



Haematological parameters of iron deficiency anaemia among infants and their correlation with the psychosocial developments

Awaz Muhammed Ameen Anwar* Adil Abozaid Eissa**

Abstract

Background and objectives: Iron deficiency anaemia is one of the most widespread micronutrient deficiencies in the world. Our goal was to investigate how Iron deficiency anaemia affects the haematological parameters and the psychosocial development of affected infants.

Methods: A follow-up study was conducted from January, 2022 to September, 2022 at Heevi Paediatric Teaching Hospital in Duhok. A total of 58 children with Iron deficiency anaemia were involved in this study. Also, 58 children with normal iron status were recruited and served as control. The Ages & Stages Questionnaires®, Third Edition were used to evaluate the five areas of developmental progress of enrolled infants including gross motor skills, fine motor skills, adaptability, language skills, and social skills.

Results: Study has found that Serum iron for patients with iron deficiency anaemia was (g/dL) 20.82 ± 1.1 vs 77.8 ± 5 for control. Generally, patients scored lower blood count compared to control. Hence, All haematological parameters including haemoglobin, mean cell volume, mean cell haemoglobin, mean corpuscular haemoglobin returned to normal after 2 month treatment. Both groups scores in the communication and gross motor domains were not statistically significant communication: 40 ± 0.6 for patients vs. 42 ± 0.5 for controls, and gross motor: 48 ± 1.7 for patients vs. 50 ± 1.5 for controls. Whereas, fine motor, problem solving, and social behaviour are other categories that were shown to have statistically significant low scores (p -value ≤ 0.05): fine motor for patients was 36 ± 1.2 vs. 48 ± 1.5 for controls, problem solving was 33 ± 1.1 vs. 45 ± 2.0 and social behaviour was 31.5% vs. 47.5% for the control group.

Conclusion: These findings show that children with Iron deficiency anaemia have negative impact on fine motor, problem solving, Social-behaviour.

Keyword: ASQ-3, Haematological parameters, Iron deficiency anaemia IDA, Social-behaviour

Introduction:

The most prevalent nutritional issue worldwide is iron deficiency particular

among infants as a result of combination of rapid growth and insufficient iron intake so

*M.B.Ch.B, Board candidate of haematology, Kurdistan Higher Council for Medical Specialties Department of Hematology, Duhok. Directorate of Health, Duhok, Iraq, Email: dr.awaz86@gmail.com. Corresponding author

** M.B.Ch.B, FIBMS, FRCPath (Haematology) Pathology department, College of Medicine; University of Duhok; Duhok, Iraq.; adilkhr77@uod.ac



iron reserves are significantly depleted within the first year of life and it has been estimated that 5-25% of infants in high-income countries and up to 50% in low-income countries suffer from iron deficiency.¹⁻³ The World Health Organization (WHO) suggests that breastfeeding should be continued exclusively for the first six months of a baby's life.¹⁻² Iron deficiency (ID) is a worry for certain infants who are exclusively breastfed (EBF) before the age of six months, particularly in communities who are prone to the condition.¹⁻² The presence of ID in infants has been associated with slower psychomotor development, and it may also impact immunological function.³

When it comes to many metabolic processes, including oxygen transportation, synthesis of nucleic acids, and the transport of electrons, depend on iron thus ferrous deficiency during infancy can affect both growth potential and psychomotor development.⁴ A lack of iron may impair an infant's cognitive, motor, and behavioural growth, and this impairment may last even after the iron level has restored to normal. Poor motor skill coordination, behavioural problems at home and school, and low academic achievement are all long-term effects of iron deficiency in infants.⁵ High-risk individuals treated with iron have improved psychomotor and cognitive development and fewer psychiatric issues.⁶ When it comes to the link between nutrition and brain development, the first two years of life are very important⁷. The tool that should be used to assess the developmental progression of any infants, should be characterized by certain properties including; ease-of-use-, parent centric approach, non-invasive, applicable to early ages in order to detect any impending defects, not time consuming, that is why Ages & Stages Questionnaires®, Third Edition (ASQ®-3) had been used in the current study.⁷

Our aim of conducting this study was to evaluate the possible impact of iron-deficiency anaemia (IDA) on the infants' development and the relation of impaired development to haematological parameters. Therefore, we conducted follow-up research to assess the impact of IDA on the psychosocial development of infants.

