KEMAS 21 (3) (2026) 696-707

Jurnal Kesehatan Masyarakat

http://journal.unnes.ac.id/nju/index.php/kemas

Nutritional Determinants and Molecular Insights into Anemia among Boarding School Adolescents

Kiky Martha Ariesaka[1]✉, Lintang Widya Sishartami[1], Anditri Weningtyas[1], Moh. Mirza Nuryady[2,3]

[1]Department of Medicine, Faculty of Medicine, State University of Malang, Malang, Indonesia
[2]Institute of Parasitology, Department of Biological Science and Pathology, Veterinary Medicine of Vienna, Austria
[3]Biology Education Department, Faculty of Teacher Training and Education, University of Muhammadiyah Malang, Malang, Indonesia

Article Info

Article History:
Submitted August 2025
Accepted November 2025
Published January 2026

Keywords:
anemia; adolescents; dietary diversity; hemoglobin; iron metabolism;

DOI
http://doi.org/10.15294/kemas.v21i3.35386

Abstract

Introduction: Anemia remains a significant public health problem among adolescents in developing countries such as Indonesia. Female adolescents are more vulnerable due to menstrual blood loss and increased iron needs during growth, while dietary diversity and beverage habits may further influence anemia risk. **Aim:** This study aimed to analyze factors associated with anemia, including gender, diet quality, and tea or coffee consumption, and to explore their molecular relevance using a bioinformatics approach. **Methods:** A cross-sectional study was conducted among 199 adolescents (105 males, 94 females) aged 12–17 years in a boarding school in Malang, Indonesia. Data collection included hemoglobin measurement, anthropometric assessment, and a Food Frequency Questionnaire (FFQ). Statistical analysis was performed using Chi-square and logistic regression, while bioinformatics analysis employed STRING, Cytoscape, and ShinyGO to identify key genes and pathways. **Results:** Female gender (AOR = 6.595; $p < 0.001$), adequate diet (AOR = 0.184; $p = 0.012$), and tea/coffee intake (AOR = 7.532; $p < 0.001$) were significant predictors of anemia. Bioinformatics analysis identified SLC11A2, TFRC, and HAMP as key genes regulating ferroptosis and mineral absorption pathways. **Conclusions:** Gender, dietary quality, and tea or coffee consumption significantly influence anemia in adolescents.

Introduction

Anemia is a global health problem that is still prevalent in developing countries, including Indonesia (Priliani *et al*., 2025). The WHO defines anemia as a condition where the hemoglobin level is <12.0 g/dL in adolescent girls and <13.0 g/dL in adolescent boys (WHO, 2024). Anemia is characterized by a decrease in hemoglobin levels in the blood, resulting in a reduced capacity to transport oxygen to body tissues, resulting in symptoms such as fatigue, tiredness, lethargy, impaired concentration, and decreased academic performance (H S *et al*., 2024; Killeen *et al*., 2025).

Adolescence is a crucial period characterized by accelerated physical growth, hormonal changes, and increased nutritional needs, including iron (Soliman *et al*., 2022). An imbalance between nutrient needs and intake during this period can result in anemia (Qasrawi *et al*., 2024). Data shows that the prevalence of anemia among adolescents in Indonesia increased from 18.4% to 32% between 2013 and 2018 (Reski *et al*., 2020). Anemia in adolescents has been more often associated with female gender due to blood loss during menstruation (Gonete *et al*., 2018; Sishartami *et al*., 2025). Numerous studies have

✉ Correspondence Address:
Department of Medicine, Faculty of Medicine, State University of Malang, Malang, Indonesia
Email: kiky.martha.fk@um.ac.id

pISSN 1858-1196
eISSN 2355-3596

revealed consistently elevated anemia rates among adolescent females. A study observed a prevalence rate of 40.5% in Aceh, Indonesia, with wasting and overweight status serving as important predictors (Ahmad *et al*., 2023; Khayati *et al*., 2025). Another study discovered that both hemoglobin-related knowledge and physical activity were significantly correlated with the prevalence of anemia in adolescent girls (Fitariani *et al*., 2025). However, research also shows that adolescent boys are at risk of anemia due to increased iron requirements for muscle mass development and higher levels of physical activity (Nicotra *et al*., 2023).

Boarding school environments exhibit relatively uniform dietary and physical activity patterns among students because daily meals and activities are regulated by the institution (Acciai *et al*., 2019; Ashfaq *et al*., 2023; Diana *et al*., 2025). This provides an opportunity to analyze the determinants of anemia in adolescent boys and girls in a more controlled environment. In this context, variations in hemoglobin levels between sexes may better reflect biological and behavioral differences rather than diverse external environmental influences (Barrera-Reyes & Tejero, 2019). Anemia is not solely a matter of iron deficiency but also part of a complex nutritional problem involving various biological, social, and environmental determinants (Raiten *et al*., 2023). These factors include growth and development, age, gender, physiological status, economic status, parental education, and exposure to infectious diseases such as worm infestation, schistosomiasis, malaria, tuberculosis, and HIV (Thachil *et al*., 2014; Wiafe *et al*., 2023). In addition to iron, deficiencies in other micronutrients such as vitamins A, B2, B6, B9 (folic acid), B12, C, D, E, and zinc also contribute to anemia through various mechanisms (Espinosa-Salas & Gonzalez-Arias, 2025; Pratiwi & Sudiarti, 2025). Moreover, the absorption and utilization of dietary iron are influenced by food components that can either enhance or inhibit absorption. Polyphenols found in tea and coffee, as well as phytates in grains and legumes, act as potent inhibitors of non-heme iron absorption, whereas vitamin C and certain amino acids can enhance it. Therefore, understanding the pattern of tea and coffee consumption, together with dietary diversity, becomes essential in evaluating anemia risk (Scarano *et al*., 2023).

