

## Improved Prevalence of Anemia and Nutritional Status among Japanese Elderly Participants in the National Health and Nutritional Survey Japan, 2003-2009

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### Abstract

**Objectives:** This study aimed 1) to examine the trends in the prevalence of anemia of the Japanese elderly population and 2) to evaluate the association between hemoglobin concentrations and diet and lifestyle factors, by using data from a population-based, nationwide cross-sectional survey in Japan, from 2003-2009.

**Design:** A cross-sectional nationally representative survey.

**Setting:** Japan.

**Participants:** A nationally representative sample of 10,606 community dwelling men (n=4656) and women (n=5950) aged 65 years and over.

**Measurements:** Information on anthropometry, dietary intake status, information on current medication, lifestyle habits, and blood biomarker measurements were obtained from the participants. Anemia was defined as hemoglobin concentrations <130 g/L in men and <120 g/L in women. Logistic regression analysis adjusted for subject age was applied to estimate the effect of survey year to anemia prevalence. Multiple regression analysis was applied to estimate the effect of survey year and clinical, dietary and lifestyle factors to hemoglobin values.

**Results:** Anemia prevalence was 19.3% in men and 21.7% in women. When adjusted for age, the prevalence of anemia significantly decreased by each survey year in both men (odds ratio: 0.933, 95% confidence interval: 0.899, 0.968,  $p < 0.001$ ) and women (odds ratio: 0.968, 95% confidence interval: 0.939, 0.999,  $p = 0.040$ ). The multivariate model explained 25% and 22% of the variance in hemoglobin values in men and women, respectively. In both men and women, each unit of increase in BMI, daily smoking, serum ferritin and albumin was positively associated to hemoglobin values, and age was negatively associated. After adjusting for all factors, hemoglobin values were estimated to increase 0.66 g/L per year in men, and 0.68 g/L per year in women.

**Conclusion:** Nutritional status of the Japanese elderly as observed by anemia prevalence and hemoglobin concentrations has improved in recent years.

**Keywords:** Elderly; Anemia; Hemoglobin; Medication

### Introduction

The elderly population, defined as individuals aged  $\geq 65$  years, is rapidly increasing worldwide in numbers and proportions [1]. In Japan, which is one of the most rapidly ageing societies in the world, the proportion is estimated to increase from 22.8% in 2010 to 38.8% in 2050 [2]. The Japanese also enjoy longevity compared to other countries, with life expectancy of 19.08 years in men and 23.97 years in women at 65 years (<http://www.mhlw.go.jp/toukei/saikin/hw/life/life13/index.html>). It is an urgent public health issue to maintain health in later life, without disabilities or serious morbidities. Japan may serve as an ideal model of an ageing society, for other countries facing the same trend in the future.

Anemia is a common health problem in elderly populations and the prevalence of anemia is reported to increase with advancing age [3]. In the United States (US), anemia prevalence increases with advancing age after 50 years and rises to more than 20% at age  $\geq 85$  years [4,5]. In the community dwelling elderly Japanese population, the prevalence of anemia was reported to increase with age [6]. However, this study was not conducted in a nationally representative sample and limited the highest age category to  $\leq 80$  years. A previous study using the data on adult women in the National Health and Nutrition Survey of Japan (NHNS) from 1989-2003, showed that anemia was prevalent (25.3%-26.2%) among women aged 70 years and older [7]. Recently, studies have indicated anemia as one of the factors responsible for health decline among the elderly, such as increased risk in all-cause mortality [8-11], decline in cognitive function, dementia [12] and increased fracture risk [13].

In addition, anemia is not simply a natural consequence of the aging process. Anemia in the elderly may be the result of underlying chronic conditions and nutritional deficiencies of key nutrients, such as iron, folate, and vitamin B<sub>12</sub>. Nearly one-thirds of elderly anemia cases are due to nutrient deficiencies, according to the US National Health and Nutrition Survey [4]. Very few studies have examined the anemia risk and nutrient intake in the elderly population, and these results are inconsistent. Meng et al. [14] examined anemia prevalence and nutrient intakes in Chinese elderly women, but did not describe the association between anemia prevalence and protein, iron, or vitamin C intake; while Thomson et al. [15] showed that low intake of protein, iron, vitamin B<sub>12</sub>, folate or vitamin C were associated with greater risk of anemia in post-menopausal women. In order to promote a balanced diet in the elderly to prevent anemia, we need to identify dietary and life-style factors that are related to anemia risk. In the previous Japanese study [6], hemoglobin concentrations were reported to be higher in younger cohorts. The changes in diet and lifestyle may have a profound effect on the nutritional status of the Japanese elderly, and this should be examined in nationally representative samples, such as the NHNS.

