The Turkish Journal of Pediatrics 2018; 60: 22-31
DOI: 10.24953/turkjped.2018.01.004

Original

Investigation of the frequency of iron insufficiency among infants in a population in which routine iron supplementation is implemented

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Received: 20th July 2017, Revised: 17th August 2017, Accepted: 30th August 2017

SUMMARY: Çullas-İlarslan NE, Günay F, İleri DT, Elhan AH, Ertem M, Arsan S. Investigation of the frequency of iron insufficiency among infants in a population in which routine iron supplementation is implemented. Turk J Pediatr 2018; 60: 22-31.

Iron deficiency anemia (IDA) represents the most common cause of anemia worldwide. Because of potential irreversible neurodevelopmental impairment, its prevention during infancy is essential. We aimed to investigate the frequency of iron insufficiency among infants in a population which routine iron supplementation is implemented; and to examine related risks. A total of 501 infants, aged 9-15 months, were screened with complete blood count and serum ferritin. Infants were divided into two groups. [Group 1 (iron insufficient), [Group 1a: Iron deficiency (ID), Group 1b: IDA (IDA)], Group 2 (Iron sufficient (IS)]. Anemia was recognized in 122 (24.3%) infants. Microcytosis was observed in 110 (90.2%) of anemic infants. Group 2 accounted for 49.5% (n=248) whereas 152 (30.3%) and 101 (20.2%) infants belonged to Groups 1a and 1b, respectively. Multiple logistic regression analysis showed that male gender (OR=1.53; 95%CI 1.07 and 2.17), receiving >500 ml/day cow's milk (OR=2.77; 95%CI 0.87 and 8.83) and incompliance to iron supplementation (OR=2.51; 95%CI 1.75 and 3.60) were distinctive characteristics of Group 1 while prevalence of iron insufficiency was higher in infants consuming less formula (OR=3.10; 95%CI 2.00 and 4.80). The most frequent reasons for incompliance were consideration of supplementation as unnecessary (n=69, 31.1%) and neglection (n= 59, 26.6%). Our study demonstrated a high frequency of iron insufficiency among infants in a setting utilizing national iron supplementation and "incompliance" to iron as the most evident risk factor for iron insufficiency. Effective counseling of families by health care providers concerning importance of compliance to iron prophylaxis is essential for prevention of iron insufficiency. We also suggest screening of infants for ID as well as IDA in settings with high frequency of iron insufficiency.

Key words: anemia, infancy, iron deficiency, iron deficiency anemia, iron supplementation.

Anemia is defined as hemoglobin (Hb) -2SD below the mean Hb concentration adjusted for age and gender.[1,2] Iron deficiency anemia (IDA) represents the most common cause of anemia worldwide.[3,4] Irreversible neurodevelopmental impairment, particularly apparent in the first few years of life, is the most relevant clinical outcome of IDA which may also be observed in iron deficiency (ID).[5-9]

There has been an obvious decline in the prevalence of IDA in infants in industrialized nations throughout the last decades related with increased encouragement of breastfeeding, iron fortified infant formulas and complementary food, routine screening of anemia and prophylactic iron implementation.[4] The current prevalence of ID is 8% and IDA is 1-2% in toddlers in the United States of America

This study was presented at the 60th Turkish National Pediatric Congress, November 9th-13th 2016, Antalya, Turkey.

(U.S.A).[10,11]

IDA is a challenging health problem especially for developing countries, basically related with inadequate iron-rich food consumption, lower education and limited opportunity to reach health services.[12] Current prevalence of anemia in children aged 5-59 months in Turkey was reported as 30% (95% CI 9 and 64) by WHO while regional previous data show rates of 15-60%.[2,13-16]

Despite initiation of national iron supplementation project to infants in 2004, we believe that iron insufficiency still serves as an unsolved health issue in Turkey as we observe high rates in our daily practice. As a result, we hypothesized that iron supplementation in infancy is essential but not sufficient for prevention of iron insufficiency without *"compliance"*.

Primary aim of this study was to investigate the frequency of iron insufficiency and associated risk factors among infants in a population which routine iron supplementation is implemented. Our secondary aim was to examine reasons for incompliance.