Adolescent nutritional status, as measured by body mass index (BMI), is also closely related to hemoglobin levels (Enggardany *et al*., 2021). Several studies have shown that overweight or obese adolescents have a lower risk of anemia compared to those with a normal BMI. Furthermore, sociodemographic factors such as parental education and income, as well as menstrual status in girls, also influence the incidence of anemia (Hamed *et al*., 2024) (Ani *et al*., 2025). Although numerous studies have examined anemia in adolescent girls, studies directly comparing boys and girls in controlled boarding environments are still limited in Indonesia (Handayani *et al*., 2024; Putri *et al*., 2025; Sari *et al*., 2022). This study provides novelty by analyzing hemoglobin levels, nutritional factors, and nutritional status associated with anemia in male and female adolescents in a boarding school setting. The homogeneity of dietary and physical activity patterns in the boarding school setting allows for a more accurate comparison of biological and behavioral factors influencing anemia. This study aimed to analyze hemoglobin levels and nutritional determinants associated with anemia in male and female adolescents in a boarding school setting. Furthermore, this study integrated a bioinformatics approach to elicit gene interactions that encompass key factors in a significant determinant. Through this approach, the study focused not only on epidemiological approaches but also on molecular biological mechanisms, making it more comprehensive.

Methods

This study used a descriptive analytical design with a cross-sectional approach. The study took place at a boarding school in Malang City, which was selected purposively. Inclusion criteria included: (1) active students aged 12–17; (2) willingness to participate in all measurements; and (3) good health with no history of blood transfusions or chronic diseases. Respondents undergoing anemia therapy or with blood disorders such as thalassemia were excluded from the study. Sample size calculations were performed using G*Power software version 3.1.9.7 using the t-test (Means: Difference between two independent groups). The parameters used included a one-tailed test, a medium effect size (d = 0.5), a significance level (α) of 0.05, and a power of 0.95. This study involved 199 students—105 males and 94 females. This study has received ethical approval from the Health Research Ethics Committee of the State University of Malang, under permit number 27.03.07/UN32.14.2.8/LT/2025. All participants were explained the purpose and procedures of the study and signed an informed consent form before participating in the study.

Data collection was conducted in July 2025. Data were collected once using two main instruments: a structured questionnaire and a Food Frequency Questionnaire (FFQ). The structured questionnaire consisted of multiple-choice and short-answer questions. Dietary pattern data were obtained from a structured questionnaire containing four components: breakfast habits (4 questions), snacking habits (4 questions), fast food consumption habits (3 questions), and fiber consumption habits (6 questions). Breakfast and snacking habits were categorized as frequent if consumed >5 times/week and infrequent if consumed ≤5 times/week. Fast food consumption was categorized as frequent if consumed ≥2 times/week and infrequent if consumed <2 times/week. Consuming sources of fiber (vegetables and fruit) was categorized as frequent if consumed >3 times/week and infrequent if consumed ≤3 times/week (Nur, 2008).

Respondents' food consumption quality was assessed based on the total score of the FFQ. Scores were determined based on the frequency of consumption of each food group. A score of 50 was given for consumption ≥3 times per day, 25 for 1 time per day, 15 for 3–6 times per week, 10 for 1–2 times per week, 5 for 2 times per month, and 0 for never consumption (Nababan & Nurdin, 2023). The food consumption score reflects the diversity of a subject's dietary intake in a one-month period. The quality of a subject's food consumption was categorized into three categories: low (FFQ score <611), adequate (FFQ score 611-1114), and good (FFQ score >1114). Anthropometric measurements were conducted using an ONEMED digital scale with an accuracy of 0.1 kg for weight and a SECA stadiometer with an accuracy of 0.1 cm for height. Body mass index (BMI) was calculated by dividing weight (kg) by the square of height (m^2) and then categorized based on the WHO standards Z score for adolescents.

Hemoglobin levels were measured using an EasyTouch® GCHb hemoglobin meter using the reflective photometry method using capillary blood samples from the fingertip. The examinations were performed by trained medical personnel. Based on World Health Organization (2024) criteria, hemoglobin levels <12.0 g/dL in girls and boys aged 12-14 years and <13.0 g/dL in boys aged 15 years and older are categorized as anemia. The collected data were then cleaned and coded. Data were analyzed using IBM SPSS Statistics version 30 for MacOS. Descriptive analysis was used to display the distribution of respondents. Comparison of average hemoglobin levels between male and female adolescents was analyzed using the independent t-test. The correlation between anemia (yes/no) and categorical variables was analyzed using the Chi-square test, where if the conditions are met (there is an expected count of less than 5 in more than 20% of cells), otherwise the analysis is carried out using Fisher's Exact Test or Kolmogorov-Smirnov Test. A multivariate test was conducted with simple logistic regression. A p-value <0.05 was considered statistically significant.

The selected genes were subjected to a protein–protein interaction (PPI) network analysis using the STRING database (https://string-db.org/) with a minimum interaction confidence score set at >0.4. The resulting interaction network was imported and visualized in Cytoscape (version 3.10.4) (https://cytoscape.org/). To identify the most critical genes within the network, the CytoHubba plugin was employed, ranking the top 10 hub genes based on the Maximum Clique Centrality (MCC) algorithm. To explore the functional relevance of the identified genes, Gene Ontology (GO) (https://www.geneontology.org/) and Kyoto Encyclopedia of Genes and Genomes (KEGG) (https://www.genome.jp/kegg/) pathway enrichment analyses were performed. These analyses were conducted using ShinyGO version 0.85 (https://bioinformatics.sdstate.edu/go/), focusing on the enriched biological processes, cellular components, and molecular functions associated with iron metabolism. An FDR threshold of 0.05 was applied to determine statistical significance.

Result and Discussion

Table 1 shows a comparison of the characteristics of adolescents who were not anemic and those who were anemic. Most respondents were female, with an average age of 14.25 ± 1.68 years. The analysis showed a significant difference by gender (p = 0.004). Female adolescents were more likely to experience anemia (11.1%) than male adolescents (4.5%). This condition may be caused by blood loss during menstruation and increased iron requirements during growth (Wulandari *et al*., 2025). These findings are consistent with previous studies, which indicated that adolescent girls are more vulnerable to iron deficiency anemia. This vulnerability arises not only from blood loss but also from the genetic regulation of iron absorption and distribution (Arifah *et al*., 2025). In females, the expression of the HAMP gene, which modulates the hormone hepcidin, tends to rise due to hormonal factors (Greenwood *et al*., 2023), potentially obstructing iron absorption via SLC11A2 and its release through SLC40A1 (Prajapati *et al*., 2024). This renders teenage girls more vulnerable to iron insufficiency, despite comparable food consumption (Stubbendorff *et al*., 2025). Besides, this result also demonstrates the need to integrate gender aspects into nutrition education and anemia counseling. This gender-based counseling should be conducted routinely in boarding schools to raise awareness of more vulnerable women and ensure their adherence to iron supplementation. Furthermore, boarding school menus should also be gender-sensitive, as women require higher levels of iron.

