ORIGINAL ARTICLE

Risk Factors of Iron Deficiency Anemia among Children under Two Years Old in the Southeast of Iran: A Case–Control Study

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Abstract

Background: Iron deficiency anemia in children is one of the most important challenges in the global health system. Also, it is one of the main problems in Iran, especially in the southern regions. Therefore, the aim of this study was to investigate the factors affecting iron deficiency anemia in children under two years of age.

Methods: This case-control study was conducted on children under two years of age in Sistan and Baluchestan Province in the southeast of Iran with the highest birth rate in 2020. In the study, 760 children were divided into case and control group (380 vs 380). A standard information form was used for collecting data, and the data were analyzed using SPSS-21 by chi-square test and logistic regression.

Results: There were significant associations between the child's iron deficiency anemia and the type of child nutrition (P=0.000), history of child's food allergies (P=0.021), child's congenital anomalies (P=0.009), maternal body mass index (P=0.083), number of previous pregnancies (P=0.035), history of abortion and stillbirth (P=0.027), use of postpartum supplementation (P=0.004), mother's anemia (P=0.000), family marriage (P=0.001), father's job (P=0.017), father's anemia (P=0.000), and father's addiction (P=0.007). Also, based on multivariate regression, the most important predictor of iron deficiency anemia in children was father's addiction (OR=1.720; 95% CI: 1.067 – 2.773).

Conclusion: The findings showed that parental factors could play an important role in causing iron deficiency anemia in children. These risk factors can be improved and prevented by promoting health education, increasing parental awareness and knowledge, and improving the lifestyle of families. Therefore, holding educational and counseling classes for parents is especially recommended.

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Introduction

The World Health Organization (WHO) defines anemia as level of hemoglobin under12 gr/dl in women and under13 gr/dl in men.[1] Iron deficiency anemia is a major challenge in the healthcare system that affects about 3.5 billion people worldwide.[2] Almost 25% of the world's population suffers from anemia, and iron deficiency

is the cause of half of all anemias.[3] This disease leads to irreparable consequences for the people's physical and mental health and the comprehensive community development.[4]

WHO has introduced iron deficiency anemia as one of the most effective risk factors of years with disabilities and death.[5] Iron deficiency anemia can affect different age groups, but children under 5 years old are the most vulnerable ones because of the rapid growth of the organs, a diet without enough iron, nutrient deficiency and sensitivity to cow's milk protein.[6] About 50 percent of children under the age of five in developing countries have iron deficiency anemia.[7] Studies have shown that iron deficiency anemia in children under the age of three in the United States is about four percent.[8] Overall, 24.8 percent of the world's population (1.62 billion people) have iron deficiency anemia and a significant number of these people are children under five years of age.[9] High rates of patients with iron deficiency anemia are seen in developing countries (approximately 50 percent of the global burden of anemia).[10]

Various studies have been done on the prevalence of iron deficiency anemia in children group in Iran. Studies have shown that among children under six years old, the prevalence of iron deficiency anemia in male gender (17.7%) was higher than female gender (14.4%)[6]. Akbari in this study found that the prevalence of anemia in Iranian population aged under 18 years was estimated to be 13.9% (95% CI: 10.8-17.1).[11]

If iron deficiency anemia is diagnosed late, it can lead to detrimental and irreversible consequences, including immune system disorders, brain metabolism disorders, damage to the central nervous system, behavioral disorders, damage to the optic and auditory nerves, decreased intelligence quotient (IQ), impaired concentration, learning and academic failure, anorexia, heart failure, dental injury, and hair loss.[12] Therefore, prevention of iron deficiency anemia can have beneficial effects on improving the child's health, academic achievement, increasing the efficiency of human resources, and reducing the incidence of diseases and even mortality. Also, it can be a valuable and effective investment in society's future prospects.[13]

Although the incidence of iron deficiency anemia in children in Iran is lower than in some developing countries, in comparison with industrialized countries, it is significant. Prevention of iron deficiency anemia in Iranian children is an important health priority.[6] Since iron deficiency anemia is a multifactorial disease, the identification of these factors can have a significant impact on the adoption of strategic and preventive measures by health policymakers and reduce the number of children with this disease.

Sistan and Baluchestan is one of the most deprived provinces in Iran and has unfavorable socio-economic conditions; this factor has led to less access to primary healthcare,[14] especially the use of iron drops for children, poor nutrition, and wrong lifestyle in the households of this region.[15, 16]

Few studies have been done to identify the effective factors on the occurrence of iron deficiency anemia in children in this province; therefore, the aim of this study was to investigate the factors affecting iron deficiency anemia in children under two years of age.

