Family History as a Risk Factor for Iron Deficiency Anemia among Korean Adolescents: Data from the Fifth Korea National Health and Nutrition Examination Survey (KNHANES)

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Background: Iron deficiency anemia (IDA) is prevalent throughout the world. However, there is limited information regarding whether familial factors are associated with the risk of adolescent IDA.

Methods: This study evaluated the association between adolescent IDA and family history of IDA using data from the fifth Korea National Health Nutrition Survey (2010-2012). Data from 10-18-year-old children who underwent laboratory testing were analyzed.

Results: The overall prevalence of IDA was 3.1% (95% confidence interval [CI]: 2.4-4.1%), with prevalence of 0.5% among boys (95% CI: 0.2-1.3%) and 6.2% among girls (95% CI: 4.6-8.3%). The prevalence of IDA was associated with female sex (odds ratio [OR]: 13.43, 95% CI: 4.92-36.65; P<0.001) and a family history of IDA (OR: 3.12, 95% CI: 1.11-8.76; P=0.03). Other risk factors for IDA were receiving social welfare support (OR: 3.31, 95% CI: 1.45-7.56; P=0.031), low maternal education (OR: 3.12, 95% CI: 1.39-6.99; P=0.006), receiving charitable food support (OR: 2.27: 95% CI: 0.95-5.44; P=0.04), poor body-image (OR: 2.14, 95% CI: 1.16-3.93; P=0.026), and weight-loss efforts (OR: 2.42, 95% CI: 1.27-4.61; P=0.01). Nutritional supplementation protected against IDA (OR: 0.40, 95% CI: 0.19-0.82; P=0.007), although adolescents with awareness of nutritional labels had a high IDA prevalence (OR: 8.06, 95% CI: 1.71-38.05; P<0.001).

Conclusion: A family history of IDA was an independent risk factor for IDA. Further studies are needed to determine whether family-level educational interventions can reduce the risk of adolescent IDA.

Key Words: Anemia, Iron-deficiency, Adolescent, Family medical history

Introduction

Iron deficiency anemia (IDA) is prevalent in underdeveloped, developing, and even developed countries. The world-wide prevalence of iron deficiency among pre-school children is approximately 25%, and the prevalence in-
CREASES IN RURAL AREAS OR COUNTRIES WITH A LOW DEVELOPMENT INDEX [1]. THE PREVALENCE OF IDA IN SOUTH KOREA WAS 0.7% FOR MEN (95% CONFIDENCE INTERVAL [CI]: 0.3-1.0%) AND 8.0% FOR WOMEN (95% CI: 6.8-9.2%), BASED ON DATA FROM THE 5th KOREA NATIONAL HEALTH AND NUTRITION EXAMINATION SURVEY (KNHANES) [2]. THE RISK OF IDA IS ASSOCIATED WITH LOW BIRTH WEIGHT [3,4], FEMALE SEX DURING THE REPRODUCTIVE AGE [5], PROLONGED BREAST FEEDING WITH UNFORTIFIED FOOD [3], MENSES [5], LOW SOCIO-ECONOMIC STATUS [1,6], AND LOW MATERNAL EDUCATION [6]. STUDIES REGARDING IDA IN INFANCY HAVE DEMONSTRATED THAT IDA CAN LEAD TO SERIOUS COGNITIVE PROBLEMS THAT EXTEND INTO ADULTHOOD [7-10].