Table 1. Participants Characteristic

Characteristic	Non-Anemic n (%)	Anemic n (%)	p-Value
Age (years)	**Mean ± SD = 14.25 ± 1.68 (range 12–18)**		
Gender			**0.004 ***
Male	96 (48.2)	9 (4.5)	
Female	72 (36.2)	22 (11.1)	
BMI category			**1.000**
Thinness (Z < -2 SD)	4 (2.0)	1 (0.5)	
Normal (−2 SD ≤ Z ≤ +1 SD)	121 (60.8)	23 (11.6)	
Overweight (+1 SD < Z ≤ +2 SD)	21 (10.6)	5 (2.5)	
Obesity (Z > +2 SD)	22 (11.1)	2 (1.0)	
Mother's education			**1.000**
Elementary	2 (1.0)	0 (0.0)	
Junior High	11 (5.5)	4 (2.0)	
Senior High	95 (47.7)	17 (8.5)	
College/University	60 (30.2)	10 (5.0)	
Father's education			**1.000**
Elementary	3 (1.5)	0 (0.0)	
Junior High	8 (4.0)	1 (0.5)	
Senior High	80 (40.2)	16 (8.0)	
College/University	77 (38.7)	14 (7.0)	
Mother's occupation			**0.998**
Housewife	101 (50.8)	21 (10.6)	
Private sector	27 (13.6)	1 (0.5)	
Trader	16 (8.0)	3 (1.5)	

Characteristic	Non-Anemic n (%)	Anemic n (%)	p-Value
Laborer	4 (2.0)	1 (0.5)	
Teacher/Lecturer	20 (10.1)	5 (2.5)	
Father's occupation			**1.000**
Private sector	87 (43.7)	14 (7.0)	
Trader	41 (20.6)	8 (4.0)	
Farmer	2 (1.0)	0 (0.0)	
Laborer	23 (11.6)	5 (2.5)	
Teacher/Lecturer	15 (7.5)	4 (2.0)	
Breakfast habit			**0.262**
Frequent	49 (24.6)	6 (3.0)	
Infrequent	119 (59.8)	25 (12.6)	
Snack frequency			**0.124**
Frequent	57 (28.6)	15 (7.5)	
Infrequent	111 (55.8)	16 (8.0)	
Fast food consumption			**0.767**
Frequent	134 (67.3)	24 (12.1)	
Infrequent	34 (17.1)	7 (3.5)	
Fruit/Vegetable consumption			**0.343**
Frequent	66 (33.2)	15 (7.5)	
Infrequent	102 (51.3)	16 (8.0)	
Food Frequency Questionnaire (FFQ)			**0.017** *
Low (score < 661)	101 (50.8)	28 (14.1)	
Adequate (score 661–1114)	50 (25.1)	3 (1.5)	
Good (score > 1114)	17 (8.5)	0 (0)	
Tea/Coffee consumption			**< 0.001***
Yes	69 (34.7)	24 (12.1)	
No	99 (49.7)	7 (3.5)	

Source: Primary Data, 2025

Diet quality, measured using the Food Frequency Questionnaire (FFQ), showed significant results (p = 0.017). Adolescents with low FFQ scores (<661) had the highest proportion of anemia (14.1%), while there were no cases of anemia in the group with good FFQ scores (>1114). These findings suggest that the better the dietary quality, the lower the risk of anemia. A diverse diet provides sources of iron, protein, and vitamin C, which play a role in hemoglobin formation and iron absorption (Piskin *et al*., 2022). Food diversity aligns with Indonesia's general guidelines for balanced nutrition. To meet the body's nutritional needs, it is important to eat a variety of foods, such as carbohydrates, protein, vegetables, fruit, fat, dairy products, and water (Ariesaka *et al*., 2025). The Indonesian Ministry of Health has also put together a list of excellent nutrition guidelines under the phrase "Isi Piringku" (fill my plate). Isi Piringku talks about a lot of different things, such as the many kinds of cuisine that people should eat every day, like side dishes, fruits, vegetables, and staple foods. In addition to eating a variety of foods, it is also a good idea to drink eight glasses of water a day, exercise for 30 minutes a day, and wash your hands with soap (Ministry of Health of the Republic of Indonesia, 2019). In terms of balanced nutrition education, boarding schools need to implement structured meal planning by paying attention to the intake of animal protein, green leafy vegetables, and fruits rich in vitamin C (Nahdyah *et al*., 2025). These results also align with a previous study, which found that diverse food consumption is associated with better hemoglobin levels in adolescents

Table 2. Multivariate Analysis of Factors Associated with Anemia

Variables	Coefficient (B)	p-value	OR (95% CI)
Step 1			
Gender (Female)	1.836	< 0.001	6.269 (2.378 – 16.523)
Snack consumption (Frequent)	0.423	0.353	1.527 (0.625 – 3.732)
FFQ (Adequate vs Low)	−1.652	0.014	0.192 (0.051 – 0.720)
FFQ (Good vs Low)	−19.649	0.998	~0.000 (—)
Tea/Coffee consumption (Yes)	2.009	< 0.001	7.457 (2.716 – 20.474)
Constant	−3.674	< 0.001	0.025
Step 2			
Gender (Female)	1.886	< 0.001	6.595 (2.510 – 17.327)
FFQ (Adequate vs Low)	−1.694	0.012	0.184 (0.049 – 0.687)
FFQ (Good vs Low)	−19.588	0.998	~0.000 (—)
Tea/Coffee consumption (Yes)	2.019	< 0.001	7.532 (2.747 – 20.649)
Constant	−3.531	< 0.001	0.029

Source: Primary Data, 2025

(H. Li *et al*., 2025). The impact of dietary diversity on anemia occurs more through the role of supporting and inhibiting nutrients in absorption (Cai *et al*., 2023). Vitamin C, for example, facilitates the reduction of Fe^{3+} to Fe^{2+} by CYBRD1 (Lane *et al*., 2015), thereby increasing the availability of non-heme iron for transport by SLC11A2 (Fisher & Nemeth, 2017).