Material and Methods

This prospective cross-sectional study was conducted in the pediatric outpatient clinic of Ankara University Children's Hospital between April-December, 2015. The study protocol was approved by the Institutional Ethics Committee of Ankara University School of Medicine (Approval number: 02-70-15; Feb 2015). Written informed consent was obtained from the parents.

Selection criteria

Infants with a history of infection in the past two weeks, leukocytosis or high serum C-reactive protein (CRP), previous diagnosis of IDA and/or chronic disease (kidney, gastrointestinal or lung disease, congenital or acquired heart disease, neuromuscular disease, immune deficiency), prematurity (<37 weeks), low birth weight (<2,500 g) and missing informed consent were excluded.

Patient characteristics

In accordance with the approximate age of national screening for anemia held in Turkey, we included infants between 9-15 months. A total of 662 healthy infants in this age interval were admitted to our outpatient clinic during the study period. Among these, 74 parents (11.2%) refused to participate, 18 (2.7%) infants with high CRP, 29 (4.4%) with inadequate blood samples, 36 (5.3%) carrying other exclusion criteria and 4 (0.6%) diagnosed as beta-thalassemia minor later were excluded. Consequently, 501 (75.7%) infants (242 girls 48.3%) with a median age of 11 (9-15) months were evaluated.

Description of iron supplementation program implemented in Turkey

Since 2004, 10 mg/day iron supplementation is recommended for infants aged 4-12 months within the scope of a national project called "Iron-like Turkey" and screening for anemia at 9-12 months is performed by measurement of Hb. Although families are mainly consulted by family physicians or nurses in primary health care centers (PHCC), pediatricians also prescribe iron drops to prevent missed opportunities in cases who fail to visit PHCC. Families are reminded by doctors and/or nurses concerning the continuation and correct use of iron in each follow-up visit.

Our institution advises families to continue iron supplementation until age 2 in accordance with WHO recommendations for iron supplementation for infants living in developing nations.[17] Although most side effects are easily tolerated by infants, we suggest utilizing a

Table I. Reasons for Incompliance to Iron Supplementation.

	Number (n)	Percentile (%)
Consideration of iron as unnecessary	69	31.1
Neglection	59	26.6
Observed side effects	37	16.6
Taste problem	34	15.3
Did not receive any recommendation of iron	14	6.3
Worry about possible side effects	9	4.1

different preparation or switching ferrous (+2) to ferric iron (+3) if side effects are strong. Another option is to start with small doses and gradually increase the dose each day following cessation of iron for a couple of days.

All infants included in our study were started on ferric iron (+3) drops in accordance with the iron supplementation program of Turkish Ministry of Health. Iron supplementation were mostly started to infants in PHCC (n=467, 93.2%) and rarely (n=23, 4.6%) in pediatric clinics.

Data collection

Parent questionnaire: Maternal risks, demographic and socioeconomical characteristics, dietary habits, iron prophylaxis status and reasons for incompliance to iron were questioned.

Definitions

Growth parameters: Length for age (LFA), weight for age (WFA), weight for length (WFL) and body mass index (BMI) standard deviation (SD) scores (Z-scores) were calculated[18]. Z scores -2SD - 2SD were accepted as normal, < -2SD - ≥ -3SD as stunted/ underweight/ wasted; < -3SD as severely stunted, severely underweighted or severely wasted, > 2SD as overweight and > 3SD as obese.

Adequate red meat consumption: ≥3 portions/ week, ≥30 g/portion, as adapted from Olaya's study[19].

Compliance to iron: Although not defined elsewhere, we defined "compliance" to iron as ≥5 times/week for ≥4 months.

Laboratory tests

Blood samples for CBC (complete blood count) (2-3 ml) and serum ferritin (2 ml) were obtained from each patient. In order to rule out acute subclinical infection, additional blood (2 ml) was drawn for CRP measurement, as ferritin might also elevate as an acute phase reactant. CBC analysis was established using (Coulter Counter LH780) while CRP was measured with (UniCel DxC800 Synchron) device (Beckman Coulter, U.S.A). Serum ferritin was measured using the reactant Access Ferritin-33020 (Beckman Coulter, U.S.A).