Methods

Study Design

A case-control study was conducted in Zahedan, the capital of Sistan and Balochestan, in 2020. We investigated the factors affecting iron deficiency anemia in children under two years old, who were referred to health centers from February to July 2020. The study was approved by the Ethics Committee of the Research Committee of Zahedan University of Medical Sciences (Ethical approval no: IR.ZAUMS.REC.Fsa1397.90).

Sample Size

According to a previous similar study (32), considering the following formula to calculate the sample size and according to the 95% confidence interval, P=0.48 for the case group, P=0.5 for the control group, d=0.06 (maximum acceptable error) and Zα=1.96, Zβ=0.85, 380 children entered to the study as the case group and 380 children entered as the control group.

$$n = \frac{p1(1-P1) + p2(1-p2) * (z\alpha + z\beta)2}{(p1-p2)2}$$

Data Collection

First, Zahedan was divided according to the municipal districts, and then several health centers were selected from each district based on its population. In each health center, based on the number of children under two years old, convenience sampling methods was used for the case and control groups. Then, children who had done an iron deficiency anemia diagnosis test (Complete Blood Count) at the age of 6-9 months and were considered healthy by the physician's diagnosis were included in the control group. Also, children who performed CBC tests at 6-9 months of age (first stage) and repeated the test at the age of nine months to two years according to the physician's instructions (second stage) and in both stages of the CBC test, the physician confirmed the presence and persistence of iron deficiency anemia, were selected as cases.

The inclusion criteria included children under two years old, completion of the informed consent form by mother, and performance of two stages of iron deficiency anemia test at the ages of 6-9 months and nine months to two years.

Then, at the appointed time, the mothers were asked to refer their children to the health center. After providing the necessary explanations on how to conduct this research and the high value of cooperation to mothers, the data were collected by a data collection form. To gather the data, we used child and family health files and also asked the mothers. The data collection form has been validated by experts in the health field and the basis for selecting variables has been the review of several previous studies.

The data collection form included four parts. First, questions about the child: gender, birth weight (extracted from family health file), age of birth, birth rate, the person who cares for the child, presence of congenital anomalies in the child, presence of any allergies and sensitivities in the child, and use of iron supplementation before the diagnosis of iron deficiency anemia. Second, maternal questions: maternal age during pregnancy, maternal occupation and education, maternal body mass index (mothers' body mass index was extracted from the family file), type of delivery (natural or cesarean), number of previous pregnancies, multiple births, abortions and stillbirths in the mother. Third, paternal questions: father's education and father's addiction; fourth, other questions: place of residence, nationality, and ethnicity of the child.

Statistical Analysis

After collecting the data and ensuring the accuracy of the available data, the data was first entered into SPSS software version 21 (SPSS Inc., Chicago, IL, USA) and analyzed with statistical tests with a 95% confidence interval. The normality of the distribution of all variables was examined by using Kolmogorov-Smirnov test; then, Pearson Chi-square test was used to compare the proportions. Univariate and multivariate regression analyses were applied to find out the significant factors associated with iron deficiency anemia. P<0.05 was considered significant. Before data collection, informed consent form was signed by the mothers.

Results

In this study, 760 children under two years old who had the criteria to enter the study were examined. About 194 (51.1%) children with iron deficiency anemia were boys. In 75% of children with iron deficiency anemia and 83.4% of healthy children, fathers had non-government jobs. Also, 41.8% (159) of the case and 43.9 (167) of control group families were in the lower income class, respectively (Table 1).

Also, among the variables reported in Table 1, only a significant relationship was found between the father's job (P=0.01) and iron deficiency anemia in the children.

There was a significant relationship between the type of nutrition of the child (P=0.00), history of

Table 1: Comparison of family variables between children with iron deficiency anemia and healthy children

