A community-based iron supplementation program, "Iron-like Turkey", and the following prevalence of anemia among infants aged 12-23 months

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During the second year of the "Iron-like Turkey" Project, in which all children aged 4-6 months in Turkey receive iron supplementation for 5 months, we aimed to assess the utilization of iron supplementation in the field, as well as the prevalence of anemia in healthy infants aged 12-23 months, while determining a variety of sociodemographic and nutritional factors for anemia in three of the 12 NUTS (Nomenclature of Territorial Units for Statistics) regions (regions with the highest, lowest and middle under-5 malnutrition levels). In a community-based, cross-sectional survey using a multi-staged, weighted, cluster-selected sample, children aged 12-23 months with birthweight ≥2500 g, no chronic illness, no history of blood disease, and from term and singleton pregnancy were enrolled; 1589 children met the criteria. The mean±SD age of children surveyed was 17.8±3.6 months. Of the parents, 72.4% claimed that their physician had recommended iron supplementation, and 68.8% had given supplementation to their children. Overall prevalence of anemia was 7.3%. Multivariate analysis revealed that the frequency of anemia decreased significantly in older infants, when supplementation was recommended by health providers, when an infant was breastfed longer than 6 months, and when the mother received iron supplementation during pregnancy. However, anemia prevalence increased when the infant received iron supplementation at a later age (≥9 months), lived in a crowded family (≥6 persons), and when the mother had a history of iron deficiency anemia. Anemic infants had significantly lower z scores of weight for age than non-anemic ones. This survey suggests that iron supplementation during pregnancy, initiation of iron supplementation in infants at 4-6 months of age, effective counseling on supplementation, subsequent compliance, support of breastfeeding, and effective training of health care personnel are effective strategies for prevention of anemia in the community.

Key words: anemia, infants, iron supplementation, "Iron-like Turkey" project, prevalence, nutrition.

Iron deficiency anemia (IDA) is one of the most severe and widespread nutritional disorders in the world[1]. Anemic women and their infants are at greater risk of dying due to the consequences of anemia during the perinatal period[1-3]. Infantile iron deficiency (ID) impairs cognitive development, learning capacity and school performance of children from infancy through adolescence[1,4,5]. Impaired immunity due to IDA is associated with increased morbidity rates[1,6]. Given the detrimental long-term effects and high prevalence of ID (1 of the top 10 serious health problems in the modern world), its prevention in early childhood is an important

public health issue[1,7,8].

Iron deficiency (ID) commonly develops after 6 months of age if complementary foods during the weaning period do not provide sufficient absorbable iron[1,9,10]. The diet of young children tends to comprise few foods consumed in small amounts, and thus, food quality becomes critical[9]. From the three common programmatic choices (supplementation, fortification and increased consumption of iron-rich foods), the World Health Organization (WHO) recommends universal iron supplementation (IS) for children when prevalence of anemia is more than 40%[1,11,12]. Country estimates of anemia prevalence were moderate (31.5%) in preschool-age children and severe in pregnant women (40.2%) in Turkey[7].

Turkey launched a program titled "Iron-like Turkey" in 2004 to be implemented in children in all the provinces[13]. This program has an advisory board. Members of the board are from a variety of both governmental and non-governmental institutions including universities. The program includes free IS to all children under 12 months of age through primary health care facilities. All infants receive 10 mg of IS once a day starting from 4 months of age and continuing for at least 5 months. Preterm infants are advised to receive supplementation as early as 2 months of age at a dose of 2 mg/kg daily. This community-based intervention also includes provision of iron treatment for all 4–24-month-old children with IDA. During the implementation of the program, all health care providers received training with clear policy guidelines on the prevention of anemia in the community as well as the additional strategies to improve the nutritional status of infants, with strong support of exclusive breastfeeding up to 6 months of age, with continued breastfeeding along with appropriate complementary foods up to 2 years of age or beyond[13].

Before the initiation of the program, nationwide data were missing. Hospital-based studies in addition to limited local and regional data on iron status of the risk groups[14,15] were used to develop effective strategies for planning and implementing the Iron-like Turkey Program. However, nationwide interventions require effective monitoring for further planning and implementation strategies. Therefore, the advisory group recommended undertaking a nationwide study at the end of the second year to evaluate the feasibility, acceptance, compliance, outcome, and/or impact of the program. Turkey has 12 NUTS-1 (Nomenclature of Territorial Units for Statistics) regions. Every five years, a National Demographic and Health Survey is carried out in Turkey providing information on various health indicators of these regions[16]. A cross-sectional survey was planned in three different NUTS-1 regions defined according to their health indicators as low, high and middle. The aims were to assess the prevalence of anemia in healthy infants aged 12-23 months and to determine a variety of sociodemographic and nutritional predisposing factors for IDA in infants in three NUTS-1 regions in Turkey with low, high and middle health indicators.

Material and Methods

The study was a community-based, cross-sectional survey using a multi-staged, weighted, cluster-selected sample. Children aged 12-23 months, with birthweight ≥2500 g, term, with no major congenital anomalies, no chronic diseases, and no history of blood disorders such as carriers of β-thalassemia, and children from singleton and term pregnancies (gestational age ≥37 weeks) took part in the study. If more than one child was eligible per household, only one was randomly selected to participate. Children who had febrile illness on enrollment were excluded from the study.