The NHNS is an annual nationwide survey that covers approximately 5000 households in about 300 randomly selected census units defined by the Ministry of Health, Labor, and Welfare. It provides the largest available nationally representative sample with which to monitor dietary intakes, lifestyle factors, and selected biological indicators of Japanese people, including anthropometric measurements. The NHNS consists of three survey components, which are the household based dietary intake survey, the physical examination survey, and the lifestyle questionnaire survey on adults [16].

This study aimed 1) to examine the trends in the prevalence of anemia of the Japanese elderly population and 2) to evaluate the association between hemoglobin concentrations and diet and lifestyle factors, by using data from a population-based, nationwide cross-sectional survey in Japan.

## Methods

### Data source

We used the dataset from 2003-2009 NHNS, which were conducted by the Ministry of Health, Labor and Welfare, Japan. The present study was approved by the Ministry of Health, Labor and Welfare, Japan.

### Subjects

A total of 70,037 individuals aged  $\geq 1$  year participated in the NHNS from 2003 to 2009, and among these, 17,589 subjects aged  $\geq 65$  were selected for analyses. As in the United Nations Report [1], we also chose 65 years as the cutoff in the present study. We excluded subjects who lacked height and weight measurements (n=2742), had not participated in the dietary survey (n=599), and lacked blood hemoglobin, blood ferritin and blood albumin data (n=3529) or had not participated in the lifestyle questionnaire survey related to smoking history, alcohol drinking and current exercise habits (n=112). The data from the remaining 10,606 subjects were selected for analyses in the present study.

### Dietary assessment

A semi-weighed one-day household-based dietary record, with the approximate proportions by which family members shared each dish, was used to estimate nutrient and food intake. [16] The nutrient intake for each family member was estimated according to the Standard Tables of Food Composition in Japan, Fifth Revised and Enlarged Edition [17]. Energy and macronutrient intake estimated using this method highly correlated to the intake estimated using individualized diet records (Pearson's correlation coefficients;  $r=0.89-0.91$ ) [18]. Further details regarding the methods used can be found elsewhere [19]. In the present study, intakes of energy, total protein, fat, carbohydrates, sodium, potassium, calcium, iron, vitamin B<sub>12</sub>, folate, vitamin C, energy intake from cereals, and percent energy intake from cereals and 11 food groups (cereals, potatoes and starches, pulses, vegetables, fruits, fish and shellfish, meat, eggs, milk and milk products, fats, and beverages) were calculated.

### Physical examinations and lifestyle characteristics

The subjects underwent measurements for height, body weight, and abdominal circumference in the physical examination survey. Body mass index (BMI) (kg/m<sup>2</sup>) was calculated as body weight (kg) divided by the square of body height (m). Subjects also participated in the steps measurement using a standardized AS-200 pedometer (Yamasa Tokei Keiki Co., Tokyo) for a single day. Subjects also reported their current medication status regarding treatment of non-communicable disease. Current use of antihypertensives, antilipids, antiarrhythmics and antidiabetics/insulin was assessed throughout the survey period, and use of iron supplements was assessed only in 2008 and 2009. Current exercise habits were also assessed, and exercisers were defined as those reporting "exercising regularly for >30 min at a time, for >2 days/week, and for more than a year."

Through the lifestyle questionnaire, subjects reported their smoking history. Current smokers were those smoked daily. Frequency of current drinking was also assessed. The subjects chose either "never," "1-3 day(s)/month," "1-2 day(s)/week," "3-4 day/week," "5-6 day/week," or "daily" and current drinkers were categorized as those reporting daily drinking.