Tea and coffee consumption showed a highly significant association with anemia ($p < 0.001$). A total of 12.1% of adolescents who consumed tea or coffee experienced anemia, compared to only 3.5% in the non-consumer group. These results indicate that the habit of drinking tea or coffee is a significant risk factor for anemia, as has been demonstrated in previous studies (He & Chen, 2024; Lee *et al*., 2023; Wartiningsih *et al*., 2024). Over the years, more and more people have started drinking coffee. This is mostly because of how it tastes and how it makes you feel, not because of its nutritional value (Samoggia & Riedel, 2019). People of all ages, from teens to adults, now prefer coffee over other drinks. But drinking coffee can raise the risk of lower hemoglobin levels, which can lead to anemia (Nanri *et al*., 2023). In Indonesia, it is a long-standing cultural tradition to serve tea instead of water at breakfast or as an afternoon snack. This habit indirectly causes anemia by making it harder for the body to absorb iron because it has polyphenols and tannins in it. Caffeine, which is in all kinds of coffee beans and tea, can make it harder for the body to absorb iron (Rodak *et al*., 2021). Caffeine can lower blood hemoglobin levels, thereby impairing the body's ability to store and deliver oxygen to the lungs and other parts of the body. Polyphenols such as tannins and chlorogenic acid can bind to non-heme iron and form insoluble complexes, thus inhibiting iron absorption in the intestine (Scarano *et al*., 2023).

Multivariate logistic regression analysis showed that gender, diet quality (FFQ), and tea/coffee consumption were the most influential factors in anemia. Women were 6.6 times more likely to develop anemia than men (AOR = 6.595; 95% CI 2.510–17.327). Adequate diet quality acted as a protective factor, reducing the risk of anemia by 82% (AOR = 0.184; 95% CI 0.049–0.687). Conversely, tea and coffee consumption increased the risk of anemia more than sevenfold (AOR = 7.532; 95% CI 2.747–20.649). These results demonstrate a consistent relationship between dietary behavior and the biological regulation of the iron transport system.

To explore the molecular basis, bioinformatics analysis of genes involved in iron metabolism was performed on several candidate genes related to iron homeostasis. A protein–protein interaction (PPI) analysis was performed using the STRING database to determine the 10 most influential genes, including *SLC11A2, TFRC, FTH1, FTL,*

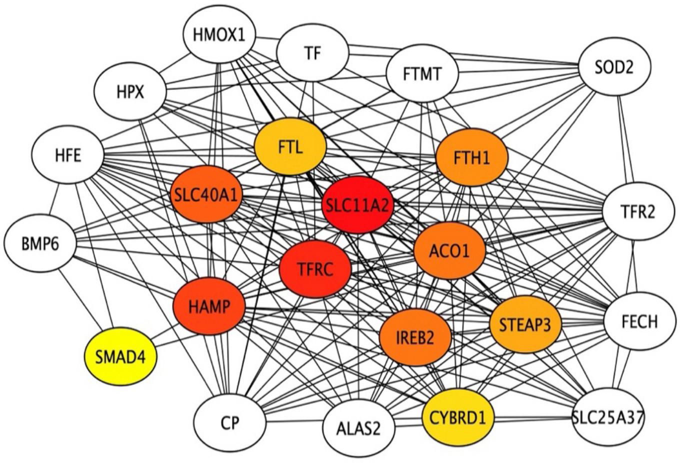

Figure 1. Protein–protein interaction (PPI) network of the iron metabolism–related genes. Node colors represent the ranking order (from red = highest rank to white = lowest rank).

HAMP, SLC40A1, IREB2, ACO1, CYBRD1, and *STEAP3* (Figure1). These genes were then used in GO and KEGG enrichment analyses to identify the dominant biological pathways.

Gene Ontology (GO) analysis confirmed these results. In the Biological Process (BP) aspect, key genes play a role in iron ion transport, iron homeostasis, and the response to iron ions (Figure 2A). This activity indicates that the body's system actively maintains stable iron levels through cellular and systemic mechanisms. When iron intake is low (low FFQ), this system fails to adapt, leading to impaired transport and inefficient accumulation of Fe^{2} for hemoglobin synthesis. In the Molecular Function (MF) aspect, dominant activities include iron-responsive element binding, oxidoreductase activity, and ferrous iron transporter activity (Figure 2B). This function confirms the role of proteins such as CYBRD1 and STEAP3 in maintaining the reduced form of iron for utilization by SLC11A2. This activity may decrease when dietary antioxidant consumption is low, or when polyphenols from tea/coffee predominate, as they compete at the enzymatic level. In the Cellular Component (CC) aspect, most genes are localized to the brush border membrane, autolysosome, and secondary lysosome (Figure 2C). These locations represent key areas for iron uptake and recycling from senescent erythrocytes. Disrupted expression in these areas can impede iron circulation and prolong recovery time from anemia.

KEGG pathway enrichment analysis revealed that the ferroptosis and mineral absorption pathways were the most significant (Figure 3). The ferroptosis pathway describes iron accumulation-dependent cell death and oxidative stress (S. Li & Huang, 2022), while the mineral absorption pathway demonstrates the direct involvement of transporter proteins in the intestinal mineral absorption process (Lu *et al*., 2023). These two pathways link the mechanisms of iron deficiency due to low intake and the inhibitory effects of tea/coffee on the iron transport system.

SLC11A2 (DMT1) is a proton-coupled divalent metal importer essential for intestinal nonheme iron uptake and for releasing transferrin-derived iron from endosomes; loss-of-function or mistrafficking variants cause microcytic hypochromic anemia often with paradoxical hepatic iron accumulation (Romero-Cortadellas *et al*., 2022). DMT1 is the principal apical transporter for dietary nonheme Fe2+ in mature enterocytes and is essential for postnatal intestinal iron absorption. Genetic ablation of Slc11a2 in mice abolishes dietary nonheme iron uptake after birth and produces severe systemic iron deficiency, demonstrating that DMT1 is the dominant intestinal $Fe2^{+}$ importer in vivo (Hounjet *et al*., 2023).