The sample size was found to be 384 children from each region, with an expected proportion at 50%, an alpha of 0.05, and a level of precision (d) of 0.05[17]. The effect of cluster sampling was overcome by making an appropriate correction for design effect, a multiple of 1.5. Since this was a community-based study, a nonresponse rate of 25% was added. The calculated sample size was at least 720 for each region. According to population data in Turkey, an overall estimation is made that 13 households should be looked for to be able to find a 12-23-month-old child. For each region, approximately 9600 households were planned to be visited. Therefore, the target total sample size of the survey was set at 28,800 households visited as a whole to reach 2200 children.

The survey was carried out from November 2006 to March 2007. The study population consisted of 12-23-month-old children, living in three different NUTS-1 regions of Turkey according to the prevalence of malnutrition (the

percentages of height for age below -3SD; high, middle and low) in the Turkey Demographic and Health Survey (TDHS) 2003[16], and "region with high malnutrition prevalence" defined as poor region (PR), "region with middle malnutrition prevalence" as middle region (MR) and "region with low malnutrition prevalence" as good region (GR)[13]. Each region had eight cities, and these cities were listed from the worst to the best using health indicators and statistical development level data provided by the Turkish Government Planning Agency[13,18]. From the lists of each region, the 2nd and 8th cities were enrolled for the study according to ballot numbers 2 and 8 as the first level clusters. In the case of PR, data were collected from Malatya and Bingöl provinces, for MR from Hatay and Adana, and for GR from Bursa and Bilecik. Then, lists of Primary Health Care Centers (PHCCs) of cities were obtained from the records of the Ministry of Health and the National Statistical Center of Turkey, in an attempt to obtain a representative sample from the overall population of three selected regions. Household Record Files (HRFs) and the number of children aged 1 year of PHCCs were updated in selected cities. First, PHCCs were listed alphabetically, and the number of HRFs of each center was noted and added cumulatively. Then, 32 center-points were selected in each region (the second level). After selection of a starting point randomly, the center-point was chosen by systematic sampling. These center-points were used to identify "PHCCs-selected" in which household clusters were selected and children were enrolled. Only PHCCs having at least 50 households were eligible for inclusion. The number of center-points was proportional to the child population size in each city: 3 Bilecik, 29 Bursa, 12 Hatay, 20 Adana, 6 Bingöl, and 26 Malatya[13]. Then, HRFs of these PHCCs were obtained from the Turkish Ministry of Health. The third stage sample selection was "household-clusters". After selection of a starting point randomly, 10 household clusters containing 30 households were chosen from each "selected-PHCCs" by systematic sampling. Then, children suitable for the study (children aged 12-23 months of age, no history record of thalassemia) in each household-cluster were enrolled for the survey. The constituted participant lists were given to community organizers.

A team of fieldworkers (nurses) and community organizers were thoroughly trained in survey methods before the start of each phase of the study. The team was accompanied and supervised daily by the program managers (SSY, BT) in order to ensure the maintenance of standard procedures. Fieldworkers identified families of selected children, obtained informed consent and referred children to the PHCC for questionnaire data, anthropometric measurements and hemoglobin (Hb) assessment. The survey questionnaire was administered to the mothers by the fieldworkers. Anthropometric data were collected at the PHCC. Weight and height of children were measured.

Capillary blood samples were obtained in two microtubes from the middle finger of the left hand of each subject using a microlance, and centrifuged to measure the hematocrit (Htc) levels. If the mean Htc value of a child was <33%, venous blood samples were taken for the following: complete blood count (Hb, Htc, mean corpuscular volume (MCV) by STKS Coulter Machine) and serum ferritin (SF). Complete blood count was analyzed within 4 hours (h) at the regional reference center. Venous blood without anticoagulants was centrifuged at 3000 rpm for 10 minutes (min) and the serum was separated, aliquotted and frozen at -20°C within 4 h of sample collection. Frozen samples were transported on dry ice to the laboratory where they were analyzed for SF by electrochemiluminescence immunoassay using commercial kits (Roche Diagnostics GmbH, Mannheim, Germany).

Anemia was defined as Hb <11.0 g/dl[1]. The ferritin cut-off point, <15 μg/L, recommended by WHO for developing countries, was used to define ID in order to compensate for the effect of infection, which can lead to elevation of the level of ferritin[1]. In cases with anemia, ID was defined as ferritin <15 μg/L or MCV <70 fL and red cell distribution width (RDW) >14.5%[1,19]. All children diagnosed as having anemia were referred to physicians of the PHCC who examined them for further evaluation. Children who were diagnosed as carriers of β-thalassemia by Hb electrophoresis during the study did not take part in the survey.

A detailed survey questionnaire, which covered areas such as socioeconomic factors, parental educational status, reproductive history (parity, birth interval), maternal anemia during pregnancy or at other times, dietary patterns of children (the duration of breastfeeding, age

of starting complementary feeding, starting age of introduction of cow's milk, and amount of cow's milk consumed daily), and history of β-thalassemia in the family, was developed from a review of the literature concerning risk factors for IDA and from expert opinion. The data on IS was based on the mothers' self-reported use. The use of three stages for recording IS use, that is, tick box data (yes or no for IS use), textual data (listing all types of medications), and the amount of boxes of iron medications used increases the likelihood that different sources of IS will be captured by the questionnaire.

