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Original article

Anemia-related subjective symptoms in the general adult population in Japan

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Abstract

Objectives: Approximately 17% of Japanese women have hemoglobin concentrations less than 12 g/dL. Therefore, anemia prevention and early intervention are crucial public health issues in Japan. This study aimed to identify the symptoms and characteristics of anemic individuals in the general adult population by comparing survey responses of individuals with anemia and without anemia visiting blood donation centers.

Materials and Methods: This cross-sectional study used self-administered questionnaires. Individuals who visited two Japanese Red Cross Society blood donation centers in Fukushima Prefecture, Japan were included. Hemoglobin levels were measured at blood donation, and the levels of 13 g/dL for men and 12 g/dL for women were defined as anemia.

Results: Of the 857 individuals analyzed, 530 were men and 327 were women, of whom 19 (3.6%) and 12 (3.7%) had low hemoglobin levels, respectively. Logistic regression analysis was performed in men, and the results showed that "lightheadedness" (odds ratio [OR]=8.4) and "depressive symptoms" (OR=3.6) were significantly associated with hemoglobin levels. None of the evaluated items were significantly associated with hemoglobin levels in women.

Conclusion: Among healthy Japanese men, those who exhibit lightheadedness and depressive symptoms have an increased risk of anemia. Lightheadedness and depressive symptoms may be indicative of undiagnosed anemia in men, which necessitates greater clinical attention.

Key words: adult, anemia, epidemiology, depression, hemoglobin levels

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Introduction

According to the World Health Organization (WHO), 40.1% of pregnant women and 32.5% of nonpregnant women worldwide experience anemia[1]. The prevalence of anemia is higher in women than in men in many regions and age groups; moreover, South Asia and Central, West, and East Sub-Saharan Africa have the highest burden[2]. Iron-deficiency anemia is more common in disadvantaged populations, such as low-income individuals[3] and refugees and immigrants from low- and middle-income countries[4]. Despite Japan being a high-income country, individuals living in Japan have lower iron intake and higher rates of anemia than those observed in people living in other countries with similar economic status. The average iron intake of Japanese women aged >20 years is 7.5 mg/day[5], which is lower than that of women living in Australia (9.7 mg/day)[6], Germany (12.3 mg/day)[7], the United Kingdom (9.4 mg/day)[8], the United States (12.3 mg/day)[9], and South Korea (14.7 mg/day)[10]. Accordingly, approximately 17% of Japanese women have a hemoglobin concentration of less than 12 g/dL, which is the WHO criterion for diagnosing anemia in adult women[5, 11]. Therefore, anemia prevention and early intervention are crucial public health issues in Japan.

Iron-deficiency anemia has been associated not only

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with physical symptoms, such as lightheadedness, shortness of breath, headache, lethargy, and fatigue, but also with cognitive impairment[12, 13], loss of concentration[14, 15], and depression[16]. Furthermore, it results in decreased athletic and academic performance among children and young people[14, 15, 17]. The relationship between anemia and depressive symptoms has been reported among various groups, including mothers, older adults, and adults in general[16, 18–20]. Similar studies have been conducted in Japan[20]; however, to our knowledge, the only study conducted in the general public relied on self-reported data on anemia and depression[21]. To reduce mental health comorbidities in Japan, the early detection and treatment of anemia in the general adult population are of utmost importance.

In this study, we conducted a questionnaire survey among visitors to a blood donation center. We aimed to identify the symptoms and characteristics specific to anemia patients in the general adult population by comparing the results of a questionnaire survey conducted between anemic and non-anemic groups.

Methods

Study design and participants

This cross-sectional study used self-administered questionnaires. Candidates for blood donation who visited two Japanese Red Cross Society blood donation centers in Fukushima Prefecture, Japan were included. This study was conducted from February 2021 to November 2021. Questionnaires were administered and filled out on the day of the patient's blood donation, and their hemoglobin levels were routinely measured. Visitors who were able to complete the questionnaire survey were deemed eligible as study participants. Taking iron pills or supplements may reduce symptoms in anemia patients; hence, such individuals were excluded.