MATERNAIDURING THE PERINATAL PERIOD CAN ALSO INFLUENCE THE CHILD’S RISK OF DEVELOPING ANEMIA, WHICH CAN ALSO LEAD TO VARIOUS HEALTH PROBLEMS [11-14]. HOWEVER, PREVIOUS STUDIES REGARDING THE INFLUENCE OF MATERNAL IDA ON THE CHILD’S RISK OF ANEMIA HAVE VARIOUS LIMITATIONS. FOR EXAMPLE, MOST STUDIES HAVE FOCUSED ON THE INFLUENCE OF MATERNAL IDA ON INFANTS AND TODDLERS, AND FEW STUDIES HAVE EXAMINED THE FAMILY-RELATED EFFECTS OF IDA AMONG OLDER CHILDREN. NEVERTHELESS, THE RISK OF IDA LATER IN LIFE CAN BE RELATED TO THE INDIVIDUAL’S SOCIO-ECONOMIC STATUS, LIFESTYLE, AND HABITS. IN THIS CONTEXT, FAMILY SETTINGS CAN INFLUENCE INDIVIDUALS’ FOOD HABITS AND PREFERENCES, LIFESTYLE (E.G., EXERCISE), NUTRITIONAL SUPPLEMENTATION, AND HEALTH INTERESTS, WHICH MIGHT ALL AFFECT THE PREVALENCE AND RISK OF IDA LATER IN LIFE.

OUR STUDY AIMED TO DETERMINE WHETHER PARENTAL IDA AFFECTED THE RISK OF IDA AMONG KOREAN ADOLESCENTS WHO WERE INCLUDED IN THE 5th KNHANES. THIS SURVEY IS SOUTH KOREA’S LARGEST NATION-WIDE CROSS-SECTIONAL STUDY, AND HAS BEEN CONDUCTED EVERY 3 YEARS SINCE 1998 BY THE KOREAN MINISTRY OF HEALTH AND WELFARE. THE 5th KNHANES (2010-2012) IS THE ONLY SURVEY THAT INCLUDED LABORATORY TESTING FOR HEMOGLOBIN, SERUM IRON, TOTAL IRON-BINDING CAPACITY, AND FERRITIN IN ADULTS AND ADOLESCENTS OVER 10 YEARS OF AGE. FURTHERMORE, THE SURVEY IS PERFORMED USING FAMILY-LEVEL UNITS, WHICH MAKES THE 5th KNHANES IDEAL FOR EXAMINING THE PREVALENCE OF ADOLESCENT IDA AND ITS RELATIONSHIPS WITH A FAMILY HISTORY OF IDA AND OTHER RISK FACTORS.

MATERIALS AND METHODS

1) STUDY POPULATION

The KNHANES participants were randomly selected using a stratified multistage sampling process, although individuals were excluded if they were in a nursing home or facility, soldiers, prisoners, or non-Koreans. Women who were pregnant, and the individuals who were in treatment of chronic disorder, including pulmonary tuberculosis, chronic renal failure requiring dialysis, various cancer, chronic rheumatoid disorders, liver cirrhosis at the time of the survey were excluded. The primary data from the 5th KNHANES were searched for records of participants who were 10-18 years old, and these participants were matched to their parents’ records. The available laboratory data included red blood cell counts, hemoglobin levels, serum iron levels, serum total iron-binding capacity, and serum ferritin levels. The participants’ records also contained data regarding various socio-economic factors, such as family income, education level, and reception of various forms of social welfare support. Finally, the records contained data regarding each participant’s physical and mental health, such as feelings of happiness and healthiness, health interests, body image, attempts and methods for losing weight, exercise, nutritional supplementation, and nutritional knowledge.

2) VARIABLE DEFINITIONS

The World Health Organization’s criteria for anemia were adopted, which identify anemia based on a hemoglobin level of <12.0 g/dL (<15 years old), <13.0 g/dL (≥15-year-old males), or <12.0 g/dL (≥15-year-old females). The presence of IDA was identified based on the coexistence of age-dependent anemia, serum ferritin levels of <15 ng/mL, and transferrin saturation of <16%.

Body mass index (BMI) was used to classify the participants as obese (BMI of ≥25 kg/m² at >18 years old or ≥95% of the age-specific reference value at <18 years old), normal weight, or underweight (BMI of <18.5 kg/m² at >18 years old or ≤5% of the age-specific reference value at <18 years old). The age-specific reference values
were obtained from the 2007 standard growth chart for Korean children and adolescents. Household income was divided into quartiles based on data from the time of the survey. Participants were considered to perform regular exercise if they performed medium-intensity exercise at least 3 times per week.