The questionnaire was pretested, revised, and then pretested again from May 2006 to June 2006 in two PHCCs in Ankara that serve as a resident continuity clinic and Hacettepe University İhsan Doğramacı Children's Hospital. During pretesting, parents completed the questionnaire after giving informed consent, and then the principal investigator interviewed them to assess the clarity and quality of each item. The questionnaire took an average of 18 min to complete. The comments of the parents resulted in minor changes in the questionnaire.

This study was reviewed and approved by the Ethical Committee of the Turkish Ministry of Health. Written informed consent was obtained from caretakers for each individual participant before enrolment.

Statistical analyses were performed with the Statistical Package for the Social Sciences (SPSS Inc., version 10.0, Chicago, IL, USA). Four age categories were used: 12 to <15 months, 15 to <18, 18 to <21, and 21-24 months of age. Z scores of weight for age, weight for height, height for age, and body mass index (BMI) for age (WAZ, WHZ, HAZ and BAZ) were calculated from the WHO Multicenter Growth Reference Study[20].

Data were presented as mean, SD or n (%) or 95% confidence interval (CI). Statistical significance level was set at a p value <0.05. To identify the predictors of anemia, we performed multiple logistic regression analysis. Of the measured indicators of anemia, only parameters with p value <0.20 and adequate available data in univariate analysis were considered in the modeling. Furthermore, independent variables that are correlated with each other were eliminated. To involve supplementation characteristics and prevent duplicate parameters, only "recommendation of IS by health providers" and "starting age for IS" were taken into analysis among the types and duration of supplementation.

Results

A total of 2339 children were present in selected HRF clusters. During the study period, 144 (6.2%) had found to change residency to places outside the project area, 148 children and their parents (6.3%) could not be found at home after repeated attempts, and 2 (0.1%) had died before the survey period. During the eligibility screening process, it was found that 330 children (14.1%) did not meet the inclusion criteria (outside the age range, chronic illness, thalassemia, febrile illness for the last 24 hours, hospitalized during survey period, low birthweight, preterm, multiple pregnancy). Of all, 101 parents (4.3%) refused to participate in the survey. Fieldworkers could not take blood samples from 25 children (1.1%). Finally, 1589 surveys were enrolled and served as the focus of this analysis. The participation rate was 67.9% (69.1% in GR, 65.5% in MR, 69.0% in PR). No statistically significant differences were noted between enrollees and those who were missed or refused to participate with respect to age and gender. The mean (95% CI) age of children surveyed was 17.8 (17.7, 18.0) months, and 52.8% were males.

Coverage of Iron-like Turkey Project: In the survey, 72.4% (n=1150) of the parents claimed that their physician had recommended IS. Most parents (66.5%, n=765) had received IS from the physician or nurse of the PHCC. Others had obtained the iron from a pharmacy with prescription of hospital physicians. Overall, parents of 1093 children (68.8%) had given IS to their children. Of those not giving IS, 46 parents said they had forgotten to give the drugs, 8 fathers had not wanted their children to take drugs and thought it was unnecessary, and 6 mothers stated that the iron bottle had broken. Of those giving supplementation, most of the children (n=840, 76.9%) had received supplementation daily; however, less than half of the children had complied with supplementation appropriately (suitable starting age for supplementation 54.2% (n=592); sufficient boxes 38.0% (n=415); desired daily dosage 38.1% (n=416)).

Side effects: 72.3% (n=790) of parents said their children experienced side effects after

taking the drug. The side effects experienced by the majority were mild, such as constipation (n=161), diarrhea (n=159), vomiting (n=141), tooth discoloration (n=228), changes in stool color (n=472), irritability (n=142), and unpleasant taste (n=410).

Anemia prevalence: The mean serum Htc value was 35.3% (SD=2.5, 95% CI=[35.3, 35.6]). Overall, 154 children (16.8%) had mean Htc value ≤33%, and blood analysis for complete blood count (CBC) and ferritin were done (Fig. 1). Of the children with further analysis, 116 had Hb <11 g/dl, MCV <70 fl and RDW ≥14.5 and were accepted as "anemic cases". The remaining 1473 children were accepted as "non-anemic cases". As a result, the overall prevalence of anemia was 7.3% and that of mild (Hb: 10-10.9 mg/dl), moderate (Hb: 9.0-9.9 g/dl), and severe anemia (Hb <9.0 g/dl) was 5.2%, 1.8% and 0.3%, respectively.

A regional pre-marriage screening program was implemented in MR due to the high prevalence of thalassemia. The questionnaire revealed that parents of 419 (26.4% of all groups and 89.5% of MR) children had admitted to a pre-marriage screening program for thalassemia carrier and 36 parents (26 mothers, 10 fathers) had thalassemia trait. Only 3 children of 36 parents had anemia (Hb <11 g/dl, MCV <70 fL, RDW >14.5%), and SF levels of these children were <10 μg/L.

Factors associated with occurrence rate of anemia: The comparison among the regions revealed that the prevalence of anemia was slightly higher for MR and GR compared to PR. However, these differences were not statistically significant (p=0.166, Table I).