The study protocol was reviewed and given ethics approval by the Japanese Red Cross Society Blood Services Headquarters (no. 2020-023) and Koriyama Women's University (no. 2018-012). A document describing the purpose and process of conducting the research was distributed to the participants to inform them that their cooperation was voluntary, and only those who provided consent were included in the survey.

Survey items

Questions on iron intake status and anemia symptoms were included to examine the factors related to anemia. The Revised Self-Administered Iron Intake Scale (RIIS)[22], a two-item screening measure of depressive symptoms[23], a communicative and critical health literacy scale[24], and items related to the presence of anemia symptoms were used to identify factors associated with hemoglobin levels, measured by blood sampling.

The RIIS was used to assess iron intake[22]. This scale was developed based on nutritional intake by food group as reported in the 2013 "National Health and Nutrition Survey", from which "iron-rich" food groups were selected as questionnaire items[22]. This part of our questionnaire comprised 12 items: 11 questions on the respondents' consumption frequency of iron-rich food groups and one question on the amount of iron supplements taken. The 11 questions on food consumption were rated on a five-item scale: 0, 0.5, 1, 2, and 4 points, which corresponded to the frequency of consuming certain food groups. One point in the RIIS is equal to an estimated 0.5 mg of iron intake; therefore, the subtotal of iron intake (mg) from iron-rich foods was estimated by summing the weighed food group scores and multiplying the total score by 0.5. The overall iron intake was calculated by adding the amount of iron intake from supplements (response to the 12th question) to this subtotal. The reliability and validity of the RIIS has been established[22, 25], including its association with a brief self-administered diet history questionnaire[26, 27].

A two-item screening measure[23] was used to assess for depressive symptoms: "During the previous month, have you often felt down, depressed, or hopeless?" and "During the previous month, have you often found little interest or pleasure in doing things?". Participants who answered "yes" to both questions were classified as having depressive symptoms. The health literacy scale comprised three items related to communicative health literacy and two items related to critical health literacy[24]. Responses were rated on a five-point Likert-type scale with scores ranging from 1 ("strongly disagree") to 5 ("strongly agree"). The mean score of the five items was used to indicate overall communicative and critical health literacy. The factors associated with hemoglobin levels from blood sampling included the presence or absence of anemia, presence or absence of anemia symptoms, and burden of menstruation. The questions related to each of these items received reposes of "yes" (1) or a "no" (0).

Our questionnaire included a question related to "skipping meals almost every day". Because Japanese people habitually eat three meals a day—breakfast, lunch, and dinner—a positive response to this question indicated that the respondent regularly missed at least one meal. The questionnaire also asked respondents to rate their agreement with the statement, "I rarely eat homemade food". This item was intended to assess whether the respondent regularly consumed fast food or other processed foods and, therefore, did not have a nutritionally balanced diet.

In addition to the survey, the Hb levels were routinely measured as part of the blood donation process. Based on the WHO's criteria, sex-specific anemia was defined as hemoglobin levels of 13 g/dL or less for men and 12 g/dL or less for women. Those who met the criteria for anemia were

classified as the "light anemia" group, while those who did not meet the criteria were classified as the "normal" group.

Statistical analysis

The χ^2 test and t-test were used to examine the characteristics of the normal and light anemia groups by sex. Multinomial logistic regression analysis was performed using stepwise selection to examine the anemia-associated factors. The odds ratios (ORs) and 95% confidence intervals were also determined. The dependent variable was the presence or absence of anemia. The independent variables were RIIS, a two-item depression scale, a health literacy scale, subjective satisfaction (one item), and anemia symptoms. All analyses were performed using the SPSS software (version 25.0; IBM Corp., Armonk, NY, USA).