Patients and methods

Patients were enrolled if they met the following criteria for IDA: a low level of CBC. Low hematocrit (Hct %), low serum ferritin .While exclusion include, Infants and children who have a history of being born prematurely or who are too small for their age. Children and babies who are suffering from protein/calorie malnutrition, rickets, malabsorption, liver disease, renal insufficiency, or any kind of anemia are said to have a chronic systemic ailment.

So, from January 2022 to Sep 2022, a follow-up study was undertaken at HIVEE Pediatric Teaching Hospital in Duhok/Iraq. The hospital includes facilities for diagnosing, treating, and monitoring iron deficiency anaemia.

The current study included a total of 58 infants that are suspected to have IDA plus their parents help to achieve this study because it needs a serial of question to be answered in ASQ-3, manual aged 6-12 months with IDA as well as other 58 age matched infants without iron deficiency, served as controls. Infant born prematurely were excluded from the current study while race, religion, or socioeconomic backgrounds were not factors taken into consideration.

A Hb concentration of less than 11.0 g/dL are considered to have anemia, according to the 1999-2002 United States National Health and Nutrition Examination Survey.⁸ At first a verbal consent was taken from all parents and the study was approved by scientific committee at Kurdistan Higher Council of Medical Specialties and ethical committee at Duhok directorate of health. Blood was drawn via venepuncture from



either the antecubital or dorsal veins and dispensed into appropriate tubes (dipotassium EDTA anticoagulant and gel tubes) for measuring haematological [Complete blood count (CBC), reticulocytes] and biochemical parameters [iron, Total iron binding capacity (TIBC) and ferritin] using automated methods (Swelabo for haematological parameters and Cobas 6000 for biochemical investigations) with daily calibration to assure the validity of the results.

The Ages & Stages Questionnaires®, Third Edition (ASQ®-3) ASQ-3 was used in the current study due to its ease of administration, parent-centric approach and broad applicability across a variety of demographics.⁷⁻⁸ Five areas of performance were examined using the ASQ-3 in English version. The questionnaire form includes 1 domains in children's play: gross motor (movements of the arms, legs, and torso), fine motor (movements of the hands and fingers), Communications, problem solving, and personal-social development (play in groups and alone) (learning and understanding). Finally, numerical ratings as 10 for YES, 5 for some times and zero for No were applied.

off score with particular attention to the most affected area .Prior to enrolment, all After filling the questionnaire by the

parents, scoring and analysis done to find affected children with reference to the cut-individuals provided written informed consent from Heevi Paediatric Teaching Hospital in Duhok.

The results were presented in the form of means \pm standard deviation (SD). One-way analysis of variance (ANOVA), followed by the paired t-test, to perform statistical comparisons between the groups, and p-values of less than ≤ 0.05 were considered to be statistically significant.

Results

Table (1) compares biochemical and haematological parameters between IDA patients and controls. When compared to control patients, an infant with IDA had significantly lower results across the board. As anticipated, IDA patients' blood ferritin levels were significantly lower than those of controls (p value ≤ 0.01), as were their RBC count, haemoglobin level, haematocrit (Hct), mean corpuscular volume (MCV), mean corpuscular haemoglobin (MCH), and mean corpuscular haemoglobin concentration (MCHC). RBC distribution width (RDW) was greater in the IDA group compared to the other groups (p value ≤ 0.01).

Table (1): Changes in haematological and biochemical laboratory values of among infants with iron deficiency anaemia (IDA) compared to normal infants.