The prevalence of anemia among the age group between 12-14.9 months was significantly higher than among the age groups 18-20.9 and

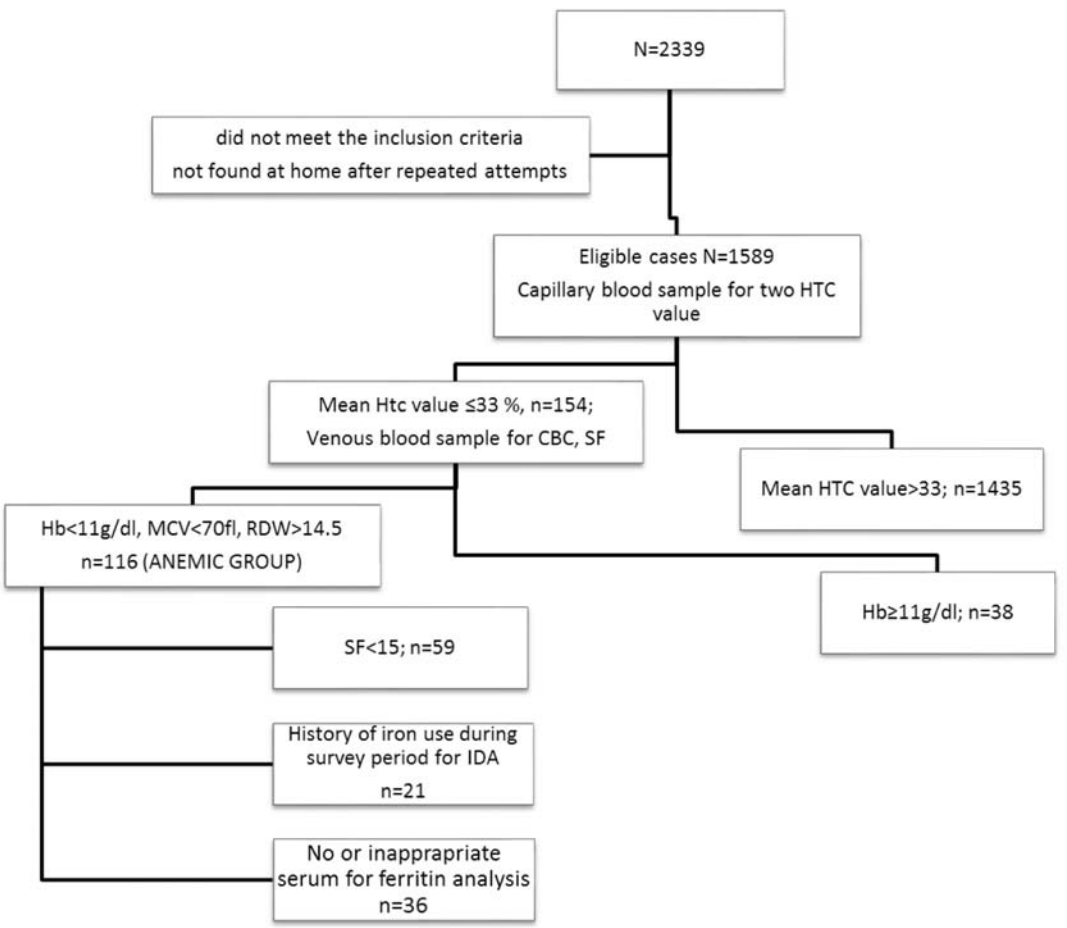

Fig. 1. Follow-up scheme of the survey.

Table I. Prevalence of Anemia among Children Aged 12-23 Months by Some Infant and Maternal Characteristics

			Cases with anemia		Odds Ratio	95% Confidence Interval
		N	n	%		
Overall		1589	116	7.30		
Region	PR	513	29	5.65	1	
	MR	468	41	8.76	1.60	0.98, 2.62
	GR	608	46	7.57	1.37	0.85, 2.21
Infantile age, months*	<15	408	43	10.54	1	
	15-17.9	432	30	6.94	0.63	0.39, 1.03
	18-20.9	364	23	6.32	0.57	0.34, 0.97
	21-<24	385	20	5.19	0.47	0.27, 0.81
Gender	Female	750	48	6.40	1	
	Male	839	68	8.10	1.29	0.88, 1.89
Delivery type	Vaginal	997	74	7.42	1	
	Cesarean section	577	41	7.11	0.95	0.64, 1.42
Parity	1	606	38	6.27	1	
	2-3	787	58	7.37	1.19	0.78, 1.82
	≥4	188	18	9.57	1.58	0.88, 2.85
Birth interval*	<2 years&	153	18	11.76	1.82	1.07, 3.10
	≥2 years or the first pregnancy	1421	97	6.83	1	
Family type	Nuclear	1230	87	7.07	1	
	Extended	359	29	8.08	1.16	0.75, 1.79
Number of household members**	<6	1208	76	6.29	1	
	≥6	381	40	10.50	1.75	1.17, 2.61
Children <5 years in the household	1	1038	72	6.94	1	
	≥2	551	44	7.99	1.16	0.79, 1.72
Maternal age, years	<25	454	35	7.71	1	
	25-29	537	38	7.08	0.91	0.57, 1.47
	30-35	391	28	7.16	0.92	0.55, 1.55
	≥35	199	14	7.04	0.91	0.48, 1.72
Maternal education level, years	<8	1057	85	8.04	1	
	≥8	532	31	5.83	0.71	0.46, 1.08
Maternal occupation**	Employed	129	2	1.55	1	
	Housewife	1416	109	7.70	5.30	1.29, 21.70
Paternal education level, years	<8	83	5	6.02	0.80	0.32, 2.02
	≥8	1495	111	7.42	1	
Parental consanguinity	Yes	319	31	9.72	1.49	0.97, 2.29
	No	1260	85	6.75	1	

Values are presented as N (total number of children), n (anemic children), % (percentages of anemic children; row percentage).