Results

We received survey responses from 1,029 participants, 857 of whom were included in the analysis, whereas 172 individuals were excluded, of whom 38 took medical iron preparations, 105 took iron supplements, 17 had no data on hemoglobin levels, and 12 did not indicate their sex. To calculate the subscale scores on the questionnaire, subscales with at least one missing response were regarded as unanswered. Of the 857 respondents, 12 (1.4%) were first-time blood donors, 836 (97.5%) had donated blood before, and 9 (1.1%) had no blood donation experience. The number of participants according to blood donation type was as follows: whole blood donation, 305 (35.6%); component blood donation, 458 (53.4%); no donation, 27 (3.2%); and no response, 67 (7.8%) (Tables 1 and 2).

Descriptive statistics for sex and hemoglobin levels are shown in Tables 1 and 2, respectively. The 857 participants included in the analysis comprised 530 men and 327 women. Among men, 511 had a normal hemoglobin level (>13.0 g/dL) and 19 (3.6%) had a light anemia level; among women, 315 had a normal hemoglobin level (>12.0 g/dL) and 12 (3.7%) had a light anemia level. Among men, the proportion of participants who experienced "lightheadedness" and "depressive symptoms" was significantly higher in the low hemoglobin group than in the high hemoglobin group. Moreover, the low hemoglobin group was significantly older than and had lower mean corpuscular volume levels than those of the high hemoglobin group. Among women, the percentage of participants who responded "diagnosed with anemia in the past" was significantly higher in the low hemoglobin group than in the high hemoglobin group (Table 3).

A logistic regression analysis of each sex was performed to examine the factors associated with hemoglobin levels (Table 3). A stepwise logistic regression analysis was performed in men, and the results showed that "lightheadedness" (OR=8.4) and "depressive symptoms" (OR=3.6) were significantly associated with hemoglobin levels. The results of the stepwise method revealed that none of the evaluated parameters were significantly associated with hemoglobin levels in women.

Discussion

This study aimed to identify the subjective symptoms and characteristics of individuals with anemia and compare them according to sex. Among men, those with lightheadedness and depressive symptoms had a higher risk of anemia than that of men without these complaints. Our finding that anemia was associated with depressive symptoms is similar to those of previous studies[16, 18–21]. For example, previous meta-analyses have reported that anemia is associated with an increased risk of maternal depression[16]. Anemia was also associated with postpartum depression in a cohort study of Japanese individuals[20]. Other than postpartum depression, cross-sectional studies in the general adult population[18] and older adults[19] have also reported an association between depressive symptoms and anemia. Few studies have reported the associated characteristics of anemia in adult men; however, our results imply a relationship between the symptoms of lightheadedness and depression among men and the presence of anemia, although it is not possible to draw conclusions based on causality owing to the cross-sectional nature of our study. Most studies on iron-deficiency anemia have been conducted in pregnant women[1, 16] and athletes[17], with only a few studies conducted in the general male population. A cohort study of 206 men with iron-deficiency anemia reported that gastrointestinal bleeding was the leading cause of iron-deficiency anemia in adult men, emphasizing the importance of gastrointestinal testing[28]. Another study based on online survey responses suggested that iron-deficiency anemia is associated with depression, but the association was assessed using the participants' self-reported data on iron-deficiency anemia and depression; therefore, its reliability may be limited[21]. Further research is required to examine the prevalence of iron-deficiency anemia in men in various countries, including Japan, and to investigate related factors.

