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SIGNATURE OF IRON DEFICIENCY ANEMIA ON NEURODEVELOPMENTAL OUTCOME AMONG UNDER-FIVE CHILDREN

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ABSTRACT **Introduction:** Growth and development are interlinked and dependent on Infant and Young Child Feeding (IYCF) practices. Iron deficiency anemia (IDA) is an important determinant of neuro-development. **Objectives:** (1) To assess IYCF practices, nutritional status, and neuro-developmental outcome using Developmental & Social Quotients (DQ & SQ) among 6-60 months-old-children with and without IDA. (2) To determine association of nutritional factors & IDA with DQ & SQ. **Materials and methods:** 6-60-months-old children, 30 each with/without IDA belonging to middle & low socioeconomic status, were enrolled during January-April 2021. Children with comorbidities/neurodevelopmental defects/genetic disorders were excluded. Birth weight (BW), IYCF practices, anthropometric measurements, complete Hemogram, DQ by Bharathraj Developmental Screening Test and SQ by Malin's adaptation of Vineland Social Maturity Scale were recorded. **Results:** Among cases, 66.7% had mild, 33.3% moderate and no-one had severe anemia. Study variables showed difference between Cases vs. Controls– Proportions; Low IYCF score < 80% ((70% vs. 13.3%), Exclusive breastfeeding (43% vs. 83%), underweight (50% vs. 10%), stunting (43% vs. 13%), wasting (47% vs. 10%), low DQ (77% vs. 0%) and impaired SQ (80% vs. 6.7%), Mean values; BW (2.79 vs. 3.08 kg), DQ (76.46 vs. 96.18), and SQ (75.32 vs. 92.41). Significant association noted between anemia and IYCF score & malnutrition; DQ & SQ with BW, IYCF score, malnutrition & anemia. 14/20 with mild and 9/10 &10/10 with moderate anemia had low DQ and SQ respectively. All those with moderate anemia were not exclusively breastfed. The relative risk for low DQ and SQ was 2.3 (CI -1.26-5.03) among those with anemia and 1.3 (CI -1.32-5.05) in moderate compared to mild anemia. **Conclusions:** Those with anemia had low BW, poor IYCF practices & malnutrition. Those with IDA had low DQ & SQ, the signature of impaired neurodevelopment. Hence, anticipatory nutrition guidance including prevention of anemia is recommended.

INTRODUCTION:

Under-five children are a vulnerable subset of population. Physical growth and brain development are interlinked and dependent on IYCF practices including micronutrient sufficiency [1,2].

According to CNNS 2016-18, among 1-4-year-old children, 20.8% had Iron deficiency anemia (IDA) [3]. IDA is an important determinant of neuro-development [4,5].

This study was undertaken to assess IYCF practices, nutritional status, and neuro-developmental outcome using Developmental & Social Quotients (DQ & SQ) among 6-60 months-old-children with and without IDA and to determine association of nutritional factors & IDA with DQ & SQ.

MATERIALS AND METHODS:

6-60-months-old children, 30 in each group with and without anemia belonging to middle and lower socioeconomic status attending Department of Pediatrics of a tertiary care teaching hospital during January 2021 – April 2021 were enrolled, based on a calculated sample size of 24 in each group [4]. IEC approval and Informed consent from parent/guardian were obtained.

Inclusion Criteria:

Cases: 6-60 months-old children with anemia, graded as per WHO,2011 criteria – mild anemia (Hb:10-11 g/dl), moderate anemia (Hb: 7-10 g/dl) and severe anemia (Hb: <7 g/dl) and

Controls: those with no anemia (Hb >11 g/dl).

Exclusion Criteria:

Children with neurological disorders, chromosomal or genetic disorders, risk factors for developmental delay like IUGR, birth asphyxia, hyperbilirubinemia, prematurity, congenital anomalies, other co-morbidities and those who have undergone surgery/ blood transfusion.