Data interpretation

Anemia was defined as Hb <11 g/dl as recommended by WHO guidelines for 6-24 months[2]. Mean corpuscular volume (MCV) < 70 fl was considered as microcytosis. Cut-off level of ferritin was accepted as 15 ng/ml as outlined by WHO guidelines for developing countries.[1] Iron deficiency was defined as low ferritin, normal Hb and MCV >70 fl. A child with low hemoglobin, low ferritin and MCV <70 fl was diagnosed as IDA. Group 1a (ID) and Group 1b (IDA) were both called "iron insufficient" (Group 1). Infants with normal Hb level, normal ferritin and MCV >70 fl were considered IS (Group 2). Groups were compared regarding associated risks.

Statistical analysis

Multiple logistic regression analysis was used to define risk factors of outcome variables (iron insufficiency, ID and IDA). Prior to logistic regression analysis, a univariate estimate was performed by means of the

Table II. Hematological Parameters of Three Groups [Group 1a (ID) and Group 1b (IDA), Group 2 (IS)].

	ID	IDA	IS
Hb (g/dl), mean±SD	11.80 ± 0.57	10.11 ± 0.75	11.91 ± 0.69
RBC (x 10^6/mm^3), mean±SD	4.69 ± 0.40	4.65 ± 0.37	4.73 ± 0.36
Hct (%), mean±SD	35.62 ± 1.84	31.77 ± 2.14	35.69 ± 2.59
MCV (fl), mean±SD	75.52 ± 3.66	67.96 ± 5.99	76.78 ± 3.54
RDW (%), mean±SD	14.73 ± 1.44	17.12 ± 1.99	14.43 ± 3.86
Ferritin (ng/ml), median (min-max)	9.65 (3-14.8)	6 (2-11.4)	24.3 (14-68)

ID: iron deficiency, IDA: iron deficiency anemia, IS: iron sufficient, Hb: hemoglobin, Hct: hematocrit, RBC: red blood cell, MCV: mean corpuscular volume, RDW: red blood cell distribution width

logistic regression analysis to evaluate the association of each independent variable with the outcome variables. Variables with P<0.25 following univariate analysis were included to the multiple logistic model along with variables of known biological importance. Chi-square test or Fisher's exact test were used for categorical variables, where applicable. For two groups, Student's t-test was used for continuous variables. Differences amongst three groups for continuous variables were evaluated by One-way analysis of variance. When p-value from one-way ANOVA statistics was statistically significant, multiple comparison test was used to know which group differs from which others. The Bonferroni correction was applied for all possible multiple comparisons. P<0.05 was considered statistically significant. Statistical analysis was performed using the SPSS statistical package (v.21.0).

Results

Median time of iron supplementation of the whole study group was 5.06 (0-11) months. Side effects of iron were constipation (n=45, 9%), vomiting (n=43, 8.6%), diarrhea (n=13, 2.6%), loss of appetite (n=5, 1%), rash (n=1, 0.2%) and discoloration of the teeth (n=1, 0.2%). Compliance to iron was reported as 55.7% (n=279). The most frequent reasons for incompliance were consideration of supplementation as unnecessary or neglection whereas side effects constituted only a small portion (Table I). The median time period of iron supplementation was observed to be longer in infants who were accepted as compliant [6.26 (4-11) months].

The hematological parameters of groups are documented in Table II. 122 (24.3%) infants had anemia while microcytosis was observed in 110 (90.2%) of anemic infants. Group 2 accounted for 49.5% (n=248) whereas 30.3% (n=152) and 20.2% (n=101) infants belonged

Table III. Comparison of Groups with Respect to Maternal Factors and Demographic Characteristics of Infants.