### Blood sampling

Venous blood was drawn into the vacuum blood collection tube that contained EDTA and was drawn at least 4 h after the last meal, at the physical examination survey. Blood was allowed to clot at room temperature and centrifuged at 1,500 g for 10 min. Serum samples were divided into separate tubes and stored at -4C until delivered to the SRL. Inc. Blood hemoglobin was determined by the sodium lauryl sulfate (SLS)-hemoglobin method, and red blood cell count and hematocrit were determined by the sheath flow direct current (DC) detection method. Serum total protein was determined by the Biuret method, serum albumin by bromocresol purple method, and blood ferritin by chemiluminescent enzyme immunoassay. All analyses were performed by the SRL. Inc., (153 Komiya-cho, Hachioji, Tokyo, 192-0031 Japan).

### Definitions of anemia

In this study, anemia was defined according to the WHO definition as hemoglobin concentrations <130 g/L in men and <120 g/L in women [20].

### Statistical analysis

All analyses were separately performed for men and women. Results are expressed as means ± SD or medians for continuous variables, and proportions (%) for categorical variables. To assess the normality of the distribution of continuous variables, the Kolmogorov-Smirnov test was applied. For normally distributed variables such as blood hemoglobin and blood albumin concentrations, the student's t-test was applied to compare the results between anemic and non-anemic subjects. Blood ferritin concentration, energy, nutrients, and food intakes were skewed; therefore, the Mann-Whitney U test was used to examine these variables. Chi-square tests were applied to compare categorical variables between anemic and non-anemic subjects.

For continuous variables, the univariate regression analysis was applied, and for categorical variables, the logistic regression analysis was applied to examine the effect of survey year. Logistic regression analysis adjusted for subject age was applied to estimate the effect of survey year to anemia prevalence. The general linear regression analysis was applied to estimate the effect of survey year, clinical, dietary and lifestyle factors to hemoglobin values. Each selected variable was separately included in the general linear regression model (univariate model). In the next step, all variables were included in the model (multivariate model). The estimated changes in hemoglobin values for each unit of variable (estimate) and their standard errors, 95% confidence interval of estimate (lower and upper limits), standardized partial regression coefficients, t values, and generalized coefficients of determination statistics (R<sup>2</sup>) were calculated. An R<sup>2</sup> for the multivariate model was shown separately for men and women.

For all analyses, two-tailed P values <0.05 were considered to indicate statistical significance. The SPSS software version 19.0 for

Windows (SPSS Inc., Chicago, IL, USA) was used to perform all analyses.

### Results

Physical characteristics, intake of energy and selected nutrients (/d), Intake of selected food groups (g/d), and blood biomarker values are summarized for men (Supplementary -Table 1) and women (Supplementary -Table 2). In both men and women, mean age (p<0.01) and height (p<0.05) of the subjects increased significantly over time. Mean body weight, waist circumference, and BMI significantly increased in men (all p<0.01), but mean BMI significantly decreased in women (p<0.05). Mean number of steps per day was also significantly decreased only in women (p<0.01). The trend in intake of energy, nutrients, and food groups differed between men and women. Changes in energy, protein, and calcium intakes were not significant in men, but decreased in women (all p<0.01). Intakes of sodium, iron, vitamin B<sub>12</sub>, energy from cereals significantly decreased in both men and women (both p<0.01). Intakes of cereals significantly decreased (p<0.01) and intakes of vegetables and meat increased (both p<0.05) in both men and women. In women, intakes of fish/shellfish and milk/milk products significantly decreased (p<0.01), and intakes of beverages significantly increased (p<0.05). The trend for blood biomarker values was similar between men and women. Red cell count, hematocrit values, hemoglobin values, serum ferritin values significantly increased (all p<0.01), and serum total protein and albumin values decreased (both p<0.01).

Proportion of selected health status, blood biomarker status, medication and lifestyle habits of elderly men and women are summarized according to survey year in Table 1.