Variables		Case Frequenct (%)	Control Frequency (%)	P value
Gender	Female	186 (48.9)	195 (51.3)	0.501
	Male	194 (51.1)	185 (48.7)	
Mother's education	Illiterate and elementary	77 (20.3)	58 (15.3)	0.181
	Middle school, high school and diplomas	109 (28.7)	121 (31.8)	
	University	194 (51.1)	201 (52.9)	
Mother's job	Non-governmental job	67 (17.6)	61 (16.1)	0.801
	Governmental job	33 (8.7)	31 (8.2)	
	Housewife	253 (66.6)	255 (67.1)	
	Student	27 (7.1)	33 (88.7)	
Father's education	Illiterate and elementary	18 (4.7)	9 (2.4)	0.141
	Middle school, high school and diplomas	120 (31.6)	112 (29.5)	
	University	242 (63.7)	259 (68.2)	
Father's job	Non-government job	285 (75.5)	317 (83.4)	0.012
	Government job	82 (21.6)	54 (14.2)	
	Unemployed	13 (3.4)	9 (2.4)	
Residence place	Downtown	170(44.7)	149 (39.2)	0.892
	Suburbs	126 (33.2)	135(35.5)	
	Other urban areas	84 (22.1)	96(25.3)	
Nationality	Iranian	371 (97.6)	369 (97.1)	0.601
	Non-Iranian	9 (2.4)	11 (2.9)	
Household income level	Low-income class	159 (41.8)	167 (43.9)	0.602
	Intermediate income class	160 (42.1)	147 (38.7)	
	High income class	61 (16.1)	66 (17.4)	

*P<0.05; Statistical analysis method: Chi-square test

Table 2: Comparison of children's demographic variables between children with iron deficiency anemia and healthy ones

Variable		Case Frequency (%)	Control Frequency (%)	P value
Age of birth	Term	315 (82.9)	325 (85.5)	0.501
	Pre-term	52 (13.7)	43 (11.3)	
	Post-term	13 (3.4)	12 (3.2)	
Child birth rate	First to third child	285 (75.0)	305 (80.3)	0.202
	Fourth to seventh child	77 (20.3)	61 (16.1)	
	Eighth child and more	18 (4.7)	14 (3.7)	
Birth weight	Less than 2.5 kg	190 (50.0)	213 (56.1)	0.101
	2.5 – 4 kg	188 (49.5)	167 (43.9	
	More than 4 kg	2 (0.5)	0 (0)	
Use of iron supplement drops by a child before diagnosing iron deficiency anemia	Yes	188 (49.5)	203 (53.4)	0.203
	No	192 (50.5)	177 (46.6)	
History of allergy or food restriction	No	342 (90.0)	359 (94.5)	0.022
	Yes	38 (10.0)	21 (5.5)	
Who cares for the child?	Parents	278 (73.2)	279 (73.4)	0.455
	Relatives near or far	66 (17.4)	57 (15.0)	
	Neighbor	9 (2.4)	16 (4.2)	
	Private nurse	27 (7.1)	28 (7.4)	
Child's Feeding Type	Breast milk, formula and Supplemental nutrition	81(21.3)	76(20.0)	0.001
	Breast milk, cow's milk and supplemental nutrition	34(8.9)	50(13.2)	
	Formula and supplemental nutrition	33(8.7)	21(5.6)	
	Breast milk and Supplemental nutrition	178(46.9)	215(56.5)	
	Breast milk and cow's milk	13(3.5)	10(2.6)	
	Formula, cow's milk and supplemental nutrition	41(10.7)	8(2.1)	
Which is less than five times a week consumed?	Meat	285 (75.0)	296 (77.9)	0.501
	Bread or cereals	6 (1.6)	6 (1.6)	
	Both (Meat and Bread or cereals)	16 (4.2)	2 (0.5)	
	None	73 (19.2)	76 (20.0)	

P<0.05; Statistical analysis method: Chi-square test

allergy or food restriction in child (P=0.02) and child's iron deficiency anemia (Table 2).

There was a significant association between iron deficiency anemia and pattern addiction (P=0.007), pattern anemia (P=0.00), maternal body mass index (0.08), maternal number of previous pregnancies (P=0.035), history of abortion and stillbirth in the mother (P=0.02), maternal anemia (P=0.000), and use of supplements after childbirth (P=0.004) (Table 3).

Most parents of children studied had non-familial marriage (456 parents or 60%). Also, a significant relationship was found between iron deficiency anemia in children under two years old and familial marriage of parents in the two groups (P=0.001).

On multivariate regression, the factors associated with iron deficiency anemia in children under two years old were the father's addiction, consumption of supplementary pills after delivery, and history of congenital malformations in children. Children whose mothers never had consumed supplementary pill after delivery or had consumed it irregularly were 1.758 times more likely to have severe iron deficiency anemia than children whose mothers had always and regularly used supplementary pills after delivery. Children with a history of congenital malformation were 2.034 times more likely to have severe iron deficiency anemia than those without congenital malformation (Table 4).