		Iron insufficient	Iron sufficient	p value
Parity	1	119 (47.0)	126 (50.8)	0.399
	>1	134 (53.0)	122 (49.2)	
Interpregnancy interval (years)	<2	23 (9.1)	31 (12.5)	0.219
	≥2	230 (90.9)	217 (87.5)	
Chronic disease during pregnancy	Yes	22 (8.7)	27 (10.9)	0.409
	No	231 (9.3)	221 (89.1)	
IDA during pregnancy	Yes	127 (50.2)	105 (42.3)	0.078
	No	126 (49.8)	143 (57.7)	
Iron suppl. during pregnancy	Yes	168 (66.4)	174 (70.2)	0.366
	No	85 (33.6)	74 (29.8)	
Age (months)	9-11.99	131 (51.8)	129 (52.0)	0.958
	12-15	122 (48.2)	119 (48.0)	
Gender	Female	109 (43.1)	133 (53.6)	0.018
	Male	144 (56.9)	115 (46.4)	
Length for age Z-score	<-2	23 (9.1)	17 (6.9)	0.591
	-2-+2	218 (86.2)	221 (89.1)	
	>2	12 (4.7)	10 (4.0)	
Weight for age Z-score	<-2	12 (4.7)	10 (4.0)	0.637
	-2-+2	236 (93.3)	230 (92.8)	
	>2	5 (2.0)	8 (3.2)	
Weight for length Z-score	<-2	18 (7.1)	10 (4.0)	0.312
	-2-+2	226 (89.3)	230 (92.8)	
	>2	9 (3.6)	8 (3.2)	
Body mass index Z-score	<-2	18 (7.1)	16 (6.5)	0.940
	-2-+2	224 (88.6)	222 (89.5)	
	>2	11 (4.3)	10 (4)	

IDA: iron deficiency anemia, suppl: supplementation

to Group 1a and 1b, respectively. A total of 253 (50.5%) infants were iron insufficient.

Rate of multiparity and IDA during pregnancy was higher and iron supplementation in pregnancy was lower in Group 1 without statistical significance (Table III).

Age distribution of infants and growth parameters were similar in both groups. Predominance of male gender was significant in Group 1 (p=0.018) (Table III).

Duration of exclusive breastfeeding was longer (p<0.001), ratio of infants still receiving breastmilk was higher (p<0.001) and number of infants receiving more than half of daily feedings with formula was less (p<0.001) in Group 1. Although not significant, more infants consumed >500 ml/day cow's milk in Group 1 (p=0.073). Consumption of red meat, timing

Table IV. Comparison of Dietary Habits, Iron Prophylaxis Status and Socioeconomic Characteristics of Group 1 (Iron insufficient) and Group 2 (IS).

		Iron insufficient	Iron sufficient	p value
Exclusive breastfeeding (months)	<4	56 (22.1)	100 (40.3)	<0.001
	4.1-6	180 (71.2)	136 (54.9)	
	>6	17 (6.7)	12 (4.8)	
Infants still receiving breastmilk	Yes	204 (80.6)	164 (66.1)	<0.001
	No	49 (19.4)	84 (33.9)	
Receiving > ½ of daily feeding as formula	Yes	37 (14.6)	86 (34.7)	<0.001
	No	216 (85.4)	162 (65.3)	
Introduction of complementary food (months)	<4	29 (11.5)	25 (10.1)	0.949
	4-5.99	54 (21.3)	56 (22.6)	
	6	147 (58.1)	143 (57.7)	
	>6	24 (9.1)	24 (9.7)	
Adequate red meat consumption	Yes	62 (24.5)	56 (22.6)	0.612
	No	191 (75.5)	192 (77.4)	
Introduction of cow's milk (months)	<12	40 (15.8)	49 (19.8)	0.248
	≥12/not yet	213 (84.2)	199 (80.2)	
Amount of daily received cow's milk (ml)	≤500/not yet	242 (95.7)	244 (98.4)	0.073
	>500	11 (4.3)	4 (1.6)	
Received iron recommendation	Yes	241 (95.3)	246 (99.2)	0.008
	No	12 (4.7)	2 (0.8)	
Iron dose (mg/kg)	<1	140 (55.3)	127 (51.2)	0.637
	1-2	90 (35.6)	95 (38.3)	
	>2	23 (9.1)	26 (10.5)	
Initiation of iron (months) *	4-5	206 (86.6)	197 (86.8)	0.942
	≥6	32 (13.4)	30 (13.2)	
Duration of iron supplementation (months)	0-3.99	82 (32.4)	48 (19.4)	0.003
	4-7.99	120 (47.4)	133 (53.6)	
	≥ 8	51 (20.2)	67 (27)	
Proper use of iron (≥5/week)	Yes	137 (54.2)	182 (73.4)	< 0.001
	No	116 (45.8)	66 (26.6)	
Compliance to iron supplement	Yes	113 (44.7)	166 (66.9)	< 0.001
	No	140 (55.3)	82 (33.1)	
Maternal education (years)	<8	122 (48.2)	107 (43.1)	0.254
	≥8	131 (51.8)	141 (56.9)	
Paternal education (years)	<8	98 (38.7)	96 (38.7)	0.995
	≥8	155 (61.3)	152 (61.3)	
Monthly income	< MW	7 (3)	5 (2.2)	0.451
	1-1.99 MW	117 (50.2)	104 (45.4)	
	≥ 2 MW	109 (46.8)	120 (52.4)	