3) Statistical analysis

The KNHANES is designed to provide a complex and representative sample of participants, based on stratification, clustering, and unequal weighting. All statistical analyses were performed according to the relevant strata, clusters, and weightings from the guidelines regarding the use of primary KNHANES data, which are published by the Korean Centers for Disease Control and Prevention [15]. Prevalences of IDA and their 95% CI were calculated and compared using the chi-square test. In addition, the chi-square test was used to evaluate the associations between IDA prevalence and socioeconomic, personal, and family factors. Two-sided P-values of <0.05 were considered statistically significant. All statistical analyses were performed using IBM SPSS software (version 22.0; IBM Corp., Armonk, NY).

Results

The 5th KNHANES included 31,596 randomly selected individuals from 11,520 families, with a total of 25,534 participants (M:F=1.18:1). A total of 2,918 adolescents aged 10 to 18 (M:F=1.15:1) completed the laboratory test. Fig. 1 shows the study flow chart.

The overall prevalence of IDA was 4.5% (95% CI: 4.1-4.8%), which was similar to the result from a previous study of IDA [2]. The prevalence of IDA in adolescents was 3.1% (95% CI: 2.4-4.1%).

Several variables were analyzed to identify the risk associated with IDA (Table 1). Female sex was a risk factor for IDA (odds ratio [OR]: 8.2, 95% CI: 7.5-8.8), although male sex was not (OR: 0.9, 95% CI: 0.7-1.2), and this difference was statistically significant (P<0.001). Adolescent girls showed a higher risk of IDA than adolescent boys (P<0.001). The socioeconomic variables exhibited inconsistent associations with adolescent IDA. For example, a high prevalence of adolescent IDA was associated with receiving social welfare support (P<0.03), low maternal education (P<0.006), and receiving charitable food support (P<0.04). A family history of IDA was also associated with a high prevalence of IDA (P<0.03). In addition, the prevalence of IDA was associated with poor body image (P<0.026) and weight control efforts (P<0.01). Nutritional supplement was associated with decreased IDA in adolescents (P<0.007), although nutrition education did not have a significant impact on IDA reduction (P<0.08). However, adolescents who were aware of nutritional labels had a high prevalence of IDA (P<0.001).

The multivariate model included all of the variables from Table 1, and the results are shown in Table 2. Low household income, receiving social welfare support, and low maternal education were not significant risk factors. However, the risk of adolescent IDA was independently associated with a family history of IDA (P<0.03), female sex (P<0.04), no nutritional education (P<0.01), and awareness of nutritional labels (P<0.009). Interestingly, unlike in the univariate analysis, obesity was independently associated with IDA (P<0.001). However, IDA was not significantly associated with poor body image (P<0.007), weight control efforts (P<0.019), nutritional supplementation (P<0.866), or use of nutritional labels (P<0.622).

![Fig. 1. Study flow chart.](image-url)
### Table 1. Prevalence and risk of iron deficiency anemia according to various factors