In the context of adolescent anemia, the mechanisms mentioned above are relevant to environmental and behavioral factors

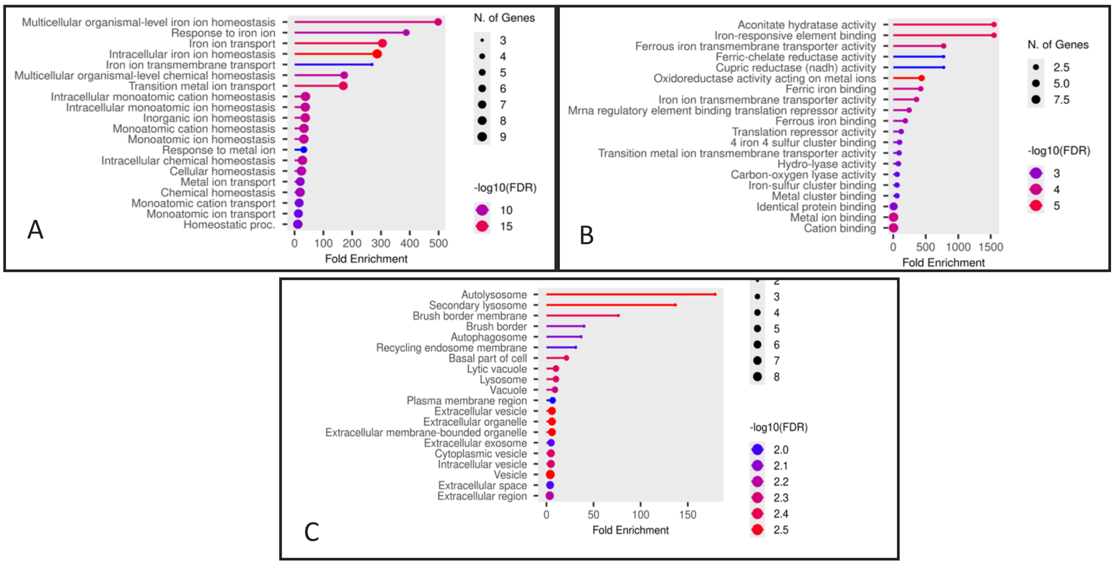

Figure 2. GO enrichment of the top 10 hub genes (A) Biological Process, (B) Molecular Function, and (C) Cellular Component

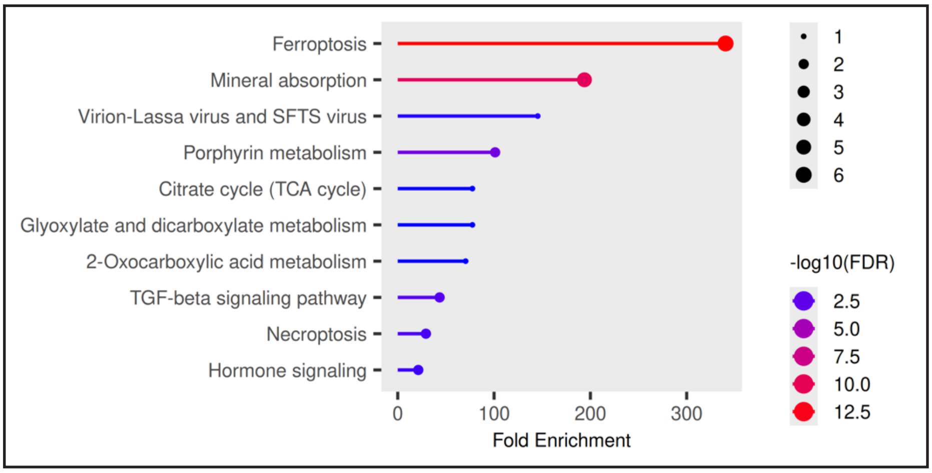

Figure 3. KEGG pathway enrichment of the top 10 hub genes.

that interfere with T1DM activity. Frequent tea or coffee consumption leads to high concentrations of polyphenols that chelate non-heme Fe^{3+} in the intestinal lumen, leading to decreased iron circulation (Scarano *et al.*, 2023), triggering upregulation of hepcidin reuptake inhibitor (HAMP), which suppresses ferroportin (SLC40A1) and subsequently limits basolateral iron export, creating a reverse cycle that impedes iron absorption and utilization (Pagani *et al.*, 2019). Low dietary diversity also mitigates anemia by reducing the intake of essential cofactors required for optimal T1DM function. Enzymes such as CYBRD1 and STEAP3, which catalyze the reduction of Fe^{3+} to Fe^{2+} in the brush border membrane, depend on electron donors such as vitamin C, amino acids, and adequate protein intake (Wallace, 2016). A diet lacking fruits, vegetables, and animal protein limits the availability of reduced iron and may even decrease SLC11A2 expression through nutrient-sensitive signaling pathways.

The female gender is associated with this molecular network due to hormonal modulation of iron-regulating genes. Estrogen has been shown to increase hepcidin expression, indirectly suppress ferroportin-mediated export (Bustamante-Barrientos *et al.*, 2021), and may reduce feedback signals that support T1DM synthesis. When combined with menstrual iron loss and inadequate dietary intake, these hormonal effects reduce T1DM inhibition at both the intestinal and erythroid levels. Consequently, adolescent girls experience limited bioavailable iron—dietary inhibition, cofactor depletion, and intrinsic hormonal regulation converging to limit erythroid iron supply even when systemic stores appear adequate.

Taken together, the results of this study indicate that the incidence of anemia in adolescents is influenced not only by demographic factors such as gender but also by consumption patterns and drinking habits, which can affect iron metabolism. Statistical analysis showed that women have a higher risk of anemia, while a diverse diet plays a protective role against anemia, and tea or coffee consumption significantly increases the risk. These results are consistent with the biological mechanisms identified through bioinformatics analysis, in which key genes such as SLC11A2, TFRC, and HAMP play a central role in regulating body iron homeostasis. PPI and pathway enrichment analyses confirmed that the main pathways involved are ferroptosis, mineral absorption, and porphyrin and iron metabolism, which are functionally closely linked to the processes of hemoglobin formation and iron transport in tissues.

