed higher percentage of mothers with antenatal anaemia (74%) compared to the control group (28%). Similarly children in the IDS group also showed higher percentage of mothers with antenatal anaemia (42%) when compared to controls.Out of 150 children, 68% had associated symptoms and 32% had no associated symptom. Children with IDA gave more complaints, namely, decreased appetite (30%) followed by intermittent abdominal pain(24%), dull in activity (14%), easy fatiguability (6%) and irritability (4%) when compared to IDS group who didn't have too many complaints except for 10% having intermittent abdominal pain and 4% having decreased appetite. In the control group, 2 children (4%) gave complaints of decreased appetite. Out of the 150 children, 75.3% were term and 24.7% were preterm as seen in **table 1** and in the IDA group 36% were preterm and 64% were term, when compared to control group where only 22% were preterm and 78% were term. In IDS group 16% were preterm and 84% were term. Of the total 150 children, 56% of the children were weaned early and 44% children were weaned at 6 months as seen in **table 1.** 78% were weaned early in the IDA group and in the IDS group 56% were weaned early when compared to the control group (34%). In the IDA group, out of the 39 children who were weaned early, 28 chidren (71.7%) were stopped with breast feeding and started on cows milk and complementary feeds. Comparing the percentages of children of each group having PEM in **table 1,** it showed that in the IDA group, 22% had grade 1 PEM , 62% had grade 2 PEM, 14% had grade 3 PEM and 2% children who had mild anaemia had no PEM when compared to the control group where 94% had no PEM and 6% had grade 1 PEM. In the IDS group 56% had no PEM, 34% had grade 1 PEM and 10% had grade 2 PEM. Comparing the peripheral smears of the children of the various groups in **Table 2** shows that in the IDA group, out of the 50 children, 39 children (78%) had Microcytic hypochromic anaemia and 11 children (22%) had Dimorphic anaemia. On evaluating the cognitive function of the children as seen in **table 3,** of the total

150 children 2% were bright normal, 47% were average, 39.3% were dull normal and 11.3% were borderline. Vineyard social maturity scale grading and calculation of social quotient within the groups shows that in IDA group there were no children with bright normal social grade, 22% were average, 48% were dull normal and 30% were borderline when compared to the control group where 6% were bright normal, 74% were average, 20% were dull normal and none were borderline. In IDS group, there were none with bright normal, 46% were average, 50% were dull normal and only 4% were borderline.

SEX	**IDA**	**IDS**	**CONTROL**
MALE	39(78.0%)	27(54.0%)	26(52.0%)
FEMALE	11(22.0%)	23(46.0%)	24(48.0%)
ANTENATAL ANEMIA	IDA	IDS	CONTROL
PRESENT	37(74.0%)	21(42.0%)	14(28.0%)
ABSENT	13(26.0%)	29(58.0%)	36(72.0%)
MATURITY	IDA	IDS	CONTROL
TERM	32(64.0%)	42(84.0%)	39(78.0%)
PRETERM	18(36.0%)	8(16.0%)	11(22.0%)
EARLY WEANING	IDA	IDS	CONTROL
YES	39(78.0%)	28(56.0%)	17(54.0%)
NO	11(22.0%)	22(44.0%)	33(66.0%)
PEM GRADE	IDA	IDS	CONTROL
GRADE 0	1(2.0%)	28(56.0%)	47(94.0%)
GRADE 1	11(22.0%)	17(54.0%)	3(6.0%)
GRADE 2	31(62.0%)	5(10.0%)	0(0.0%)
GRADE3	7(14.0%)	0(0.0%)	0(0.0%)

Table 1 Depicting Comparative Statistics Of The Three Groups With Reference To The Gender, Mother's Anaemia Status, Early Weaning And Grade Of Pem

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Smear	**Iron Deficiency Anemia**	**Iron Deficiency Status**	**Control**
Microcytic hypochromic anaemia	39(78.0%)	0(0%)	0(0%)

Normocytic Normochromic anaemia	0(0%)	50(100%)	50(100 %)
Dimorphic anemia	11(22.0%)	0(0%)	0(0%)
Total	50(100%)	50(100%)	50(100 %)