Discussion

The study aimed to investigate the factors affecting iron deficiency anemia in children under two years old in the southeast of Iran. The results of the present study showed that 51% of children with iron deficiency anemia were boys, and there was no significant relationship between anemia and gender among the study population. In this regard, some studies showed that there was no significant relationship between iron deficiency anemia and child gender.[17, 18] However, two studies showed that most of the children with iron deficiency anemia were boys.[14, 15]

In this study, almost half of the mothers in both groups had a university education. No significant association was found between iron deficiency anemia and the mother's education of children studied in the case and control groups .Dalili et al.[19] found that most mothers of children with anemia (87.4%) and most mothers of healthy children (77.9%) had education less than undergraduate degree.

Table 3: Comparison of specific variables of the parents between children with iron deficiency anemia and healthy children in Zahedan, 2020

Variable		Case Frequency (%)	Control Frequency (%)	P value
Father's addiction	No	287 (75.5)	317 (83.4)	0.007
	Yes	93 (24.5)	63 (16.6)	
**Father's anemia	No anemia	229 (60.3)	303 (79.7)	0.001
	Thalassemia	14 (3.7)	10 (2.6)	
	Iron deficiency anemia	92 (24.2)	51 (13.4)	
	Hemophilia	10 (2.6)	0 (0.0)	
	Other cases	33 (8.7)	16 (4.2)	
Mother's age during pregnancy	Under the age of 18	48 (12.6)	48 (12.6)	0.200
	18 - 25 years old	121 (31.8)	138 (36.3)	
	26-30 years old	78 (20.5)	57 (15)	
	31-35 years old	63 (16.6)	71 (18.7)	
	Older than 35 years	70 (15.4)	66 (17.4)	
Mother's Body Mass Index	Less than 18.5	95 (25.5)	85 (22.4)	0.080
	18.5 - 24.9	127 (33.4)	161 (42.4)	
	24.9 - 29.9	85 (22.4)	75 (19.7)	
	30 and more	73 (19.2)	59 (15.5)	
Type of delivery	Natural delivery	328 (86.3)	341 (89.7)	0.140
	Cesarean delivery	52 (13.7)	39 (10.3)	
Number of previous pregnancies	Had no previous pregnancy	199 (52.4)	231 (60.8)	0.030
	Once	59 (15.5)	58 (15.3)	
	2-4 times	67 (17.6)	60 (15.8)	
	5-10 times	41 (10.8)	20 (5.3)	
	More than 10 times	14 (3.7)	11 (2.9)	
Multi pare history	Yes	37 (9.7)	30 (7.9)	0.370
	No	343 90.3)	350(92.1)	
A history of abortion or stillbirth	Yes	77 (20.3)	54 (14.2)	0.020
	No	303 (79.7)	326 (85.8)	
Anemia in the mother	No anemia	196 (51.6)	271 (71.3	0.001
	Thalassemia	19 (5.0)	8 (2.1)	
	Iron deficiency anemia	156 (41.1)	91 (23.9)	
	Hemophilia	4 (1.1)	0 (0)	
	Other cases	5 (1.1)	10 (2.6)	
Consumption of supplementary pill after delivery	At all	67(17.6)	47 (12.4)	0.004
	Rarely	105 (27.6)	77 (20.3)	
	Sometimes	137 (36.1)	161 (42.4)	
	Always and regular	71 (18.7)	95 (25.0)	

*P<0.05; Statistical analysis method: Chi-square test. **The father's anemia variable had missing data of about 0.5%.

Table 4: Multiple regression models of factors associated with iron deficiency anemia

Variable		95% CI for Exp (B)*	B**	P value***
Father's addiction	No	1		
	Yes	1.720 (1.06 – 2.77)	0.542	0.020
Consumption of supplementary pill after delivery	Always and regular	1		
	At all, Rarely, sometimes	1.758 (1.21 – 2.54)	0.564	0.003
History of congenital malformations in children	No problem	1		
	Kind of congenital malformations	2.034 (1.35 – 3.06)	0.710	0.001

*CI: Confidence Interval; **Beta coefficient; ***P<0.05; Statistical analysis method: multivariate regression analysis

Results of some studies showed that there was no relationship between maternal education and iron deficiency anemia in children.[20, 21]

The present study showed that most fathers of children with iron deficiency anemia (75%) as well as most fathers of healthy children (83.4%) had non-governmental jobs. There was a significant relationship between iron deficiency anemia in the child and the father's job in the case and control groups. In the study of June et al.,[22] 40.6% of fathers were self-employed. Vergaa et al.[23] found that there was a relationship between the father's job and iron deficiency anemia in children so that the rate of iron deficiency anemia in the children of unemployed fathers was higher than others.