PR: Region with high malnutrition prevalence. MR: Region with middle malnutrition prevalence. GR: Region with low malnutrition prevalence.

*p<0.05, **p<0.01.

&: for women with previous children; calculated by taking the difference between the enrolled child and the previous child.

21-24 months, in descending order (p= 0.024, Table I). Regarding gender distribution, boys were found to be more anemic (8.1% vs 6.4%; p=0.192) than girls. However, this difference was not statistically significant.

Table II. Prevalence of Anemia among Children Aged 12-23 Months by Maternal Anemia and IS

			Cases with anemia		Odds Ratio	95% Confidence Interval
		N	n	%		
IS during pregnancy	Present(+)	1085	75	6.91	0.84	0.56, 1.25
	Absent(-)	504	41	8.13	1	
Maternal history of IDA*	Present(+)	855	73	8.54	1.49	1.00, 2.21
	Absent(-)	694	41	5.91	1	
IS in mothers with a history of IDA*	Present(+)	742	57	7.68	0.50	0.28, 0.91
	Absent(-)	113	16	14.16	1	
IS in mothers without history of IDA	Present(+)	332	17	5.12	0.76	0.40, 1.44
	Absent(-)	362	24	6.63	1	
Starting time for IS	No iron usage	504	41	8.13	1	
	Trimester 1	389	23	5.91	0.71	0.42, 1.20
	Trimester 2	405	31	7.65	0.94	0.58, 1.52
	Trimester 3	193	16	8.29	1.02	0.56, 1.87
Duration of maternal IS, month	No iron usage	504	41	8.13	1	
	<2	176	17	9.66	1.21	0.67, 2.19
	2-4.99	358	22	6.15	0.74	0.43, 1.27
	≥5	444	30	6.76	0.82	0.50, 1.34

Values are presented as N (total number of children), n (anemic children), % (percentages of anemic children; row percentage).
IS: Iron supplementation. IDA: Iron deficiency anemia. *p<0.05, **p<0.01.

The prevalence of anemia was significantly higher among those having birth spacing of <2 years than of those having a longer period or being the first pregnancy (11.8% vs. 6.8%, respectively; p=0.026, Table I).

Maternal education (≥8 years vs. <8 years) showed weak statistical evidence as a risk factor for anemia (p=0.109). Occupational status of the mother was a variable with the highest effect for anemic infant: 1.6% for infants with working mothers, 7.7% for infants with housewife mothers. Delivery type of the enrolled infant, maternal age, paternal education, family type, and the number of children under the age of 5 years in the household were not found to be significantly associated with anemia (Table I). However, the risk of anemia was 1.75 times higher in families with ≥6 household members than that in smaller families.

As shown in Table II, 1085 mothers were on IS during pregnancy, and maternal anemia was detected in 855 mothers during their lifetime. The percentage of anemic infants with anemic mothers was significantly higher than that of anemic infants with nonanemic mothers (8.5% vs. 5.9%, respectively; p=0.049). For the infants with no history of maternal anemia, the prevalences of infant anemia did not change with maternal IS. However, the rate of occurrence of infantile anemia was found to be significantly less in anemic mothers who received IS than that in anemic mothers who did not (7.7% vs. 14.2%, respectively; p=0.022). Starting time and duration of maternal IS had no significant effect on the prevalence of infant anemia.

For infants whose physician had recommended IS (n=1150), the prevalence of ID was 7.1%. Among these 1150 children, the prevalence of ID was 6.8% in children who received IS, and it was 14.0% in children who did not (p=0.038, Table III). Infants who received IS earlier (4.0-5.9 months of age) had the lowest prevalence of anemia (4.9%, p=0.020). The prevalence of anemia was significantly lower among infants taking recommended boxes for IS, 4.6%, as compared with infants taking no IS, 14.0% (p=0.031). The type of iron preparation (last pharmaceutical form), daily dosage given and the frequency of IS in a week did not significantly affect the occurrence of anemia.

In infants whose breastfeeding was discontinued before 6 months of age, the risk of anemia was significantly higher than in those with later discontinuation (10.5% for <6 months, 5.6%

Table III. Effect of Infantile IS on Prevalence of Anemia among Children Aged 12-23 Months