This study is not without limitations. First, the cross-sectional study design cannot confirm a causal relationship between dietary patterns, tea or coffee consumption, and the incidence of anemia. The relationship found is associative, so longitudinal research is needed to determine the direction of the relationship. Second, the assessment of diet quality using the FFQ relies on respondents' memory, so the potential for recall bias is unavoidable. Third, anemia was measured solely based on hemoglobin levels without analysis of serum iron status, ferritin, or inflammatory markers, which could provide a more comprehensive picture of the body's iron status. Furthermore, although bioinformatics analysis successfully identified key genes involved in iron metabolism, these results are still predictive and theoretical in nature and need to be validated through gene expression assays or in vivo protein analysis.

Conclusion

Anemia in adolescents is influenced by biological and behavioral factors, namely female gender, low diet quality, and tea or coffee consumption habits. In addition, bioinformatics analysis supports these findings by identifying key genes such as SLC11A2, TFRC, and HAMP, which are involved in the ferroptosis pathway and mineral absorption, thus explaining the molecular mechanisms that link dietary habits to iron metabolism. These findings indicate the importance of gender-based nutrition education, increasing the diversity and intake of iron-rich foods, and reducing tea or coffee consumption at mealtimes.

Acknowledgments

The authors would like to express their sincere gratitude to Universitas Negeri Malang (UM) for the institutional support and research facilities provided throughout this study.

References

Acciai, F., Yedidia, M., DeWeese, R., Martinelli, S., & Ohri-Vachaspati, P., 2019. School Food and Physical Activity Environment: A Longitudinal Analysis of four School Districts in New Jersey. *The Journal of Adolescent Health: Official Publication of the Society for Adolescent Medicine*, 65(2), pp.216–223.

Ahmad, A., Azizah, A.P.N., Arnisam, A., Phebe, N., & Arifin, S.R., 2023. Anemia and Wasting in Adolescent Girls: A Cross-Sectional Study in Aceh, Indonesia. *Jurnal Gizi Dan Pangan*, 18(Supp.1), pp.11–13.

Ani, L.S., Sumiati, L.N., & Ds, N.K.A.D.U., 2025. Sociodemographic Factors and Adolescent Attitudes Towards Family Planning Programs Related to Adolescent Marriage in Bali Province. *Jurnal Kesehatan Masyarakat*, 21(1), pp.136–146.

Ariesaka, K.M., Weningtyas, A., Sishartami, L.W., Iftitahurroza, H.T., Wibisono, T.A.N., Putri, A.L.A., Wiratama, A.L., & Bakhtiar, F.Y., 2025. Peningkatan Pengetahuan Pengolahan Makanan Sehat untuk Pencegahan Stunting pada Komunitas PKK Desa Sumberejo. *Lumbung Inovasi: Jurnal Pengabdian Kepada Masyarakat*, 10(3), pp.666–674.

Arifah, I., Almayda, M.B., Widyani, Z., Zahra, Q.A., Nuraisyah, S.R., & Werdani, K., 2025. Role of Health Programs Utilization and Social Factors on Adolescent Anemia Status. *Jurnal*

Kesehatan Masyarakat, 20(4), pp.796–807.

Ashfaq, M.M., Jawed, N., Safdar, N.F., & Bhutto, A.A., 2023. Breakfast Patterns in Relation to Physical Activity Among School Adolescents in Karachi, Pakistan. *Journal of Health, Population and Nutrition*, 42(1), pp.116.

Barrera-Reyes, P.K., & Tejero, M.E., 2019. Genetic Variation Influencing Hemoglobin Levels and Risk for Anemia Across Populations. *Annals of the New York Academy of Sciences*, 1450(1), pp.32–46.

Bustamante-Barrientos, F.A., Méndez-Ruette, M., Ortloff, A., Luz-Crawford, P., Rivera, F.J., Figueroa, C.D., Molina, L., & Bátiz, L.F., 2021. The Impact of Estrogen and Estrogen-Like Molecules in Neurogenesis and Neurodegeneration: Beneficial or Harmful?. *Frontiers in Cellular Neuroscience*, 15, pp.636176.

Cai, Z., Li, L., Feng, J., Raat, H., Wu, Y., Zhou, H., & Rozelle, S., 2023. Dietary Diversity and Its Contribution to the Magnitude of Anaemia among Pregnant Women: Evidence from Rural Areas of Western China. *Nutrients*, 15(17), pp.3714.

Diana, R., Setyaningtyas, S.W., & Arimbi, A.N., 2025. Food Preferences, Eating Habits, and Nutritional Status of Full-Day School Students in Urban Areas: Preferensi Makanan, Kebiasaan Makan, dan Status Gizi Anak Sekolah Full-day di Perkotaan. *Amerta Nutrition*, 9(1), pp.169–175.

Enggardany, R., Hendrati, L.Y., & Hairi, N.N., 2021. Relationship between Body Mass Index (BMI) and Anemia Among Adolescent Indonesian Girls (Analysis of The Indonesia Family Life Survey 5th Data). *Amerta Nutrition*, 5(4), pp.347–352.

Espinosa-Salas, S., & Gonzalez-Arias, M., 2025. *Nutrition: Micronutrient Intake, Imbalances, and Interventions*. StatPearls. StatPearls Publishing.

Fisher, A.L., & Nemeth, E., 2017. Iron Homeostasis During Pregnancy. *The American Journal of Clinical Nutrition*, 106, pp.1567S-1574S.

Fitariani, S., Masruroh., Mawarti, H., & Nasrudin., 2025. Anemia Among Adolescent Girls: A Global Review of Prevalence, Risk Factors, and Interventions. *Nurse and Holistic Care*, 5(2), pp.121–134.

Gonete, K.A., Tariku, A., Wami, S.D., & Derso, T., 2018. Prevalence and Associated Factors of Anemia Among Adolescent Girls Attending High Schools in Dembia District, Northwest Ethiopia, 2017. *Archives of Public Health*, 76, pp.79.