According to the results, most of children with iron deficiency anemia (90%) and most of the healthy

children (94.5%) had no history of allergy, intolerance, or food restriction. There was a significant relationship between iron deficiency anemia and history of allergy or food restriction in the samples. Some studies have shown that cow's milk can cause iron deficiency anemia in infants before the age of one due to the baby's sensitivity to cow's milk protein.[9, 24]

The finding showed that 46.8% of children with iron deficiency anemia and 56.6% of healthy children ate breast milk and supplemental nutrition. Also, there was a significant relationship between the type of child nutrition and iron deficiency anemia in the samples. Qershi et al.[25] stated that in the case group, 60% of infants were fed using breast milk, 10% with formula, and 30% with a combination of breast milk, formula and cow's milk. A study showed that breastfeeding with complementary foods and formula or breast milk with cow's milk and formula can be associated with iron deficiency anemia in children, and cow's milk is the biggest nutritional risk in terms of iron deficiency anemia. A study by Zanin et al.[26] showed that nutritional factors affected the occurrence of iron deficiency anemia in children. The results of a study by Luo et al.[27] in China revealed that children who are breastfed after 6 months have lower hemoglobin levels and a higher prevalence of iron deficiency anemia than children who have been breastfed since birth; also, breastfed children have higher hemoglobin levels and lower iron deficiency anemia than those who use formula.

Most children with iron deficiency anemia (72.9%) and most healthy children (84.5%) had no history of congenital anomalies. There was a significant relationship between the history of children's congenital malformations and iron deficiency anemia in children. A study by Kanchana et al.[28] showed that iron deficiency anemia was more common in children with gastroenteritis. Karimi's study[29] showed that one of the main causes of anemia in children was the loss of blood through the gastrointestinal tract due to parasitic infections. Research has shown that anemia occurs more frequently in children with colitis, chronic kidney disease, celiac, ulcers of the stomach and pancreas, and inflammatory bowel disease.[30]

Results showed age of most mothers of children with iron deficiency anemia (31.8%) as well as most mothers of healthy children (36.3%) was in the 18-30 range during pregnancy. The results showed that there was no significant relationship between childhood iron deficiency anemia and maternal age during pregnancy. The study of Arulparithi.[31] showed that there was no significant relationship between iron deficiency anemia in children and maternal age. However, the study of Patron et al.[32] showed the chance of developing iron deficiency anemia was more in children of mothers who were under 18 years old at the time of the first delivery.

According to the results, only 41.1 and 23.9 of mothers in the case and control groups had iron deficiency anemia, respectively. There was a significant difference between iron deficiency anemia in children and maternal anemia. Lee showed that 15.4% of mothers had iron deficiency anemia and a direct relationship was found between iron deficiency anemia in children and mothers.[30] Some other studies showed a strong association between maternal iron deficiency anemia and pediatric iron deficiency anemia.[33] This can be due to wrong lifestyle, improper nutritional habits in the family, financial poverty to provide iron-containing foods, lack of awareness of mothers about the effects of iron, wrong perception of the side effects of using iron pills in women and girls, irregular use of iron pills in women and girls, menstrual bleeding, and failure to compensate for the resulting anemia.[34]

The finding showed most fathers of children with iron deficiency anemia (75.5%) as well as most fathers of healthy children (83.4%) were not addicted to cigarettes, alcohol, or any drugs, opioids or stimulants during pregnancy or breastfeeding. A significant relationship was found between iron deficiency anemia in children and father's addiction. A study by Al-alimi et al.[35] showed that there was a relationship between parents' smoking, use of opioids, stimulants, and the development of iron deficiency anemia in children.

Strengths and Limitations

To the best of our knowledge, this is the first study on the subject of antenatal anemia and iron deficiency in Zahedan. An obvious limitation is the small number of publications on iron deficiency among children in Zahedan and the substantial variations in terms of the parameters assessed. This limits the comparability among the reported studies.

Conclusion

In general, various factors, such as parental factors, can play an important role in causing iron deficiency anemia in children. All the risk factors of anemia can be improved and prevented by promoting health education, increasing parental knowledge, and improving the lifestyle of families. Therefore, holding educational and counseling classes for parents is especially recommended.

Authors' Contribution

Fatemeh Setoodehzadeh: main idea, supervision of the research project, revision of draft of the manuscript, revision of the final manuscript. Mohammad Khammarnia: scientific advisor of the research project, Supervision of proposal writing and project implementation, revision of the manuscript draft. Zeinab

Almasi: Statistical advisor of the research project, data analysis. Kosar Rezaei and Mostafa peyvand: literature search, writing proposal, data collection, writing the draft of the manuscript.

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Conflict of Interest: None declared.

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