			Anemia		Odds Ratio	95% Confidence Interval
		N	N	%		
IS recommended by health providers	Yes	1150	82	7.13	0.91	0.60, 1.38
	No	439	34	7.74	1	
Mother gave infant IS as recommended*	Yes	1093	74	6.77	0.45	0.20, 0.97
	No	57	8	14.04	1	
Starting age for IS, months*	4-5.9	592	29	4.90	1	
	6-8.9	289	26	9.00	1.92	1.11, 3.32
	9-12	164	16	9.76	2.10	1.11, 3.97
Duration of iron in infants whose doctor had advised IS, months	0	57	8	14.04	1	
	0.1-0.9	62	7	11.29	0.78	0.26, 2.31
	1-1.9	273	15	5.49	0.36	0.14, 0.89
	2-3.9	310	18	5.81	0.38	0.16, 0.92
	≥4	421	30	7.13	0.47	0.20, 1.08
Frequency of IS, times per week	0	57	8	14.04	1	
	1-2	38	3	7.89	0.53	0.13, 2.12
	3-5	120	5	4.17	0.27	0.08, 0.86
	6-7	840	59	7.02	0.46	0.21, 1.02
Total dosage given, elementary iron mg/day	0	57	8	14.04	1	
	<7	285	19	6.67	0.44	0.18, 1.06
	8-12	416	26	6.25	0.41	0.18, 0.95
	≥12	285	24	8.42	0.56	0.24, 1.33
Total boxes used*	0	57	8	14.04	1	
	Low <2	294	24	8.16	0.54	0.23, 1.28
	Recommended	415	19	4.58	0.29	0.12, 0.71
	High >5	185	16	8.65	0.58	0.23, 1.44
Type of iron preparation (last pharmaceutical form)	Fe^{++}	620	46	7.42	1.18	0.70, 1.98
	Fe^{+++}	361	23	6.37	1	

Values are presented as N (total number of children), n (anemic children), % (percentages of anemic children; row percentage). IS: Iron supplementation.
*p<0.05, **p<0.01.

for 6-11.9 months, 6.9% for ≥12 months; p<0.050, Table IV). Both the starting age and the amount of daily cow's milk consumption were associated with an increased prevalence of anemia. As the starting age for the consumption of cow's milk was delayed, the risk of anemia declined (8.6% for infants <12 months and 4.7% for infants ≥12 months; p=0.042). Early (the first age to start cow's milk <12 months) or heavy cow's milk consumption (≥ 500 ml/day) increased the occurrence rate of anemia significantly more than in late-start and less cow's milk consumption (8.5% vs. 5.8%, respectively; p=0.036).

The prevalences of wasting (<-2 WHZ), underweight (<-2 WAZ), and stunting (<-2 HAZ) were 1.5%, 0.9%, and 10.9% based on WHO standards, respectively. BAZ was <-2 z score in 1.7% of children. Anemic infants had lower WAZ than non-anemic ones (0.32±0.90 vs. 0.55±1.06, respectively, p=0.025, Table V). Similarly, WAZ was negatively correlated with Htc value (r=-0.057, p=0.025). The presence of anemia had no significant effect on the other anthropometric measurements (Table V).

Medical history revealed that presurvey Hb analyses were performed for 30% of the children enrolled. The highest rate for anemia (13.3%) was found in infants with a history of anemia and the lowest prevalence (5.2%) was found in infants with prior normal blood analysis (p<0.001, Table IV). Presence of any hospitalization regardless of the cause during lifetime of children had no effect on the occurrence of anemia.

As seen in Table VI, multiple logistic regression

Table IV. Prevalence of Anemia by Dietary Habits and Health Status of Children Aged 12-23 Months

			Anemia		Odds Ratio	95% Confidence Interval
		N	N	%		
Presence of breastfeeding during study period	Present	596	45	7.55	1.06	0.72, 1.56
	Absent	990	71	7.17	1	
Duration of breastfeeding, month*	<6	306	32	10.46	1	
	6-11.99	303	17	5.61	0.51	0.28, 0.94
	≥12+	973	67	6.89	0.63	0.41, 0.99
Starting age for cow's milk consumption, month*	<12	791	68	8.60	1	
	≥12	426	20	4.69	0.52	0.31, 0.87
Daily cow's milk consumption	No consumption	327	23	7.03	0.80	0.49, 1.31
	≥500 ml	128	14	10.94	1	
	200-499 ml	541	45	8.32	0.74	0.39, 1.39
	<200 ml	549	30	5.46	0.47	0.24, 0.92
Cow's milk consumption; starting age <12 mo or amount ≥500 ml*	No consumption	327	23	7.03	0.62	0.31, 1.24
	No	731	42	5.75	1	
	Yes	834	71	8.51	1.53	1.03, 2.27
Previous history of blood count analysis and anemia***	Anemia	300	40	13.33	1	
	Normal	174	9	5.17	0.35	0.17, 0.75
	No analysis	1115	67	6.01	0.42	0.27, 0.63
Previous history of hospitalization for infant	Yes	419	31	7.40	1.02	0.67, 1.56
	No	1170	85	7.26	1	

Values are presented as N (total number of children), n (anemic children), % (percentages of anemic children; row percentage).
*p<0.05, **p<0.01, ***p<0.001.

Table V. Z Scores of Anthropometric Measurements of Children according to Presence of Anemia among Children Aged 12-23 Months

	Anemic toddlers (n=112)		Non-anemic toddlers (n=1440)		Mean difference	95% Confidence Interval
	Mean	Standard deviation	Mean	Standard deviation		
Weight for height, z score	0.61	1.27	0.83	1.27	-0.23	-0.48, 0.02
Height for age, z score	-0.21	1.48	-0.12	1.64	-0.09	-0.41, 0.23
Weight for age , z score*	0.32	0.90	0.55	1.06	-0.23	-0.43, -0.03
Body mass index for age, z score	0.68	1.45	0.90	1.39	-0.22	-0.49, 0.06

*p<0.05.

analysis (method=enter) indicated significantly lower prevalence for anemia in children aged 18-20.9 months and 21-23.9 months compared to those aged 12-14.9 months (odds ratio [OR]=0.50 [95%CI 0.28, 0.91] and 0.44 [95%CI 0.24, 0.81], respectively); in children who were breastfed ≥6 months compared with those breastfed <6 months (OR=0.56 [95%CI 0.35, 0.91]); and in children with presence of maternal IS during the gestational period compared with those with absence of maternal IS (OR=0.60 [95%CI 0.36, 1.00]).