Study Parameters:

Socio-demographic data as per Modified Kuppuswamy scale 2021, Birth weight (BW), IYCF practices and present diet were recorded using a structured questionnaire. IYCF score was calculated based on 10 key indicators; Early initiation of breastfeeding, Exclusive breastfeeding during first 6 months, Breastfed until 1 year of age, Continued breastfeeding during 12-23 m of age, Ever bottle fed 0-23 m, Complementary foods given from 6-8 months of age, Minimum dietary diversity, Minimum meal frequency, Minimum acceptable diet and Consumption of iron-rich/ iron- fortified foods. From the questionnaire, Yes was scored as one and No as zero and interpreted as Good > 80%, Fair 50-80% and Poor < 50%. Anthropometric measurements recorded using standardized techniques were analyzed using WHO growth charts. Complete Hemogram by automated machine was interpreted for presence of anemia and evidence of Iron deficiency using RBC indices and RDW.

DQ was assessed by Bharathraj Developmental Screening

Test, developed for Indian children, which consists of 88 items representing age specific behavioral characteristics. DQ from mental age and chronological age of the child was calculated using the DQ calculator incorporated within the test folder and categorized into- Normal ($\geq$85) and Low (<85).

SQ was assessed by Malin's adaptation of Vineland Social Maturity Scale, customized for Indian children, which consists of 89 items; Social skills in the following areas of communication (listening, speaking, writing), daily living skills (general self-help, eating and dressing), motor skills (fine and gross including locomotion), occupational skills, self-direction and socialization (interpersonal relationships, play and leisure and coping skills). Scores obtained were made into age equivalent score and expressed as social age, Normal ($\geq$85) and Impaired (<85).

RESULTS:
The Male:Female ratio and socio-economic status were comparable between the groups. Among cases, 66.7% had mild, 33.3% moderate and no-one had severe anemia. There were statistically significant differences between Cases and Controls in the study; mean BW (2.79 vs. 3.08 kg), low IYCF score < 80% (70% vs. 13.3%), exclusive breastfeeding during first six months (43% vs. 83%), underweight (50% vs. 10%), stunting (43% vs. 13%), wasting (47% vs. 10%), low DQ $\geq$85 (77% vs. 0%) impaired SQ $\geq$85 (80% vs. 6.7%), mean DQ (76.46 vs. 96.18) and mean SQ (75.32 vs. 92.41) respectively. All those with moderate anemia were not exclusively breastfed during first 6 months and had low IYCF score < 80% (Table 1). Analysis of nutritional status showed that among cases, 50% were underweight, 43.3% had stunting and 46.7% had wasting compared to 10% ,13.3% and 10% among controls respectively (Table 2). Among cases, 23.3% had normal DQ & 20% had normal SQ compared to 100% & 93.3% among controls respectively (Table 3).

There was a significant association between low IYCF score and malnutrition & anemia (p <0.05). Similarly, significant association was noted between low BW, low IYCF score, malnutrition & anemia with low DQ & SQ (p <0.05). 2/7 Cases and 2/30 Controls with normal DQ had impaired SQ, suggesting a dissociation between the two. 14/20 with mild anemia had low DQ and SQ. 9/10 &10/10 with moderate anemia had low DQ & SQ respectively. The relative risk for low DQ and SQ was 2.3 (CI -1.26-5.03) among those with anemia and 1.3 (CI -1.32-5.05) in moderate compared to mild anemia.

DISCUSSION:
In this study among 6-60-month-old children with anemia, more than two third had moderate and the rest had mild IDA. Anemia is an important public health issue in India. As per CNNS 2016-18[3], it was 40.6% among 12-59-months-old and 67.1% among 6-59-months-old children in NFHS-5 data 2019-20[6]. Gebreegziabiher G reported a prevalence of 53.2% anemia among 6-11-months-old infants[7] from Ethiopia. This highlights the increased iron requirement during the younger age-group, which warrants intake of iron rich/iron fortified foods and iron supplements.

Among controls, 86.7% had good IYCF score >80% and in cases only 30% had good IYCF score. Indicators for assessing IYCF practices (WHO 2021) has suggested an IYCF indicator score based on 17 parameters[8]. In this study, IYCF score was calculated based on 10 indicators as the study was designed prior to the release of the above document. Only 43.3% were exclusively breastfed during first 6 months among cases, whereas among controls 83.3% were exclusively breastfed. Study done by Anjali et al., had reported that, among 6-24-months-old children, majority with anemia were not exclusively breastfed, Complementary feeding was not initiated at 6 months and had poor IYCF practices[9].