*(among infants whose families initiated iron supplementation), MW: minimum wage

of introduction of solid food and cow's milk were similar between groups (Table IV).

Duration of iron supplementation was shorter (p=0.003) and compliance to iron was lower (p<0.001) while less infants received iron recommendation (p=0.008) and used iron in a proper frequency (p<0.001) in Group 1 (Table IV).

Maternal, paternal education and monthly income were similar between two groups (Table IV).

Comparison of three groups (Group 1a, 1b and 2): p <0.0167 (0.05/3) was considered as significant following Bonferroni correction. Similar results with two group comparisons were obtained (Table V). Both Group 1a and 1b received iron less frequently than required (p<0.001), were less compliant to iron (p<0.001) and received less formula (p<0.001) in comparison with Group 2 while Group 1b accounted for other differences. In addition to two group comparisons, infants with IDA were more likely to be born from multiparous pregnancies (p=0.009) and less educated mothers (p=0.008).

Multiple logistic regression analysis model (we included one variable in case of related variables) revealed higher prevalence of iron insufficiency in male infants, in infants receiving >500 ml/day cow's milk and in infants who were incompliant to iron. Infants who received more formula instead of cow's milk showed less prevalence of iron insufficiency (Table VI).

Discussion

Iron deficiency anemia carries major health consequences along with social and economic issues. Main reasons for IDA among infants are increased iron requirements because of rapid growth and inadequate intake of iron from dietary supply.[20]

Previous studies from Turkey investigating iron insufficiency in children mostly included school-aged children, consisted of small size, offered regional data and variations existed in definitions of IDA and ID.[13-16] Since 2004,

Table V. Summary of The Statistically Significant Comparison Findings Amongst Three Groups (Group 1a (ID) and Group 1b (IDA), Group 2 (IS).

Parameters		ID	IDA	IS	p value
Parity	1	83 (54.6)	36 (35.6)	126 (50.8)	0.009
	>1	69 (45.4)	65 (64.4) *	122 (49.2)	
Gender	Female	72 (47.4)	37 (36.6)	133 (53.6)	0.015
	Male	80 (52.6)	64 (63.4) **	115 (46.4)	
Exclusive breastfeeding (months)	<4	47 (30.9)	9 (8.9)	100 (40.3)	<0.001
	4.1-6	99 (65.1)	81 (80.2)	136 (54.8)	
	>6	6 (3.9)	11 (10.9)*	12 (4.8)	
Infants still receiving breastmilk	Yes	115 (75.7)	89 (88.1)	164 (66.1)	<0.001
	No	37 (24.3)	12 (11.9)*	84 (33.9)	
Receives > ½ of daily feeding as formula	Yes	32 (21.1)	5 (5)	86 (34.7)	<0.001
	No	120 (78.9)	96 (95)**	162 (65.3)	
Received iron recommendation	Yes	147 (96.7)	94 (93.1)	246 (99.2)	0.006
	No	5 (3.3)	7 (6.9)**	2 (0.8)	
Duration of iron supplementation (months)	0-3.99	45 (29.6)	37 (36.6)	48 (19.4)	0.007
	4-7.99	78 (51.3)	42 (41.6)	133 (53.6)	
	≥ 8	29 (19.1)	22 (21.8)**	67 (27)	
Proper use of iron (≥5/week)	Yes	89 (58.6)	48 (47.5)	182 (73.4)	<0.001
	No	63 (41.4)	53 (52.5)**	66 (26.6)	
Compliance to iron supplement	Yes	74 (48.7)	39 (38.6)	166 (66.9)	<0.001
	No	78 (51.3)	62 (61.4)**	82 (33.1)	
Maternal education (years)	<8	62 (40.8)	60 (59.4)	107 (43.1)	0.008
	≥8	90 (59.2)	41 (40.6)*	141 (56.9)	