Table 2 Distribution Of Peripheral Smear Amongst The Three Groups

Table 3: Comparison of the vinel and scale for social maturity grading amongst the three groups

GRADES	IRON DEFICIENCY ANEMIA	IRON DEFICIENCY STATUS	CONTROL
BRIGHT NORMAL	0(0.0%)	0(0.0%)	3(6.0%)
AVERAGE	11(22.0%)	23(46.0%)	37(74.0%)
DULL NORMAL	24(48.0%)	25(50.0%)	10(20.0%)
BORDERLINE	15(30.0%)	2(4.0%)	0(0.0%)

DISCUSSION

In this study, higher prevalence of anaemia was noted in male children. The male predominance maybe due to sheer coincidence or maybe because of increased concern of parents towards male children leading to increased incidence of male admission. This study shows that in the IDA group majority of children had mothers with antenatal anaemia when compared to control. This shows that antenatal anaemia in the mother can lead to early development of iron deficiency in children, which can contribute to low birth weight and preterm birth. Lidna ray et al conducted study on effects of maternal anaemia on pregnancy outcome and found that IDA in pregnancy is a risk factor for preterm delivery. Such a finding was also supported by this study where increased preterm deliveries were seen in the IDA group followed by in the IDS group. Also perhaps the deficient iron stores of the mother contribute to the reduced fetal iron stores which get diminished earlier resulting in earlier development of IDA and cognitive function impairment in pre school children.

In this study, amongst the children who were weaned early majority of them were in the IDA group this clearly shows that early weaning, discontinuation of breast milk, introduction of cows milk and faulty weaning practice contributes to IDA. Gibson et al found in his study that ID among young children is multifactorial. However consumption of foods with lower bioavailability like cow milk is likely most important factor especially in developing countries.

In this study majority of PEM cases were in the IDA group, this shows that IDA, especially moderate to severe anaemia and other deficiencies caused by improper weaning practices and inadequate dietary intake hamper the physical growth of the children which in turn predisposes them to more infections resulting in a worsening of nutrition intake resulting in a vicious cycle.

Previous reviews on this field of study concluded that ID has a negative impact on cognition behaviour and motor skills that can have long term complications. ID seems to impact the hippocampus, and cognitive dysfunction might be due to mitochondrial damage. [10,11] In addition, changes to brain dopamine metabolism is presumed to occur. Some studies correlate the Hb levels to cognitive functions while others report an improvement in cognitive function after iron supplementation. This study also revealed that not only iron deficiency anaemia but even an iron deficiency status can have deleterious effects on the cognition of children.

LIMITATIONS OF STUDY

The sample size for this study was small and it was conducted for a short period of 15 months. Further studies with a larger sample size and long term follow up is required to establish the cognitive impairment due to iron deficiency and the efficacy of starting iron supplements in helping reverse these changes in both these groups.

CONCLUSION

This study shows that both iron deficiency anaemia and iron deficiency status hamper the cognitive function of the children when compared to children without iron deficiency. It was found that the common and possible reasons for iron deficiency in infants and young children are antenatal anaemia, faulty weaning practices and malnutrition. If subtle effects of iron deficiency in infancy lay the ground for later problems in cognitive and behavioural functioning, then a large, unrecognised population of children could be at risk for cognitive and behavioural effects owing to iron deficiency, a nutritional problem that needs to be prevented and treated. WHO/UNICEF/UNU strongly advocate that when there is a prevalence of anaemia above 40%, a universal supplementation is required as it is not cost-effective to screen children for anaemia. Hence a better implementation of the iron supplementation and anaemia prevention program is the need of the hour to protect our future generations from a preventable cause of low cognition.

What is already known?

- Iron deficiency anaemia has a negative impact on cognition, behaviour and motor skills that can have long term complications.

What this study adds?

- The deleterious effects on cognition and behaviour begin at the stage of iron deficiency status itself giving us a therapeutic window for therapy and prevention of long term irreversible effects of the same.

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