| Factor                                | Prevalence (95% CI) | Odds ratio (95% CI) | P-value |
|---------------------------------------|---------------------|---------------------|---------|
| **Sex**                               |                     |                     |         |
| Male                                  | 0.5 (0.2-1.3)       | 13.43 (4.92-36.65)  | <0.001  |
| Female                                | 6.2 (4.6-8.3)       |                     |         |
| **Household income quartile**         |                     |                     |         |
| Quartile 1                            | 5.5 (2.6-8.4)       | 2 vs. 1             | 0.295   |
|                                      | 3.2 (1.6-4.9)       | 3 vs. 1             |         |
| Quartile 2                            | 2.2 (0.8-3.5)       | 4 vs. 1             |         |
| Quartile 3                            | 2.1 (0.6-3.6)       |                     |         |
| Quartile 4                            | 2.0 (0.5-3.6)       |                     |         |
| **Social welfare support**            |                     |                     |         |
| Yes                                   | 25.0 (11.1-38.9)    | 3.31 (1.45-7.56)    | 0.031   |
| No                                    | 9.5 (6.8-12.2)      |                     |         |
| **Paternal education**                |                     |                     |         |
| Until high school                     | 12.3 (7.1-17.5)     | 2.15 (0.98-4.72)    | 0.056   |
| College/university or later           | 7.7 (3.5-11.8)      |                     |         |
| **Maternal education**                |                     |                     |         |
| Until high school                     | 12.6 (8.8-17.2)     | 3.12 (1.39-6.99)    | 0.006   |
| College/university or later           | 6.1 (2.44-9.8)      |                     |         |
| **Family history of IDA**             |                     |                     |         |
| Yes                                   | 18.7 (8.9-28.4)     | 3.12 (1.11-8.76)    | 0.030   |
| No                                    | 6.3 (1.7-10.9)      |                     |         |
| **Charitable food support**           |                     |                     |         |
| Yes                                   | 15.8 (5.2-26.4)     | 2.27 (0.95-5.44)    | 0.040   |
| No                                    | 10.3 (7.2-13.4)     |                     |         |
| **Body image**                        |                     |                     |         |
| Poor                                  | 17.2 (10.7-23.6)    | 2.14 (1.16-3.93)    | 0.026   |
| Good                                  | 8.9 (5.9-11.8)      |                     |         |
| **Weight control efforts**            |                     |                     |         |
| Yes                                   | 14.7 (10.3-19.16)   | 2.42 (1.27-4.61)    | 0.010   |
| No                                    | 7.1 (3.7-10.4)      |                     |         |
| **Obesity (≥25 kg/m² or ≥95 percentile)** |                     |                     |         |
| Yes                                   | 10.2 (0.9-21.7)     | 0.448 (0.11-1.82)   | 0.836   |
| No                                    | 11.4 (8.5-14.3)     |                     |         |
| **Regular exercise**                  |                     |                     |         |
| Yes                                   | 15.2 (4.0-26.4)     | 0.71 (0.26-1.95)    | 0.510   |
| No                                    | 13.8 (10.0-17.5)    |                     |         |
| **Nutritional education**             |                     |                     |         |
| Yes                                   | 6.6 (1.65-11.5)     | 1.73 (0.75-4.01)    | 0.076   |
| No                                    | 12.1 (8.5-15.6)     |                     |         |
| **Nutritional supplements**           |                     |                     |         |
| Yes                                   | 6.6 (2.5-9.4)       | 0.40 (0.19-0.82)    | 0.007   |
| No                                    | 13.1 (9.2-17.0)     |                     |         |
| **Nutritional label awareness**       |                     |                     |         |
| Yes                                   | 12.7 (9.1-16.3)     | 8.06 (1.71-38.05)   | <0.001  |
| No                                    | 1.7 (0.9-4.3)       |                     |         |
| **Nutrition label use**               |                     |                     |         |
| Yes                                   | 16.8 (9.7-23.9)     | 0.57 (0.29-1.13)    | 0.147   |
| No                                    | 10.54 (6.3-14.8)    |                     |         |

IDA, iron deficiency anemia; CI, confidence interval.

### Discussion

This study evaluated IDA among Korean adolescents using nationally representative data, and revealed that the prevalence of IDA among Korean adolescents was associated with several previously reported risk factors, such as low economic status, female sex, low maternal education, and receiving social welfare [2,6,10,16,17]. Interestingly, although obesity is reportedly associated with IDA [2,18-22], we could only detect a significant relationship between obesity and IDA in multivariate analysis. Thus, further studies are needed to evaluate the relationship between IDA and obesity.