ID: Iron deficiency, IDA: Iron deficiency anemia, IS: Iron sufficient,
* different from ID and IS ** different from IS

10 mg/day national iron supplementation is carried out for infants aged 4-12 months. As a result, some recent studies inform lower rates of IDA.[20,21] Yazici et al.[21] reported childhood anemia and IDA rates as 20.8% and 6.2%, respectively. Yalcin and colleagues[22] carried out the most comprehensive clinical trial in Turkey investigating the prevalence of IDA in infants following national iron supplementation and included infants from three different NUTS-1 (Nomenclature of Territorial Units for Statistics) regions of Turkey. Most infants included in this study have received iron supplementation from family physicians or nurses of the PHCC. Prevalence of anemia was 10.54% in infants aged 12-15 months, delineating efficacy of iron supplementation. Exact prevalence of neither IDA nor ID was

Table VI. Factors Related with Anemia in Accordance with Multiple Logistic Regression Analysis.

		Univariate analysis			Multivariate analysis		
		OR	95% CI	p	Adj.* OR	95% CI	p
IDA during pregnancy				0.078			
	Yes	1.37	0.97-1.95				
	No	1.00					
Gender				0.018			0.019
	Female	1			1		
	Male	1.53	1.07-2.17		1.57	1.08-2.28	
Exclusive breastfeeding (months)				0.001			
	≤4	0.42	0.29-0.63				
	4.1-6	1					
	>6	1.07	0.50-2.32				
Infants still breastfed				<0.001			
	Yes	2.13	1.42-3.21				
	No	1					
Receiving formula > ½ of daily feeds				<0.001			<0.001
	Yes	1.00			1.00		
	No	3.10	2.00-4.80		3.62	2.27-5.77	
Daily cow's milk consumption (ml)				0.084			0.009
	≤500/not yet	1.00			1.00		
	>500	2.77	0.87-8.83		5.45	1.52-19.57	
Received iron recommendation				0.018			
	Yes	1					
	No	6.12	1.36-27.66				
Compliance to iron supplementation				<0.001			<0.001
	Yes	1.00	1.75-3.60		1.00	1.78-3.80	
	No	2.51			2.60		
Monthly income				0.041			
	<MW	1.76	0.79-3.92				
	1-1.99 MW	0.71					
	≥2MW	1	0.49-1.04				

*Adj: adjusted, IDA: iron deficiency anemia, MW: minimum wage.

represented as ferritin was not measured in all infants. Inversely, Unal and colleagues[23] reported higher rates of ID (34.8%) and IDA (36%) in infants following national iron supplementation. This study is limited with its small size and inclusion of infants with acute infection.

It is well known that IDA represents the tip of the iceberg as prevalence of ID is higher. As both conditions are related to developmental disturbances which may be irreversible, diagnosis of both is crucial.[5-9] Our measurement of both CBC and plasma ferritin showed iron insufficiency in half of the infants, comparable with the recent WHO report and Unal et al.'s study.[2,23] On the other hand, our data conflicts with results of Yalcin et al.'s[22] study. Although both studies shared similarities such as using the same cut-off values for Hb and ferritin, recruiting infants who received iron from PHCC and similar compliance rates of iron supplementation, we encountered a higher rate of iron insufficiency. Moreover, ours was a single-center study held in one NUTS-1 region while Yalcin et al.[22] studied infants from three different NUTS-1 regions which represented lower income and higher malnutrition, therefore expected to carry a higher risk of iron insufficiency. Lower rate of iron deficiency anemia encountered by Yalcin et al.[22] might be due to enrollment of infants previously diagnosed as IDA and had already received therapeutic dose of iron.