Greenwood, A., von Hurst, P.R., Beck, K.L., Mazahery, H., Lim, K., & Badenhorst, C.E., 2023. Relationship Between Vitamin D, Iron, and Hepcidin in Premenopausal Females, Potentially Confounded by Ethnicity. *European Journal of Nutrition*, 62(8), pp.3361–3368.

H, S.S., Kumar, M., Choudhary, T., Katewa, V., & Sharma, P., 2024. Prevalence of Iron Deficiency Anemia and Iron Deficiency Without Anemia Among Moderate and Severely Acute Malnourished Children. *Cureus*, 16(7), pp.e65633.

Hamed, M., Zaghloul, A., Halawani, S.H., Fatani, B.A., Alshareef, B., Almalki, A., Alsharif, E., ALhothaly, Q.A., Alhadhrami, S., & Abd Elmoneim, H.M., 2024. Prevalence of Overweight/Obesity Associated With Anemia Among Female Medical Students at Umm Al-Qura University in Makkah, Saudi Arabia: A Cross-Sectional Study. *Cureus*, 16(3), pp.e57081.

Handayani, R., Anggraeni, E., Handayani, Y., Sari, M.P., & Yuningsih., 2024. Early Detection of Anemia in Adolescent Girls Through Nutritional Status Examination and Iron Panel Analysis (Tibc, Serum Iron, Iron Saturation). *The Indonesian Journal of Public Health*, 19(2), pp.344–355.

He, Y., & Chen, J., 2024. Severe Iron-Deficiency Anemia After Short-Term Moderate Consumption of Green Tea in Woman: A Rare Case Report. *Heliyon*, 10(17), pp.e36666.

Hounjet, J., Groot, A.J., Piepers, J.P., Kranenburg, O., Zwijnenburg, D.A., Rapino, F.A., Koster, J.B., Kampen, K.R., & Vooijs, M.A., 2023. Iron-Responsive Element of Divalent Metal Transporter 1 (Dmt1) Controls Notch-Mediated Cell Fates. *The FEBS Journal*, 290(24), pp.5811–5834.

Khayati, Y.N., Rahayu, T., Handayani, O.W.K., Widowati, E., & Ningrum, D.N.A., 2025. Maternal Characteristics, Malnutrition, and Pregnancy Complications with the Incidence of Low Birth Weight in an Industrial Environment. *Jurnal Kesehatan Masyarakat*, 21(1), pp.183–191.

Killeen, R.B., Kaur, A., & Afzal, M., 2025. *Acute Anemia*. StatPearls. StatPearls Publishing.

Lane, D.J.R., Bae, D.-H., Merlot, A.M., Sahni, S., & Richardson, D.R., 2015. Duodenal Cytochrome b (DCYTB) in Iron Metabolism: An Update on Function and Regulation. *Nutrients*, 7(4), pp.2274–2296.

Lee, D., Jung, W., & Shin, D.W., 2023. Association of Coffee or Green Tea with Ferritin or

Hemoglobin in Premenopausal Women. *Korean Journal of Family Medicine*, 44(2), pp.87–94.

Li, H., Moosavian, S.P., Ghanbari, N., Mirlohi, S.H., & Rahimlou, M., 2025. Association of Dietary Diversity and Odds of Anemia in Children and Adolescents: A Systematic Review and Meta-Analysis of Observational Studies. *BMC Nutrition*, 11, pp.83.

Li, S., & Huang, Y., 2022. Ferroptosis: An Iron-Dependent Cell Death form Linking Metabolism, Diseases, Immune Cell and Targeted Therapy. *Clinical & Translational Oncology*, 24(1), pp.1–12.

Lu, X., Luo, C., Wu, J., Deng, Y., Mu, X., Zhang, T., Yang, X., Liu, Q., Li, Z., Tang, S., Hu, Y., Du, Q., Xu, J., & Xie, R., 2023. Ion Channels and Transporters Regulate Nutrient Absorption in Health and Disease. *Journal of Cellular and Molecular Medicine*, 27(18), pp.2631–2642.

Ministry of Health of the Republic of Indonesia., 2019. *Minister of Health Regulation Number 28 of 2019 Concerning Recommended Nutritional Adequacy for the Indonesian People*. Database Peraturan| JDIH BPK.

Nababan, T.P., & Nurdin, N.M., 2023. Profil Asupan dan Status Gizi pada Responden yang Memiliki Kebiasaan Menonton Video Mukbang: Intake Profile and Nutritional Status of Respondents Who Have a Habit of Watching Mukbang Videos. *Jurnal Ilmu Gizi dan Dietetik*, 2(2), pp.133–140.

Nahdyah, S., Ahmad, M., Hadju, V., As'ad, S., & Jumrah., 2025. Giving Moringa Soy Milk on Weight Gain and Upper Arm Circumference of Pregnant Women. *Jurnal Kesehatan Masyarakat*, 21(2), pp.434–442.

Nanri, H., Hara, M., Nishida, Y., Shimanoe, C., Iwasaka, C., Higaki, Y., & Tanaka, K., 2023. Association Between Green Tea and Coffee Consumption and Body Iron Storage in Japanese Men and Women: A Cross-Sectional Study from the J-MICC Study Saga. *Frontiers in Nutrition*, 10, 1249702.

Nicotra, D., Arieli, R., Redlich, N., Navot-Mintzer, D., & Constantini, N.W., 2023. Iron Deficiency and Anemia in Male and Female Adolescent Athletes Who Engage in Ball Games. *Journal of Clinical Medicine*, 12(3), pp.970.

Nur, R.I.A., 2008. *Faktor-faktor yang Berhubungan dengan Obesitas Berdasarkan Persen Lemak Tubuh pada Remaja di Smait Nurul Fikri Depok Tahun 2008*. Universitas Indonesia Library; Fakultas Kesehatan Masyarakat Universitas Indonesia.

Pagani, A., Nai, A., Silvestri, L., & Camaschella, C., 2019. Hepcidin and Anemia: A Tight Relationship. *Frontiers in Physiology*, 10.

Piskin, E., Cianciosi, D., Gulec, S., Tomas, M., & Capanoglu, E., 2022. Iron Absorption: Factors, Limitations, and Improvement Methods. *ACS Omega*, 7(24), pp.20441–20456.