Infants, and pregnant or premenopausal women are age groups that are at-risk for IDA, and previous studies have usually evaluated these groups [3,4,11,12,23,24]. However, adolescence is an important period of rapid growth and development, which require adequate nutritional supplies. In addition, adolescents are still influenced by their family circumstances and lifestyle, as well as other social interactions with classmates and peers. However, few studies have evaluated IDA among adolescents [25,26] and the duration of the "maternal effect" remains unclear, as previous studies have focused on the association of maternal anemia or iron...
Table 2. Multivariate analysis of risk factors for iron deficiency anemia

|                      | Odds ratio (95% CI) | P-value |
|----------------------|---------------------|---------|
| Sex                  | 22.04 (1.11-438.82) | 0.043   |
| Household income quartile | 1.75 (0.79-3.87) | 0.083   |
|                      | 2 vs. 1             |         |
|                      | 3 vs. 1             |         |
|                      | 4 vs 1              |         |
| Social welfare support | 0.66 (0.02-28.31) | 0.828   |
| Charitable food support | 4.19 (1.45-12.15) | 0.023   |
| Family history of IDA | 4.51 (1.09-18.69) | 0.034   |
| Low paternal education | 0.39 (0.09-1.82) | 0.221   |
| Low maternal education | 6.82 (0.96-48.44) | 0.055   |
| Poor body image      | 1.61 (0.26-9.93)   | 0.607   |
| Weight control efforts | 2.34 (0.44-12.55) | 0.319   |
| Obesity              | 4.53 (0.86-23.93)  | 0.001   |
| Regular exercise     | 1.89 (0.21-17.73)  | 0.574   |
| No nutritional education | 6.82 (1.08-4.31)| 0.012   |
| Nutritional supplementation | 0.85 (0.13-5.69)| 0.866   |
| Nutritional label awareness | 8.1 (1.7-38.5)| 0.596   |
| Nutritional label use | 0.64 (0.11-3.78) | 0.622   |

IDA, iron deficiency anemia; CI, confidence interval.

deficiency and IDA among neonates, infants, or toddlers [11,12,14,21,24]. In this context, maternal knowledge and feeding practices affect their children’s risk of IDA [6,21], although the child’s preferred foods and eating habits might change over time and be affected by their family members, classmates, or peers.

Obesity in children and adolescents is a disease entity that can be influenced by the family setting [27-29]. In addition, children with type 2 diabetes mellitus tend to have family members with type 2 diabetes [30]. Also, adolescents with a parental history of diabetes have increased risks of overweight/obesity, hypertension, and metabolic syndrome [31]. In this context, the present study revealed that a family history of IDA was significantly associated with an increased risk of adolescent IDA, which might be similar to the familial relationships for other chronic disorders mentioned above (e.g., obesity, diabetes mellitus, and metabolic syndrome). However, cause-result relationship of the familial factors and increased prevalence of adolescent IDA is still weak. Therefore, close mechanisms of the familial effect to the occurrence of IDA should be further investigated. Interestingly, Korean schools provide lunch programs for school-aged children, with middle- and high-school students also having access to dinner programs. Thus, individual-level differences in meal contents are mainly attributable to breakfast, inter-meal snacks, and weekend meals.

The present study revealed that lifestyle factors (e.g., regular exercise) did not protect against IDA. In addition, poor body image and efforts to lose weight were associated with increased risks of IDA, which suggests that these factors might lead to nutritional imbalance and deficiency. The relationship between nutritional label awareness and IDA is difficult to interpret, although it is possible that adolescents might focus on calorie contents instead of health-promoting nutrients. This possible relationship might be related to the same mechanism as the relationships between IDA and poor body image or efforts to lose weight. Nevertheless, the present study has limited ability to explain the underlying factors, and further studies are needed to understand and develop risk models for examining the relationship between familial factors and adolescents with IDA. Furthermore, the present study revealed that nutritional education did not protect against IDA, which indicates that current education interventions are not effectively improving health and nutrition knowledge in Korean adolescents aged 10 to 18. Moreover, maternal education level was significantly related to the prevalence of IDA among adolescents, which suggests that maternal knowledge and interest regarding nutrition and health still exert some effect on their children’s health.

**Conclusion**

The present study revealed that the development of IDA in adolescents was related to a family history of IDA. Therefore, additional studies are needed to better understand the relationship between family setting and adolescent IDA. Furthermore, additional measures should be developed to prevent IDA among adolescents, and it is possible that family-level educational interventions may help address this issue.
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