Our study revealed no significant associations between other survey items and anemia in men, and no significant associations were found between any survey items and anemia in women. These results may be due to the relatively high mean hemoglobin level of the anemic group in this study and the fact that only a few patients showed symptoms of severe anemia. The prevalence rates of anemia in our study population were 3.6% in men and 3.7% in women, which were extremely low compared with the 32.5% prevalence rate reported in a previous study[1]. Additionally, the mean hemoglobin levels of the light anemic group in this study were 12.3 g/dL in men and 11.7 g/dL in women, value close

Table 1 Number and percentage of patients with light anemia and normal hemoglobin levels by sex (χ^2 test)

	Male (n=530)						Female (n=327)					
	Light anemia* (n=19)		Normal* (n=511)		*P*-value	Phi or Cramer's V	Light anemia* (n=12)		Normal* (n=315)		*P*-value	Phi or Cramer's V
	n	%	n	%			n	%	n	%		
Fatigue												
Yes	5	26.3%	81	15.9%	0.213	0.05	1	8.3%	78	24.8%	0.306	0.07
No	14	73.7%	430	84.1%			11	91.7%	237	75.2%		
Shortness of breath												
Yes	3	15.8%	43	8.4%	0.223	0.05	2	16.7%	56	17.8%	1.000	0.01
No	16	84.2%	468	91.6%			10	83.3%	259	82.2%		
Stiff shoulders or headaches												
Yes	4	21.1%	95	18.6%	0.766	0.01	7	58.3%	161	51.1%	0.771	0.03
No	15	78.9%	416	81.4%			5	41.7%	154	48.9%		
Lightheadedness												
Yes	5	26.3%	19	3.7%	0.001	0.20	2	16.7%	31	9.8%	0.346	0.04
No	14	73.7%	492	96.3%			10	83.3%	284	90.2%		
Facial pallor												
Yes	0	0.0%	3	0.6%	1.000	0.01	0	0.0%	5	1.6%	1.000	0.02
No	19	100.0%	508	99.4%			12	100.0%	310	98.4%		
Chew on ice												
Yes	0	0.0%	8	1.6%	1.000	0.02	0	0.0%	5	1.6%	1.000	0.02
No	19	100.0%	503	98.4%			12	100.0%	310	98.4%		
Dieting experience												
Yes	3	15.8%	97	19.0%	1.000	0.02	7	58.3%	144	45.7%	0.557	0.05
No	16	84.2%	414	81.0%			5	41.7%	171	54.3%		
No awareness of taking iron												
Yes	7	36.8%	164	32.1%	0.627	0.02	5	41.7%	145	46.0%	1.000	0.02
No	12	63.2%	347	67.9%			7	58.3%	170	54.0%		
Skipping meals every day												
Yes	3	15.8%	40	7.8%	0.194	0.05	0	0.0%	32	10.2%	0.616	0.06
No	16	84.2%	471	92.2%			12	100.0%	283	89.8%		
Not eating home-cooked meals												
Yes	3	15.8%	27	5.3%	0.086	0.08	0	0.0%	14	4.4%	1.000	0.04
No	16	84.2%	484	94.7%			12	100.0%	301	95.6%		
Living alone												
Yes	3	15.8%	68	13.3%	0.731	0.01	3	25.0%	58	18.4%	0.474	0.03
No	16	84.2%	443	86.7%			9	75.0%	257	81.6%		
Menstruation interferes with work												
Yes							1	8.3%	21	6.7%	0.573	0.01
No							11	91.7%	294	93.3%		
Heavy menstruation												
Yes							4	33.3%	71	22.5%	0.481	0.05
No							8	66.7%	244	77.5%		
Experience of being diagnosed with anemia												
Yes	3	15.8%	44	8.6%	0.234	0.05	7	58.3%	87	27.7%	0.044	0.13
No	16	84.2%	465	91.4%			5	41.7%	227	72.3%		
Experience of taking iron supplements												
Yes	17	89.5%	480	93.9%	0.334	0.03	7	58.3%	242	76.8%	0.166	0.08
No	2	10.5%	31	6.1%			5	41.7%	73	23.2%		
Subjective health perception												
Very good	4	21.1%	100	19.6%	0.500	0.00	6	50.0%	76	24.1%	0.356	0.12
Good	14	73.7%	370	72.4%			6	50.0%	224	71.1%		
Neither	0	0.0%	23	4.5%			0	0	5	1.5%		
Bad	0	0.0%	17	3.3%			0	0	9	2.8%		
Very bad	1	5.3%	1	0.2%			0	0	1	0.3%		
Depressive symptoms												
Yes	6	33.3%	54	10.7%	0.011	0.13	1	8.3%	49	15.8%	0.700	0.04
No	12	66.7%	451	89.3%			11	91.7%	262	84.2%		

*Male: Normal Hb >13.0 g/dL; Female: Normal Hb >12.0 g/dL.