In accordance with our study, Dömellof et al.[24] also reported male predominance in infantile IDA. Proposed mechanisms are sex differences in ferritin, iron metabolism, body composition and hormonal factors.[25]

Similar with Abdullah et al.[26], we observed longer duration of breastfeeding and less formula intake in iron insufficiency. Support for breastfeeding is an effective preventive measure against iron insufficiency because of its high bioavailability. Nevertheless, iron reserves run out after the first 4-6 months of life, raising the need for extra iron intake so forth.[25] Iron fortification of food and/or commercial formulas and iron supplementation are effective strategies for prevention of iron insufficiency in infants. As Turkey's policy against IDA is mainly iron supplementation, we strongly believe that it is essential for all infants to receive iron regardless of the feeding practices.

Infants should receive 30% of daily iron needs from the diet. Heme sources have higher bioavailability. A study from Colombia reported higher Hb in infants receiving adequate meat.[19] We demonstrated inadequate red meat consumption as it takes a while for infants to receive sufficient meat. This finding also emphasizes the necessity of iron supplementation.

An exact definition of "compliance" to iron supplementation is lacking in the literature. A study from Mexico calculated adequate compliance by using the number of days the supplement was consumed and the field staff visited to administer the syrup[27]. We could not use this method because we questioned parents retrospectively. Because we had to take infants younger than 1 year into consideration, we accepted minimum iron use as "4 months" when defining compliance and observed lower prevalence of iron insufficiency in compliant infants. Yalcin et al.[22] found also lower prevalence of anemia in infants who were initiated iron earlier and received recommended amount of total boxes. Another study demonstrated IDA in 2% and ID in 20% of infants receiving iron while rates were 30% and 26%, respectively, in infants who failed to receive prophlaxis.[14] Shibukawa et al.[12] found IDA prevalence as 41.5% in infants in Brazil following institution of iron prophylaxis and linked failure of their program to low adherence to iron.

We think that the main reason of iron incompliance was ineffective counseling of families by health care providers as many incompliant families considered supplementation as unnecessary or just neglected. We also believe that current use of iron must be questioned in each child visit. Another study also concluded that the more information parents received, the more they administered iron to their infants.[28]

Comparison of three groups revealed multiparity and less maternal education as additional risk factors of IDA. Lopez-Florez et al.[27] have drawn attention to lower maternal education as a risk factor for incompliance to iron in infants. We believe that multiparity may also increase risk of IDA of infants as it's linked

with maternal anemia.[29]

Multivariate logistic regression analysis reported consumption of excessive cow's milk as an additional risk factor for iron insufficiency. Studies relate this finding due to its low iron content, possible occult gastrointestinal bleedings and inhibiton of dietary iron absorption[26,30,31]. Health care providers should encourage families against offering excessive amount of cow's milk to their children.

There are several limitations of this study. Including infants from one NUTS-1 region is the first limitation. Secondly, we have not recorded whether the families lived in the urban or the rural areas of Ankara. Third, recording the amount of daily consumption of green vegetables and citrus fruits which increase absorption of dietary iron would be of value. Last, our definition of *"compliance"* to iron supplementation might not be adequate for older infants as they should have received iron longer.

Prevention of iron insufficiency is crucial to avoid irreversible neurodevelopmental disturbance. Effective counseling of families by health care providers concerning negative impacts of iron insufficiency and importance of compliance to iron prophylaxis is essential. In addition, avoidance of excessive amount of cow's milk ingestion must be suggested and each well child visit should cover evaluation of the current use of iron. We also suggest measurement of serum ferritin levels besides CBC to diagnose ID as well as IDA in settings with high frequency of iron insufficiency.

Acknowledgements

We thank the children and their parents for participation in our study. We are also grateful to Leyla Zümrüt Uysal (Professor of Pediatric Hematology and Oncology, Ankara University School of Medicine) and Professors of Pediatrics from Yale New Haven Children's Hospital (Eugene D. Chapiro, Brian Forsyth, John Mishel Leventhal, Carol Weitzman, and George Lister) for their contribution to our study design and Zeynep Bıyıklı Gençtürk for her help in our statistical analysis.

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