Anemia was more prevalent among those who were underweight, stunted and wasted, as reported in earlier studies. A Danish cohort study had highlighted the association of multiple nutrition problems coexisting in the same individual[10].

Among controls, all had normal DQ and only 2 children had impaired SQ. However, among cases, 76.7% had low DQ and 80% had impaired SQ suggesting poor neurodevelopmental outcome. This study is unique as it included social quotient, along with developmental quotient. The finding that 2/7 Cases and 2/30 Controls with normal DQ had impaired SQ, suggesting a dissociation between the two, highlights the need for including social skills, along with developmental assessment.

Mean BW was lower among cases compared to controls. Malnutrition was also higher among cases. Kirkegaard H had reported that those with increased BW and adequate weight gain in infancy had higher IQ. It also emphasized that those with greater height and head circumference had higher IQ[10]. Study by Tasnim S showed that breastfeeding contributed to cognitive and psychosocial development and also emphasized that breastfed infants had higher motor skills and IQ scores[11]. Lund L K had observed that children with VLBW and SGA had significantly more mental health problems[12]. Liu J in his study noted that malnourished children showed impairment in social behavior[13].

A double blinded study by Walter T, on infants up to 15 months old showed that children with anemia had significantly lower psychomotor and mental developmental Index scores than control group[4]. Iron deficiency with or without anemia has been reported to adversely affect infant social-emotional behavior[14].

A study by SS Yalcin showed that supplementation of iron for healthy infants for a short 3-month duration had a change in transferrin saturation, but there was no change in developmental score, highlighting the point that prevention using iron prophylaxis is better than treating after the adverse outcome occurs[15]. In this study, IDA showed significant association with low SQ and DQ (RR 2.3: CI -1.26-5.03) compared to those without anemia and added risk among those with moderate anemia compared to those with mild anemia (RR 1.3: CI -1.32-5.05). Thus, IDA had an adverse signature on the neurodevelopmental outcome of infants and young children with a gradation from mild to moderate anemia.

CONCLUSIONS:
BW and IYCF practices were important determinants of physical and neurodevelopmental status. Those with anemia had low BW, poor IYCF practices, malnutrition and low DQ and impaired SQ. This study warrants urgent focus on maternal and infant nutrition, periodic monitoring of IYCF practices, nutritional status as well as developmental and social quotients for timely recognition and early intervention for better outcomes. Social quotient may not always tally with development.

This study highlights the need for including social skills in the intervention packages for comprehensive care. Intake of iron rich/iron fortified food and ensuring supply and compliance to the life cycle approach of iron and folic acid supplementation under the 'Anemia Mukt Bharat' programme, should be prioritized to reach all the eligible beneficiaries. The finding that IDA, both mild and moderate anemia, add an adverse signature on the neurodevelopmental outcome of infants and young children, with a gradation from mild to moderate anemia is an eyeopener. Hence, anticipatory nutrition guidance including prevention and treatment of anemia is

recommended. A large multicentric follow up trial can throw more light on the effect of IYCF practices and anemia on physical growth as well as neurodevelopmental outcome and the chances of reversibility after intervention.

Limitations:

- Follow up data after nutritional intervention, effect of correction of anemia on developmental and social maturity outcomes were not undertaken.
- Confounding factors like maternal malnutrition and maternal anemia were not studied.
- A larger sample size can throw more insight into this.