Table VI. Infantile and Maternal Factors Affecting Infant Anemia according to Multiple Logistic Regression (Enter) Analysis among Children Aged 12-23 Months

	Odds Ratio	95% Confidence Interval	Sig.
Region			0.074
GR vs. PR	1.80	1.02, 3.16	0.041
MR vs. PR	1.86	1.04, 3.34	0.037
Infant's age, months*			0.027
15-17.9 vs. <15.0	0.70	0.41, 1.18	0.176
18-20.9 vs. <15.0	0.50	0.28, 0.91	0.024
21-23.9 vs. <15.0	0.44	0.24, 0.81	0.008
Sex [male vs. female]	1.30	0.86, 1.98	0.215
Recommendation of iron by health providers [yes vs. no]	2.31	0.94, 5.68	0.067
Starting age for infant's IS, months*			0.042
6-8.9 vs. 4-5.9	1.70	0.95, 3.05	0.074
≥9 vs. 4-5.9	2.05	1.06, 3.97	0.032
No supplementation vs. 4-5.9	2.74	1.13, 6.66	0.026
Duration of breastfeeding, months [≥6 vs. <6]*	0.56	0.35, 0.91	0.019
Use of bovine milk [≥500 ml or <12 months of age vs. others]	1.24	0.80, 1.92	0.341
Maternal schooling, years [≥8 vs. <8]	0.85	0.52, 1.37	0.497
Maternal occupation [housewife vs. employed]	3.75	0.88, 15.90	0.073
History of maternal anemia [present vs. absent]**	1.93	1.18, 3.14	0.008
Maternal IS during pregnancy [present vs. absent]*	0.60	0.36, 1.00	0.048
Birth interval [<24 months vs. first pregnancy or ≥24 months]	1.38	0.75, 2.53	0.299
Number of household members [≥6 vs. <6]**	2.18	1.36, 3.48	0.001
Constant	0.01		<0.001

IS: Iron supplementation. PR: Region with high malnutrition prevalence. MR: Region with middle malnutrition prevalence. GR: Region with low malnutrition prevalence. *p<0.05, **p<0.01.

However, this multiple logistic regression analysis (method=enter) revealed significantly higher prevalence of anemia in children who had taken IS at 9 months of age or no IS compared with those who had taken IS at 4-5.9 months of age (OR=2.05 [95% CI 1.06, 3.97] and OR=2.74 [95%CI 1.13, 6.66]; respectively); in children with history of known maternal anemia compared with those without anemia (OR=1.93 [95%CI 1.18, 3.14]); and in children who came from households with ≥6 members compared with those with <6 members (OR=2.18 [95%CI 1.36, 3.48]).

Discussion

In this survey, prevalence of anemia was 7.3% in healthy children (no history of preterm, low birthweight or chronic illness) between 1 and 2 years of age. The prevalence of ID has been reported to be 9–34% and that of IDA 3–8% in Europe[3,7,21-24]. The prevalence of IDA in previous hospital-based, local and regional data in Turkey was between 21-35%[13,14]. This study is the first of a large sample of infants from three of 12 regions in Turkey with different nutritional status and health indicators[14]. The low prevalence of anemia observed among children resident in these three regions of Turkey suggests that the previous Iron-like Turkey Project had a substantial effect on prevention of IDA. Magoni et al.[25] reported reduction of anemia prevalence by more than 50%, from 30.1% to 18.8%, after the IS project in Sumu'a, Dhaharieh and Ramadin. Unfortunately, we had no nation wide data regarding previous anemia prevalence. As a limitation of the survey, we had no control group or area due to ethical considerations. However, subanalyses of the infants revealed that infants who received supplementation in appropriate boxes had anemia at a rate around three times lower than the infants who did not receive it. Indeed, the relatively lower prevalence of anemia in PR might be attributed to high coverage of IS in infants. As

a limitation of the present study, SF levels were measured only in cases with anemia; therefore, the prevalence of ID could not be known.

The prevalence of anemia varies across countries, depending on a variety of sociodemographic and dietary factors, individual predispositions, health promotion activities, and the definition of anemia[3,15,19,21-29]. Prematurity, age, sex, ethnicity, growth rate, household socioeconomic status, maternal education levels, and intake of cow's milk and iron-fortified food products have been associated with iron status. One of the most common causes of anemia in infants is prematurity[1]. In the selected sample of the present survey, preterm, low birthweight and twin infants were detected in 8.9%, 7.3% and 2.7%, respectively. Because of the differences in supplementation guidelines and management[1,10,11], they (15.5%) were not taken into the survey. In the present study, the risks for anemia in multivariate analysis were found to be being younger (12-14.9 months of age), living in a crowded house (perhaps due to low socioeconomic status), late initiation of IS (≥6 months of age), breastfeeding <6 months, presence of maternal anemia, and absence of maternal IS during lactation period.