Table 2 Means and standard deviations in the light anemia and normal groups (t-test)

	Male (n=530)						
	Light anemia* (n=19)			Normal* (n=511)			*P*-value
	n	M	SD	n	M	SD	
Individual characteristics							
Age	19	54.4	11.8	511	46.0	12.8	0.005
Height	19	168.7	5.3	509	170.8	6.0	0.133
Weight	19	67.5	11.5	509	70.3	11.1	0.282
Hemoglobin level	19	12.3	0.5	511	15.0	1.0	0.000
Mean corpuscular volume level	19	81.6	7.1	511	89.0	6.2	0.000
Revised Self-Administered Iron Intake Scale (RIIS)							
Total score	19	5.9	3.1	511	6.0	2.4	0.876
Do you eat staple foods such as bread and rice?	19	2.8	1.3	510	2.9	1.2	0.753
Do you eat brown rice, buckwheat, or spaghetti?	19	0.4	0.5	510	0.4	0.5	0.874
Do you eat dark green vegetables?	19	0.8	0.7	506	1.1	1.0	0.215
Do you eat raw vegetables?	19	0.8	0.9	509	0.8	0.7	0.723
Do you eat stewed vegetables?	18	0.7	1.0	509	0.6	0.6	0.665
Do you eat dried foods?	18	0.4	0.6	510	0.4	0.5	0.812
Do you eat shellfish or bluefish?	19	1.3	1.1	510	1.3	0.9	0.699
Do you eat red meat?	19	1.6	1.3	510	1.5	0.9	0.826
Do you eat liver?	19	0.8	1.1	508	0.6	0.8	0.201
Do you eat bean products?	19	1.2	0.9	511	1.6	1.1	0.156
Do you eat red bean paste, sesame seeds, cocoa or chocolate?	19	0.7	1.0	511	0.7	0.8	0.972
Communicative and critical health literacy							
Communicative health literacy	19	11.0	1.9	509	11.4	2.0	0.448
Critical health literacy	19	6.7	1.3	510	6.8	1.5	0.799

	Female (n=327)						
	Light anemia* (n=12)			Normal* (n=315)			*P*-value
	n	M	SD	n	M	SD	
Individual characteristics							
Age	12	36.2	9.8	315	40.9	13.4	0.229
Height	12	159.1	4.8	315	159.2	4.8	0.927
Weight	12	58.8	8.1	314	59.2	8.7	0.884
Hemoglobin level	12	11.7	0.3	315	13.4	0.8	0.000
Mean corpuscular volume level	12	86.0	7.0	315	89.9	4.7	0.081
Revised Self-Administered Iron Intake Scale (RIIS)							
Total score	12	6.4	2.9	315	6.4	2.5	0.913
Do you eat staple foods such as bread and rice?	12	2.8	1.1	314	2.7	1.2	0.790
Do you eat brown rice, buckwheat, or spaghetti?	11	0.8	1.2	314	0.4	0.6	0.405
Do you eat dark green vegetables?	12	1.0	0.7	313	1.3	1.1	0.333
Do you eat raw vegetables?	12	1.2	0.8	315	0.8	0.8	0.157
Do you eat stewed vegetables?	11	1.0	1.1	312	0.8	0.8	0.437
Do you eat dried foods?	12	0.3	0.3	313	0.4	0.5	0.364
Do you eat shellfish or bluefish?	12	1.1	1.0	315	1.4	1.1	0.326
Do you eat red meat?	12	1.9	1.4	315	1.8	1.0	0.750
Do you eat liver?	12	0.4	0.6	314	0.4	0.7	0.920
Do you eat bean products?	12	2.0	1.1	314	1.8	1.1	0.727
Do you eat red bean paste, sesame seeds, cocoa or chocolate?	12	0.8	1.1	313	0.9	0.9	0.675
Communicative and critical health literacy							
Communicative health literacy	12	12.6	1.3	315	11.5	1.9	0.062
Critical health literacy	12	7.7	1.0	315	7.0	1.3	0.086