Table 1. IYCF Practices among Cases and Controls

Parameters		Cases (n=30)		Controls (n=30)	Significance
		Mild anemia	Moderate anemia		
Exclusive Breastfeeding	Yes	13 (43.3%)	0 (0%)	25 (83.3%)	0.001*
	No	7 (23.3%)	10(33.3%)	5 (16.7%)	
IYCF score	Good (>80%)	9 (30%)	0 (0%)	26 (86.7%)	0.005*
	Fair (50-80%)	11 (36.6%)	7 (23.3%)	4 (13.3%)	
	Poor (<50%)	0 (0%)	3 (10%)	0 (0%)	

*- Significant

Table 2. Nutritional Status among Cases and Controls

Parameters		Cases	Controls	Significance P value
Weight for Age	Normal	15 (50%)	27 (90%)	0.003*
	Underweight	15(50%)	3 (10%)	
Height for Age	Normal	17 (56.7%)	26 (86.7%)	0.010*
	Stunting	13 (43.3%)	4 (13.3%)	
Weight for Height	Overweight	0 (0%)	2 (6.7%)	0.004*
	Normal	16 (53.3%)	25 (83.3%)	
	Wasting	14 (46.7%)	3 (10%)	

*- Significant

Table 3: DQ and SQ among Cases and Controls

Parameters	Cases	Controls	Significance P value
Mean DQ	76.46±16.38	96.18±6.00	<0.001*
Normal (85-115)	7 (23.3%)	30 (100%)	<0.001*
Below normal (retardation)	23 (76.7%)	0 (0%)	
Mean SQ	75.32 ± 15.90	92.41 ±5.77	<0.001*
Normal >85	6 (20%)	28 (93.3%)	<0.001*
Impaired <85	24 (80%)	2 (6.7%)	

*- Significant

REFERENCES:
1. World Health Organization. The global prevalence of anemia in 2011, WHO report 2015. Geneva: World Health Organization; 2015. Accessible at Prevalence of anaemia in children aged 6–59 months (%) (who.int). Accessed January 12, 2021.
2. Elizabeth KE. Nutritional anemia-strategy for prevention and management. Indian J of Practical Pediatr. 2020; 22(3): 245-51.
3. Ministry of Health and Family Welfare (MoHFW), Government of India, UNICEF and Population Council. 2019. Comprehensive National Nutritional Survey (CNNS) 2016-18 National Report. New Delhi.
4. Walter T. Effect of iron deficiency anemia on cognitive skills and neuromaturation in infancy and childhood. Food and Nutrition Bulletin 2003;24(4) :S 104-10.
5. Lozoff B, Jimenez E et al. Poorer behavioural and developmental outcome more than 100 years after treatment for iron deficiency in infancy. Paediatrics 2000;105: E51.
6. Ministry of Health and Family Welfare (MoHFW), Government of India .National Family Health Survey (NFHS -5) 2019-2021.
7. Gebreegziabiher G, Etana B, Niggusie D. Determinants of Anemia among Children Aged 6-59 Months Living in Kilte Awulaelo Woreda, Northern Ethiopia. Anemia. 2014:245870.
8. Indicators for assessing infant and young child feeding practices: definitions and measurement methods. Geneva: World Health Organization and the United Nations Children's Fund (UNICEF), 2021. Available at: https://www.who.int/publications/i/item/9789240018389
9. Anjali TR, Abbas S, Elizabeth KE et al. Association between breastfeeding practices and anemia in children aged 6-60 months. Int J Contemporary Pediatr. 2019;6(5):2027-2031.
10. Kirkegaard H, Möller S, Wu C, et al. Associations of birth size, infancy, and childhood growth with intelligence quotient at 5 years of age: a Danish cohort study. Am J Clin Nutr. 2020;112(1):96-105.
11. Tasnim S. Effect of breast feeding on child development: At birth and beyond. South East Asia Journal of Public Health.2014;4(1):4-8
12. Lund, L.K., Vik, T., Lydersen, S et al. Mental health, quality of life and social relations in young adults born with low birth weight. Health Qual Life Outcomes. 2012; 10:146.
13. Liu J, Raine A. Nutritional status and social behavior in preschool children: the mediating effects of neurocognitive functioning. Matern Child Nutr. 2017;13(2): e12321.
14. Lozoff B, Clark K, Jing Yet al. Dose-Response Relationships between Iron Deficiency with or without Anemia and Infant Social-Emotional Behavior. The Journal of Pediatrics. 2008;152(5): 696-702.
15. Yalcin SS, Yurdakok K, Acikgoz D et al. Short-term developmental outcome of iron prophylaxis in infants. Pediatric Int. 2000 Dec; 42(6): 625-30.