N	Men									P trend for	Women								
	2003	4	5	6	7	8	9	Total	2003		4	5	6	7	8	9	Total	P for trend	
	722	559	632	654	624	803	662	4656	980		690	799	822	774	961	924	5950		
Age groups																			
65-69 years	34.8	32.7	32.3	30.7	30.4	31.6	33.2	32.3	0.339	35.4	34.8	35.0	31.8	29.7	30.0	30.5	32.4	<0.001	
70-74 years	32	31.1	33.5	30.7	31.3	29.4	28.4	30.9	0.073	27.8	29.9	26.8	27.5	28.8	28.2	26.6	27.9	0.611	
75-79 years	18.3	22.2	21.0	22.9	21.3	21.5	21.9	21.3	0.196	19.6	21.0	20.9	24.7	23.3	22.6	22.7	22.1	0.042	
80-84 years	10.1	10.4	9.2	11.8	11.4	13.4	10.7	11.1	0.09	10.8	9.9	11.9	9.9	11.2	12.8	12.9	11.4	0.046	
85 years+	4.8	3.6	4.0	3.8	5.6	4.0	5.7	4.5	0.305	6.4	4.5	5.4	6.2	7.1	6.5	7.3	6.2	0.1	
Overweight (BMI>24.9)	24.8	29.7	29.3	28.7	33.3	28.4	29.8	29.0	0.054	31.4	29.7	30.2	28.7	29.1	27.7	26.6	29.0	0.33	
Underweight (BMI<18.5)	8.2	6.3	3.8	5.4	4.5	3.7	3.6	5.0	<0.01	6.4	7.5	6.1	5.2	7.1	7.5	8.3	6.9	0.2	
Anemia (hemoglobin <130 g/L for men, <120 g/L for women)	23.8	18.4	19.6	20.3	17.9	17.8	17.1	19.3	0.03	25.8	20.0	17.3	23.6	19.4	23.4	20.7	21.7	<0.01	
Low serum albumin (<3.5 mg/L)	0.6	0.9	0.5	0.6	0.5	1.1	0.3	0.6	0.51	0.3	0.4	0.1	0.2	0.5	0.2	0.1	0.3	0.65	
Low serum ferritin (<12 µg/L)	3.9	3.2	3.5	4.1	3.8	5.0	3.0	3.8	0.55	6.6	7.2	4.4	6.4	5.4	6.9	7.7	6.4	0.11	

Currently using antihypertensives	39.9	40.8	43.7	40.2	42.3	46.2	46.1	42.9	0.058	41.4	44.6	42.1	42.8	46.8	47.6	49.4	45.0	<0.01
Currently using antilipids	14.0	11.8	10.8	9.5	13.8	12.1	15.2	12.5	0.026	21.0	21.4	23.8	22.3	22.9	24.8	26.3	23.3	0.094
Currently using antiarrhythmics	11.1	9.1	10.3	9.0	9.1	7.3	9.2	9.3	0.3	5.5	7.7	7.1	8.3	7.9	7.0	8.1	7.3	0.29
Currently using antidiabetics/insulin	9.7	10.6	10.5	9.9	12.7	10.6	12.3	10.9	0.52	5.9	6.0	7.0	8.0	7.1	8.0	7.8	7.2	0.39
Currently using iron supplements	-	-	-	-	-	1.5	1.8	-	0.63	-	-	-	-	-	1.5	2.1	-	0.32
Daily drinking	36.3	37.0	35.6	34.1	35.6	36.0	35.5	35.7	0.97	2.4	4.1	4.5	3.8	3.6	2.7	3.0	3.4	0.18
Daily smoking	64.4	64.4	62.2	48.6	52.6	61.1	57.6	58.8	<0.01	4.9	8.8	5.3	4.1	5.8	6.5	6.5	5.9	<0.01
Currently exercising	39.2	47.4	41.5	43.7	42.6	42.2	45.6	43	0.073	29.9	34.3	37.0	37.2	34.4	37.4	35.8	35.1	<0.01

**Table 1:** Proportion (%) of selected health status, blood biomarker status, medication and lifestyle habits of elderly men and women, 2003-2009, – unavailable.

The distribution of age groups did not change over time among men, but among women, the proportion of 65-69 years significantly decreased ( $p<0.01$ ) and the proportion of both 75-79 and 80-84 years significantly increased ( $p<0.01$ ). The proportion of underweight men significantly decreased ( $p<0.01$ ), but not in women. The proportion of anemic subjects significantly decreased in both men and women ( $p<0.01$ ). The proportion of men using anti-lipids increased, and women using antihypertensive increased (both  $p<0.05$ ). The proportion of subjects smoking daily significantly decreased in men ( $p<0.01$ ), but significantly increased in women ( $p<0.01$ ). The proportion of women who were currently exercising significantly increased ( $p<0.01$ ).