With respect to gender as a risk factor, the literature is also contradictory[15,26,28,29]. Domellöf et al.[26] reported that at 9 months, boys were at a 10-fold higher risk to present IDA. In our previous study, male infants at 5-7 months of age had a 2.8-fold higher risk to have Hb value <9.5 g/dl. Hadler et al.[28] confirmed that male gender was a risk factor for anemia. However, Hassan et al.[29] detected no significant difference between genders in the age group from 6-11.9 months. In the present study, we obtained non-significant sex differences in the age group from 12-23 months in univariate analysis, which disappeared in multiple logistic regression analysis. This might be due to differences in growth rates by gender and age groups[15].

Similar to Hadler et al.[28], we detected that an employed mother reduced the risk of anemia among infants in univariate analysis, which might indicate a better access to socioeconomic, health, or nutrition status. However, there was a non-significant employment difference in the prevalence of anemia in multivariate analysis. This might be due to the limited number of employed mothers.

The present study showed that the use of cow's milk at an earlier age and larger amounts increased the risk of anemia in univariate analysis. Infants have reduced gastric capacity, and therefore need diets with high iron density[9]. Cow's milk has low content and absorption of iron[30]. Also, greater consumption of cow's milk may lead to a reduction of dietary total iron intake by replacing other possible sources of iron[9,21,27]. In multivariate analysis, this effect disappeared. IS might eliminate the negative effect of faulty nutritional habits.

The iron requirement of pregnant women is at least twice as much as that of nonpregnant women[31]. However, the majority of the women in the developing world and even in developed countries do not meet iron requirements during pregnancy, which means they are likely to become anemic or iron-deficient to some degree[1,2,7,10]. In mothers with severe ID, there is little immediate effect on the newborn, but infant iron storages may be depleted at a very early stage[2,10,32,33]. In addition, the iron-deficient mother's breast-milk has a low amount of iron[34]. Thus, infants born to anemic mothers are more prone to develop anemia than infants born to mothers with a satisfactory iron balance. In previous studies, infants born to anemic mothers were found to be more anemic than infants born to nonanemic mothers[35]. Indeed, in the present study, the prevalence of anemia in infants born to mothers with a lifetime history of anemia is significantly higher than in infants born to nonanemic mothers. Meyerovitch et al.[36] also reported that there was an obvious correlation between the maternal Hb value measured right before delivery and the frequency of anemia in their offspring. As seen in the present study, IS in infants born to anemic mothers decreases the risk of developing anemia. Therefore, maternal IS should be encouraged to prevent infant anemia.

We had a limited number of malnourished infants. This might be due to the exclusion of preterm, low birthweight infants and infants with chronic illness. Anemic infants had lower WAZ than non-anemic ones. However, there was no significant difference in anemia prevalence among regions, which were taken according to malnutrition status of NUTS regions: 5.7% in PR, 8.8% in MR and 7.6% in GR. This might be due to differences in coverage of IS (68.1% in GR, 65.2% in MR, 72.9% in PR, p=0.03).

In the present study, IS starting earlier, from 4-5 months of age decreases the prevalence of anemia at 12-23 months of age. There is evidence that some infants are born with diminished iron stores[33,34,37]. Such infants could exhaust their iron endowment and become iron-deficient before 6 months of age. Indeed, Yang et al.[37] reported that the percentages of infants with ID at 6 months among 404 fully breastfed infants with a birthweight >2500 g were 6% in Sweden, 17% in Mexico, 13-25% in Honduras, and 12-37% in Ghana, and the percentages with IDA were 2% in Sweden, 4% in Mexico, 5-11% in Honduras, and 8-16% in Ghana. In Denmark, on the other hand, Michaelsen et al.[22] detected no ID with or without anemia at 6 months of age. However, children who had anemia during the infancy period generally had anemia during the survey period, even if treatment was given previously. Supplementation is an easy way of preventing the occurrence of IDA and complications[1,4,5]. Therefore, IS should be started early, when infants are 4 months of age, before the development of IDA.

Some memory biases might be seen in the daily amount and the weekly frequency of supplement use. The number of medication boxes could be checked easily. Interestingly, the number of boxes which the mother said her child had taken shows a significant effect in the occurrence of anemia in the present study. Compliance to supplementation could be followed easily by the number of boxes used. As a limitation of anemia surveys, previous diagnosis of anemia and therapy might affect the results. Some infants might have anemia previously; however, mothers might give less than needed.

The presence of IDA among term healthy young infants is likely linked to an insufficient iron supply at birth as a result of maternal iron depletion, worsened by poor iron content of weaning foods. The absence of affordable (cheap for poor families) iron-rich complementary food in developing countries and limited intake of iron-rich complementary food by infants at 6-9 months of age might also contribute to the occurrence of anemia.

This survey suggests that IS during pregnancy, IS initiation in infants by 4 months of age, effective counseling and education of mothers on supplementation, following compliance by number of boxes used support of breastfeeding, and effective training of health care personnel are effective strategies for the prevention of anemia in the community. The Iron-like Turkey Project has five major components: (a) advocacy, (b) support for effective training, (c) support for effective counseling, (d) messages and materials and a program for public education, and (e) free supplementation of iron medication to infants aged 4-12 months of age[13]. Given the high coverage rate of supplementation use in this project (68.8%) and the low prevalence of anemia (7.3%), the Iron-like Turkey Project appears to achieve its goal. As with other intervention programs, sustainability is the key to supplementation. Further studies should be done to evaluate the changes in the prevalence of anemia.

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