Parameter	IDA infants (n=58)	Control (n=58)	p value	Patient after 2 months treatment	p value
RBC (M/ μ L)	4.31 \pm 0.14	4.87 \pm 0.05	<0.05	4.85 \pm 0.05	0.041
Hb (g/dL)	9.7 \pm 0.3	13.5 \pm 0.2	<0.011	11.5 \pm 0.2	<0.01
Hct (%)	28.7 \pm 0.7	38.0 \pm 0.5	<0.031	36.0 \pm 0.5	0.03
MCV (fL)	64.7 \pm 1.1	78 \pm 0.5	<0.041	76 \pm 2	0.03
MCH (pg)	22.4 \pm 0.5	28 \pm 0.2	<0.023	28 \pm 0.2	<0.01
MCHC (g/dL)	33.6 \pm 0.4	36.2 \pm 0.6	<0.011	36.2 \pm 0.6	<0.01
RDW (%)	16.2 \pm 0.5	12.6 \pm 0.2	<0.01	12.6 \pm 0.2	<0.01
Reticulocyte count	3.80 \pm 0.3	2.6 \pm 0.2	<0.051	2.6 \pm 0.2	0.04
Serum iron(g/dL)	20.82 \pm 1.1	77.8 \pm 5	<0.01	76.8 \pm 5	0.013
TIBC (μ g/dL)	400 \pm 20	270 \pm 25	<0.01	250 \pm 25	0.014
TS%	5.3 \pm 3.5	26.9 \pm 6.2	<0.01	30.72 \pm 6.2	<0.001
Ferritin (ng/mL)	6.9 \pm 0.6	64.1 \pm 5	<0.01	25.1 \pm 5	0.011



Iron deficiency anaemia (IDA) .RBC: Red blood cell; MCV: mean corpuscle volume; MCH: mean corpuscle haemoglobin; MCHC: mean corpuscular haemoglobin concentration; RDW: red cell distribution width. Total iron binding capacity: TIBC. TS: transferrin saturation. Results are expressed as means \pm SD; n: 58, (p value \leq 0.05) statistically significant.

Table (2) shows the results of the ASQ-3 questionnaire used by the parent to document their child's development. The

ASQ-3 comprises five subdomains, each with six items and a maximum score of 60, for a total score of 300 and higher scores indicate more developmental milestones reached. In the current study, the domains of communication and gross motor performance did not show statistically significant differences with p values $>$ 0.05 for either domain; however, the domains of fine motor, problem-solving (36, 33, and 31, respectively, for IDA, compared to 48, 45, and 47, respectively, for control).

Table (2): Age Sex Questionnaire (ASQ) Category and Result Scores

Area	Cut-off	IDA Overall score (n=58)	Control Overall score (n=58)	p value
Communication	33.6	40 \pm 0.6	42 \pm 0.5	0.4
Gross Motor	30.61	48 \pm 1.7	50 \pm 1.5	0.6
Fine Motor	40.15	36 \pm 1.2	48 \pm 1.5	0.032
Problem Solving	36.17	33 \pm 1.1	45 \pm 2	0.02
Personal-Social	35.84	31 \pm 1.5	47 \pm 0.5	0.017

Iron deficiency anaemia (IDA). Results are expressed means \pm SD; n 58; (p value \leq 0.05) significant.

The results of treating infants and young children with iron sulphate for two months also are shown in Table (3). As it demonstrates, every parameter measured in this study showed a significant recovery, with the exception of ferritin, TIBC, and transferrin saturation, which showed a modest but significant recovery.

Following 2 months of oral iron therapy in table (3), Supplementation of iron with subsequent correction of RBCs count, Hb., HcT, MCV, MCH, MCH, and ferritin bring about upward scoring value of all domains particularly of the affected domains as shown in Table(3). Even area previously normal domains as compared to that of control including communication and gross motor domains show significant changes following iron supplementation.

Table (3): Age Sex Questionnaire (ASQ) for children with IDA after 2 months of iron therapy.

Area	Cut off	IDA Overall score	IDA after 2 months of iron therapy	p value
Communication	33.6	40 \pm 0.6	43.6 \pm 0.4	0.04
Gross Motor	30.61	48 \pm 1.7	54.32 \pm 1.1	0.009
Fine Motor	40.15	36 \pm 1.2	44.2 \pm 0.9	0.043
Problem Solving	36.17	33 \pm 1.1	41.6 \pm 1.3	0.04
Personal-Social	35.84	31 \pm 1.5	39.14 \pm 0.5	0.038

Iron deficiency anaemia (IDA). Results are expressed means \pm SD; n 58; (p value \leq 0.05) significant.