The characteristics of the anemic and non-anemic subjects are summarized in Table 2. Anemic subjects were significantly older, shorter, lighter, and had lower BMI compared to non-anemic subjects, among both men and women (all  $p<0.01$ ). In men, anemic subjects had significantly lower intakes of energy and nutrients (all  $p<0.01$ ) except vitamin C, however, percent energy intake from cereals was significantly higher ( $p<0.01$ ). In women, anemic subjects had

significantly lower intakes of energy and nutrients (all  $p<0.01$ ), and their percent energy intake from cereals was also significantly higher ( $p<0.01$ ). Regarding intakes of food groups, anemic men had significantly lower intakes of cereals, pulses, vegetables, fish/shellfish, meat, fats, and beverages (all  $p<0.05$ ) compared to non-anemic men. In women, anemic subjects had significantly lower intakes of vegetables, fruits, fish /shellfish, meat, milk/milk products, fats, and beverages (all  $p<0.01$ ) compared to non-anemic subjects. All of the blood biomarker values were significantly lower in anemic subjects (all  $p<0.01$ ) compared to non-anemic subjects, among both men and women. The proportion of anemic men who were currently using anti-arrhythmics or anti-diabetics/insulin was significantly higher (both  $p<0.01$ ) than non-anemic men, and the proportions of current daily drinking, daily smoking, and exercising were significantly lower (all  $p<0.05$ ). The proportion of anemic women who were currently using anti-hypertensives or anti-arrhythmics was significantly higher (both  $p<0.01$ ) than non-anemic women, and the proportions of current daily drinking, daily smoking, and exercising were significantly lower (all  $p<0.05$ ).

Physical characteristics	Men				P value	Women				P value
	Anemic (n=900)		Non-anemic (n=3756)			Anemic (n=1289)		Non-anemic (n=4661)		
	Mean ± SD	Median	Mean ± SD	Median		Mean ± SD	Median	Mean ± SD	Median	
Age, years	76.0 ± 6.6	75	72.5 ± 5.5	72	<0.001	76.1 ± 6.8	76	72.8 ± 5.9	72	<0.001
Height*, cm	159.7 ± 6.4	160.1	161.7 ± 6.3	161.8	<0.001	146.2 ± 6.5	146.5	148.4 ± 5.9	148.5	<0.001
Weight*, cm	56.1 ± 8.8	55.5	62.3 ± 9.2	62	<0.001	47.9 ± 8.3	47	52 ± 8.3	51.3	<0.001
Abdominal circumference*, cm	81.8 ± 8.6	82	86.9 ± 8.2	87	<0.001	82.2 ± 10.3	82	85.7 ± 10.1	86	<0.001
BMI*	21.9 ± 3	21.9	23.8 ± 3	23.7	<0.001	22.4 ± 3.4	22.1	23.6 ± 3.5	23.3	<0.001
Number of steps/(d)	5333 ± 3981	4578	6128 ± 4069	5366	<0.001	4257 ± 3333	3509	5252 ± 3594	4631	<0.001
Intake of energy and selected nutrients/(d)										