*Male: Normal Hb >13.0 g/dL; Female: Normal Hb >12.0 g/dL. M: mean; SD: standard deviation.

Table 3 Logistic regression analysis with the hemoglobin value as a dependent variable (stepwise method)

	OR	OR 95% CI		*P*-value
		Lower	Upper	
Male (Cox-Snell R^2=0.03, Nagelkerke R^2=0.13)				
Lightheadedness	8.4	2.5	28.1	0.001
Depressive symptoms	3.6	1.2	10.9	0.027

OR: odds ratio; CI: confidence interval.

to the lower limit of normal group. As blood donors, the participants in this study were healthier than average. Severely anemic or unhealthy individuals were excluded from donating blood. Most participants donated blood multiple times, and those taking iron pills or supplements were excluded from the analysis. The strength of this study was the use of hemoglobin levels based on blood collection results as a method for assessing anemia in blood donors. Blood sampling is the most reliable method for assessing anemia. However, this study has several limitations. The first limitation was selection bias. The study population comprised visitors from two blood donation centers in Fukushima, Japan. The vast majority (97.5%) of participants had donated blood two or more times, suggesting a relatively high level of interest and awareness about anemia and other health-related issues. Hence, further surveys targeting a wider range of populations including different regions and age groups are warranted. Second, we were unable to adequately adjust for confounding factors associated with anemia, especially disease and health factors. As the study participants were blood donors, they did not include pregnant women or those on medication, and only a few were considered severely ill. Third, because this was a cross-sectional study, caution should be observed when inferring causal relationships between anemia and related factors. These limitations suggest that the results of this study should be interpreted with caution. The mean age of the male participants was 54.4 years, while that of the female participants was 46.0 years, indicating a significant age difference of 8.4 years. As age increases, the likelihood of having certain diseases or receiving treatments also increases, which raises the possibility that depressive symptoms and lightheadedness may not be directly caused by anemia but rather by the effects of these underlying conditions or treatments. However, candidates for blood donation possibly include those without severe medical conditions and not under medical treatment.

Conclusion

Among healthy Japanese men, those who exhibit lightheadedness and depressive symptoms have an increased risk of having anemia. Although further studies are needed, the results suggest that complaints of lightheadedness and depressive symptoms may be indicative of undiagnosed anemia in men, necessitating greater clinical attention.

Conflict of interest: There are no conflicts of interest.

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Ethics approval and consent to participate: The study was reviewed and approved by the Japanese Red Cross Society Blood Services Headquarters (no. 2020-023) and Koriyama Women's University (no. 2018-012). A document describing the purpose and implementation of the research was distributed to the participants to inform them that their cooperation was based on free will, and only those who provided consent were included in the survey.

Consent for publication: Not applicable

Data availability statement: The datasets generated and/or analyzed during the current study are available from the corresponding author upon reasonable request.

Author contributions: Shinya Ito: conceptualization, methodology, formal analysis, writing–original draft preparation, and acquisition of financial support for the project leading to this publication. Satoko Okabe: conceptualization and methodology. Niro Ujiie: supervision and project administration. Mina Watanabe: investigation, resources, and data curation. Norihiko Watanabe: investigation, resources, and data curation. Kenji Ishida: investigation, resources, and data curation. Aya Goto: methodology, writing, review and editing, and supervision.

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