Discussion

Many different appraisal tools are available to assess the development of the infants. The tool that has been utilized in the current study to evaluate the developmental progress in enrolled infants is the ASQ@-3. Which is the most widely used across many countries because of its high validity, reliability, accuracy, cost effectiveness, easy of scoring (in just minutes), utilization in unmatched sample of diverse children, a great way to partner with parents and make the most of their expert knowledge, and finally because of fun and engaging for kids.⁸⁻⁹ Also, evidence showed that assessment of the earlier development associated with the greater the chance of affected children to reach his or her potential.¹⁰

Iron is essential for infant and child neurologic development. Studies have shown that iron is required for proper neuro-myelination, neurogenesis, and brain cell differentiation, all of which can affect sensory systems, learning, memory, and behaviour. Iron is indeed a cofactor for enzymes involved in the synthesis of neurotransmitters.¹¹⁻¹² Not surprisingly, Iron deficiency anaemia, one of the world's most common nutrient deficiencies, affects roughly one-third of the world's population.¹³

In our observations, comparable RBCs indices to those made by Janus,¹⁴ and Aulakh,¹⁵ who found that the average MCV was 74 fl, the average MCH was 20 pg, the average MCHC was 28 percent, and the average haemoglobin was 7.6 g/dL in IDA patients.¹⁴⁻¹⁵ In this study, the mean value of serum iron in infant with IDA was 20.82g/dL, which was much lower than the value in the control group, which was 77g/dL. In a study done on child patients, the mean was found to be 22.7g/dL, which is very close to what we found. Interesting result can be found with Total iron binding capacity TIBC 400µg/dL in IDA participant this result come into agreement with study conducted by Lee and his

colleague were found 413.6 µg/dL, Research have proven that TIBC is linked with IDA.¹⁶⁻¹⁷

Brotanek et al. employed transferring saturation, free erythrocyte protoporphyrin, and serum ferritin levels as their primary IDA predictors. Domell of et al. also used standard IDA markers, such as haemoglobin, mean corpuscular volume (MCV), and ferritin. But they also looked at other markers like zinc protoporphyrin saturations and transferrin saturations. In our study ferritin recorded were recorded at (6.9 ng/mL) in IDA infant which are very similar to other paper conducted by Brotanek.¹⁸

The impact of anaemia on children's brain and behaviour development may be linked to the fact that anaemia causes haemoglobin to carry less oxygen to the brain and slows down the body's energy metabolism; also it may be linked to cellular iron deficiencies other than heme like enzymes.¹⁹⁻²⁰ Our findings are backed up by data from other studies that show relationships between low IDA and child behaviour in term of communication and problem solving and child behaviour²¹. In accordance with our findings, Mehner²² and his team found in their research child with IDA deficiency developed impaired fine motor, solving problem and abnormal behaviour compared to non-anaemic child.²²

Studies have shown that IDA during the first two years of life is associated with impaired psychomotor development and behavioural abnormalities. It has been demonstrated that these effects continue after several months of iron therapy, disregarding correction of all iron dietary parameters.²³ The outcomes of this examination demonstrate that aberrant ASQ-3 scores were widespread across three domains in children from Duhok region.

According to finding, all haematological parameter was returned to normal level with ex caption of little effect on ferritin level after 2-month treatment. studies have proven that longer period of treatment



needed for whole recover of ferritin level, researcher have also argued that 2-3 month are good duration for oral iron sulphate substitution.²⁴

Conclusion

Iron deficiency anaemia associated with long-term consequences on mental and cognitive abilities, thus monitoring and early supplementation of iron is recommended in early infancy to prevent long term psychosocial sequelae.

Conflict of Interests

The authors declare that they have no conflict of interest regarding this paper.