Total energy, kcal	1980 ± 543	1924	2109 ± 552	2061	<0.001	1649 ± 438	1602	1718 ± 448	1687	<0.001
Total protein, g	72.7 ± 24.3	70.2	78.3 ± 24.6	76	<0.001	62.7 ± 21.2	60	66.9 ± 21.4	65.1	<0.001
Fat, g	45.7±21.3	42.8	49.8 ± 21.9	47.1	<0.001	39.8 ± 18.5	36.8	43.7 ± 19	41.5	<0.001
Carbohydrates, g	299 ± 89	289	306 ± 89	297	<0.001	255 ± 74	245	259 ± 72	252	<0.001
Sodium, mg	4766 ± 1917	4488	4912 ± 1960	4621	0.033	4234 ± 1711	4003	4337 ± 1730	4084	0.043
Potassium, mg	2669 ± 1032	2550	2794 ± 1003	2691	<0.001	2430 ± 930	2309	2621 ± 999	2507	<0.001
Calcium, mg	574 ± 299	513	603 ± 291	555	0.001	547 ± 300	499	591 ± 294	545	<0.001
Iron, mg	9.0 ± 3.4	8.6	9.4 ± 3.6	8.9	0.002	8.4 ± 5.4	7.7	8.7 ± 3.4	8.2	<0.001
Vitamin B <sub>12</sub> , µg	8.3 ± 8.5	5.8	9.3 ± 10.1	6.4	0.004	6.6 ± 6.3	4.6	7.5 ± 7.5	5.3	<0.001
Folate, µg	373 ± 180	346	387 ± 183	359	0.014	345 ± 150	316	364 ± 159	343	<0.001
Vitamin C, mg	146.0 ± 143.5	115.7	152.2 ± 151.1	120.9	0.134	156.3 ± 208	117.6	171.2 ± 215.2	127.3	<0.001
Energy intake from cereals, kcal	876 ± 306	830	907 ± 320	865	0.003	699 ± 236	678	695 ± 231	672	<0.001
Percent energy intake from cereals, %	45.2 ± 12.7	44.6	43.7 ± 12.1	43	<0.001	43.3 ± 12.3	42.5	41.4 ± 11.7	40.6	<0.001
Intake of selected food groups, g/d										
Cereals	507.2 ± 188.8	479	524.8 ± 192.7	500.0	0.003	405 ± 146	390.0	398.9 ± 136.2	389.3	0.3
Potatoes and starches	75.1 ± 91.0	50.0	67.1 ± 79.6	46.7	0.149	66.3 ± 80.8	45.0	66.5 ± 79.7	45.0	0.957
Pulses	71.7 ± 82.8	50.0	76.1 ± 80.9	52.6	0.031	64.9 ± 70	48.0	70.7 ± 76.9	50.0	0.068
Vegetables	323.2 ± 192.2	289.0	341 ± 191	315.7	0.002	305.2 ± 175.8	274.3	325.1 ± 177.5	299.9	<0.001
Fruits	156.5 ± 159.8	120.0	162.4 ± 161.5	130.0	0.191	156.8 ± 154.2	130.0	180.9 ± 160.7	153.0	<0.001
Fish and shellfish	101.5 ± 86.8	85.0	112.5 ± 87.4	100.0	<0.001	83.1 ± 67	75.0	91.5 ± 71.8	81.3	<0.001
Meat	51.7 ± 56.3	40.0	61.3 ± 60.5	50.0	<0.001	41.2 ± 45.2	30.0	48 ± 49.8	38.4	<0.001
Eggs	34.8 ± 34.4	32.5	34.5 ± 33.4	34.0	0.869	30.8 ± 30.4	28.5	30.6 ± 31	25.5	0.766
Milk and milk products	104.4 ± 141.4	18.3	110.1 ± 134.8	41.2	0.068	103.7 ± 127.7	40.0	115.9 ± 131.7	84.0	0.001
Fats	7.5 ± 8.7	5.0	8 ± 8.9	5.7	0.03	6.2 ± 7.4	4.0	6.8 ± 7.5	4.8	0.002
Beverages	684.8 ± 524.4	600.0	780.8 ± 515.2	710	<0.001	593.8 ± 443.3	519.0	621.8 ± 421.5	577.0	0.003
Blood biomarkers										
Red cell count*, 10 <sup>4</sup> /mm <sup>3</sup>	388 ± 41	390.0	462 ± 37	460	<0.001	375 ± 33	376	434 ± 31	431	<0.001
Hemoglobin*, g/L	119 ± 11	122.0	146 ± 10	145	<0.001	112 ± 8	114	13.2 ± 8	132	<0.001
Hematocrit*, %	38 ± 3.3	38.6	45.5 ± 3.2	45.3	<0.001	36.2 ± 2.6	36.5	42.1 ± 2.7	41.8	<0.001
Serum total protein, mg/L	7.3 ± 0.5	7.3	7.4 ± 0.5	7.4	<0.001	7.3 ± 0.5	7.3	7.5 ± 0.4	7.4	<0.001
Serum albumin, mg/L	4.2 ± 0.3	4.2	4.4 ± 0.3	4.4	<0.001	4.2 ± 0.3	4.2	4.4 ± 0.3	4.4	<0.001
Serum ferritin, µg/L	93.3 ± 152.9	56.0	124.9 ± 127.3	96.0	<0.001	62.6 ± 115.5	39.0	74.8 ± 61	61.0	<0.001
Medication and lifestyle habits (%)										
Currently using antihypertensives	45.3		42.3		0.097	48.5		44		0.004