Prajapati, M., Zhang, J.Z., Chong, G.S., Chiu, L., Mercadante, C.J., Kowalski, H.L., Antipova, O., Lai, B., Ralle, M., Jackson, B.P., Punshon, T., Guo, S., Aghajan, M., & Bartnikas, T.B., 2024. Manganese Transporter SLC30A10 and Iron Transporters SLC40A1 and SLC11A2 Impact Dietary Manganese Absorption. *BioRxiv*, 2024.

Pratiwi, R., & Sudiarti, T., 2025. Nutritional Status of Children Aged 6-59 Months Based on Composite Index of Anthropometric Failure. *Jurnal Kesehatan Masyarakat*, 21(2), pp.348–359.

Priliani, L., Harahap, A.R., Satyagraha, A.W., Noviyanti, R., Apriyana, I., S.Biotek, I.N., Sudoyo, H., & Malik, S.G., 2025. Mapping Anemia Prevalence Across Indonesia. *Asia Pacific Journal of Clinical Nutrition*, 34(3), pp.430–439.

Putri, F., Suyanto, S., Restila, R., Laksono, A.D., & Sundjaya, T., 2025. Exploring the Role of Nutritional Status and Anthropometric Factors in Anemia Among Adolescent Girls in Pekanbaru, Indonesia. *SAGE Open Medicine*, 13.

Qasrawi, R., Badrasawi, M., Al-Halawa, D.A., Polo, S.V., Khader, R.A., Al-Taweel, H., Alwafa, R.A., Zahdeh, R., Hahn, A., & Schuchardt, J.P., 2024. Identification and Prediction of Association Patterns Between Nutrient Intake and Anemia Using Machine Learning Techniques: Results from a Cross-Sectional Study with University Female Students from Palestine. *European Journal of Nutrition*, 63(5), pp.1635–1649.

Raiten, D.J., Moorthy, D., Hackl, L.S., & Dary, O., 2023. Exploring the Anemia Ecology: A New Approach to an Old Problem. *The Journal of Nutrition*, 153(Suppl 1), pp.S1–S6.

Reski, R.N., Hadju, V., Indriasari, R., & Muis, M., 2020. Anemia, Chronic Energy Deficiency and Their Relationship in Preconception Women. *Enfermería Clínica*, 30, pp.76–80.

Rodak, K., Kokot, I., & Kratz, E.M., 2021. Caffeine as a Factor Influencing the Functioning of the Human Body-Friend or Foe? *Nutrients*, 13(9), pp.3088.

Romero-Cortadellas, L., Hernández, G., Ferrer-Cortès, X., Zalba-Jadraque, L., Fuster, J. L., Bermúdez-Cortés, M., Galera-Miñarro, A.M., Pérez-Montero, S., Tornador, C., & Sánchez, M., 2022. New Cases of Hypochromic Microcytic Anemia Due to Mutations in the SLC11A2 Gene and Functional Characterization of the G75R Mutation. *International Journal of Molecular Sciences*, 23(8), pp.4406.

Samoggia, A., & Riedel, B., 2019. Consumers' Perceptions of Coffee Health Benefits and Motives for Coffee Consumption and Purchasing. *Nutrients*, 11(3), pp.653.

Sari, P., Herawati, D.M.D., Dhamayanti, M., & Hilmanto, D., 2022. Anemia among Adolescent Girls in West Java, Indonesia: Related Factors and Consequences on the Quality of Life. *Nutrients*, 14(18), pp.3777.

Scarano, A., Laddomada, B., Blando, F., De Santis, S., Verna, G., Chieppa, M., & Santino, A., 2023. The Chelating Ability of Plant Polyphenols Can Affect Iron Homeostasis and Gut Microbiota. *Antioxidants*, 12(3), pp.630.

Sishartami, L.W., Ariesaka, K.M., Weningtyas, A., Iftitahurroza, H.T., Wiratama, A.L., & Wibisono, T.A.N., 2025. *Effectiveness of Anemia Counseling and Screening Programs in Improving Health Knowledge of High School Students*, pp.93–99.

Soliman, A., Alaaraj, N., Hamed, N., Alyafei, F., Ahmed, S., Shaat, M., Itani, M., Elalaily, R., & Soliman, N., 2022. Nutritional Interventions During Adolescence and Their Possible Effects. *Acta Bio Medica : Atenei Parmensis*, 93(1), pp.e2022087.

Stubbendorff, A., Borgström Bolmsjö, B., Bejersten, T., Warensjö Lemming, E., Calling, S., & Wolff, M., 2025. Iron Insight: Exploring Dietary Patterns and Iron Deficiency Among Teenage Girls in Sweden. *European Journal of Nutrition*, 64(3), pp.107.

Thachil, J., Owusu-Ofori, S., & Bates, I., 2014. Haematological Diseases in the Tropics. *Manson's Tropical Infectious Diseases*, pp.894-932.e7.

Wallace, D.F., 2016. The Regulation of Iron Absorption and Homeostasis. *The Clinical Biochemist Reviews*, 37(2), pp.51–62.

Wartiningsih, M., Brotosudarmo, T.H.P., Gonaldy, V.A., Juliasih, N.N., Silitonga, H., & Tanzilia, M.F., 2024. Effect of Coffee Drinking Habit to Blood Pressure and Hemoglobin Levels on Women of Childbearing Age. *Journal of Epidemiology and Public Health*, 9(3), pp.276–283.

WHO., 2024. *Guideline on Haemoglobin cut offs to Define Anemia in Individuals and Populations*. WHO.

Wiafe, M.A., Ayenu, J., & Eli-Cophie, D., 2023. A Review of the Risk Factors for Iron Deficiency Anaemia among Adolescents in Developing Countries. *Anemia*, 2023, pp.6406286.

Wulandari, C., Putri, P.H., Mutiarani, A.L., Nuriannisa, F., Hisbullah, F.J., Mabruroh, F.N.L., Lu'luah, J., & Solekha, M., 2025. Anemia in Pregnancy Based on Rural and Urban Areas. *Jurnal Kesehatan Masyarakat*, 21(1), pp.126–135.