References

1. Yang Z, Lönnerdal B, Adu-Afarwuah S, et al. Prevalence and predictors of iron deficiency in fully breastfed infants at 6 month of age: comparison of data from 6 studies. *Am J Clin Nutr.* 2009; 89(5):1433-40.
2. McLean E, Cogswell M, Egli I, et al. Worldwide prevalence of anaemia, WHO Vitamin and Mineral Nutrition Information System, 1993-2005. *Public Health Nutr.* 2009 A; 12(4):444-54.
3. Eissa AA, Mirza SS. The relevance of *Helicobacter pylori* Infection to iron deficiency anemia in Duhok City. *Iraqi JMS.* 2021; 19(1): 33-8.
4. Lichtman MA, Williams WJ. Williams's manual of hematology, 6th edition. New York: McGraw-Hill, Medical Pub. Division; 2003.
5. Killip S, Bennett JM, Chambers MD. Iron deficiency anemia. *Am Fam Physician* 2007;75: 671-8.
6. Szajewska H, Rusczyński M, Chmielewska A. Effects of iron supplementation in nonanemic pregnant women, infants, and young children on the mental performance and psychomotor development of children: a systematic review of randomized controlled trials. *Am J Clin Nutr.* 2010; 91(6):1684-90.
7. Singh A, Yeh Ch, Blanchard Sh. Ages and Stages Questionnaire: a global screening scale. *Bol Med Hosp Infant Mex.* 2017; 74(1):5-12.
8. Lipkin PH, Macias MM; council on children with disabilities, section on developmental and behavioural pediatrics. Promoting Optimal Development: Identifying Infants and Young Children with Developmental Disorders through Developmental Surveillance and Screening. *Pediatrics.* 2020; 145(1):e20193449.
9. Council on Children with Disabilities; Section on Developmental Behavioral Pediatrics; Bright Futures Steering Committee; Medical Home Initiatives for Children with Special Needs Project Advisory Committee. Identifying infants and young children with developmental disorders in the medical home: an algorithm for developmental surveillance and screening. *Pediatrics.* 2006; 118(1):405-20. doi: 10.1542/peds.2006-1231. Erratum in: *Pediatrics.* 2006; 118(4):1808-9. PMID: 16818591.
10. Beam M, Paré E, Schellenbach C, Kaiser A, Murphy M. Early developmental screening in high-risk communities: implications for research and child welfare policy. *The Advanced Generalist: Soc. Work Res.* 2015;1(3/4):18-36.
11. Iannotti LL, Tielsch JM, Black MM, et al. Iron supplementation in early childhood: health & benefits risks. *Am J Clin Nutr.* 2006;84(6):1261-76.
12. Domellöf M, Braegger C, Campoy C, et al. ESPGHAN Committee on Nutrition. Iron requirements of infants and toddlers. *J Pediatr Gastroenterol Nutr.* 2014; 58(1):119-29.
13. World Health Organization. (2008). Worldwide prevalence of anaemia 1993-2005: WHO global database on anaemia. / Edited by Bruno de Benoist, Erin McLean, Ines Egli and Mary Cogswell. World Health Organization.
<https://apps.who.int/iris/handle/10665/43894>



14. Janus J, Moerschel SK. Evaluation of anemia in children. *Am Fam Physician*. 2010 15; 81(12):1462-71.
15. Aulakh R, Sohi I, Singh T, Kakkar N. Red cell distribution width (RDW) in the diagnosis of iron deficiency with microcytic hypochromic anemia. *Indian J Pediatr*. 2009; 76(3):265-8.
16. Brittenham, GM. Disorders of iron metabolism: iron deficiency and overload. *Hematology: Basic Principles and Practice*, 2000; 3: 397–428.
17. Lee JH, Hahn JS, Lee SM, et al. Iron related indices in iron deficiency anemia of geriatric Korean patients. *Yonsei Med J*. 1996;37(2):104-111.
18. Brotanek JM, Gosz J, Weitzman M, Flores G. Iron deficiency in early childhood in the United States: risk factors and racial/ethnic disparities. *Pediatrics*. 2007; 120(3):568-75.
19. Domellöf M, Dewey KG, Lönnerdal B, et al. The diagnostic criteria for iron deficiency in infants should be re-evaluated. *J Nutr*. 2002;132(12):3680-3686.
20. Halis H, Bor-Kucukatay M, Akin M, et al. Hemorheological parameters in children with iron-deficiency anemia and the alterations in these parameters in response to iron replacement. *Pediatr Hematol Oncol*. 2009; 26(3):108-18.
21. Yang W, Liu B, Gao R, et al. Association of anemia with neurodevelopmental disorders in a nationally representative sample of US children. *J Pediatrics* .2021, 228, 183–9.
22. Mehner, CL, Gretchen JD, Madiha AM, et al. The association of cumulative risk scoring with ASQ-3 outcomes in a rural impoverished region of Guatemala. *Pediatric Dimensions*. 2019; 4 (4).
23. Walter, T. Effect of iron-deficiency anaemia on cognitive skills and neuromaturation in infancy and childhood. *Food Nutr Bull*. 2003; 24: S104-S110.
24. Tunnessen WW Jr, Oski FA. Consequences of starting whole cow milk at 6 months of age. *J Pediatr*. 1987; 111(6 Pt 1):813-6.