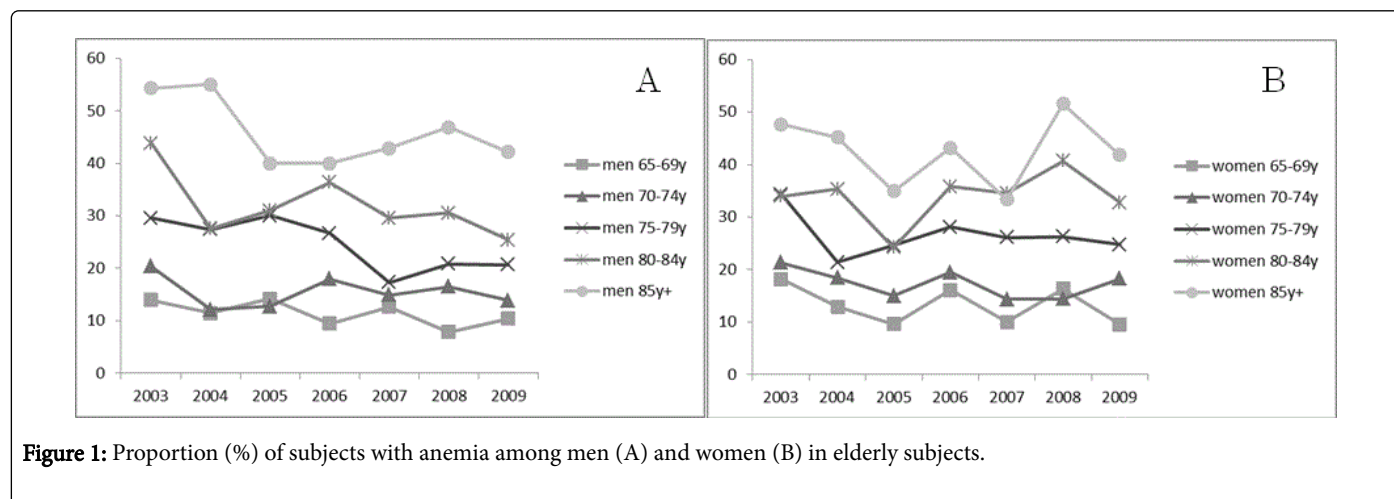


Currently antilipids using	12.7		12.4		0.823	21.7		23.7		0.119
Currently antiarrhythmics using	13.1		8.4		<0.001	9.1		6.8		0.006
Currently antidiabetics/insulin using	13.3		10.3		0.008	7.5		7		0.549
Daily drinking	24.4		38.4		<0.001	2.5		3.6		0.044
Daily smoking	55.1		59.6		0.013	4.6		6.3		0.021
Currently exercising	38.4		44.1		0.002	29		36.8		<0.001

**Table 2:** General characteristics of anemic and non-anemic elderly in the National Health and Nutrition survey, Current exercisers were defined as those reporting “exercising regularly for >30 min at a time, for >2 days/week, and for more than a year.” \* T-tests for other continuous variables, Mann-Whitney’s U-tests were applied, and for categorical variables, chi-square tests were applied.

The proportion of anemic subjects according to five-year age groups and survey year are shown in Figure 1 (A: men, B: women). According to the logistic regression analysis grouped by sex and five-year age groups, the odds ratio for anemia significantly decreased by each survey year in 75-79 years aged men (odds ratio: 0.904, 95%

confidence interval: 0.840, 0.972, p=0.007), but not in other sex and age groups. When adjusted for age, the odds ratio for anemia significantly decreased by each survey year in both men (odds ratio: 0.933, 95% confidence interval: 0.899, 0.968, p<0.001) and women (odds ratio: 0.968, 95% confidence interval: 0.939, 0.999, p=0.040).



**Figure 1:** Proportion (%) of subjects with anemia among men (A) and women (B) in elderly subjects.

Table 3 shows the association between hemoglobin values and factors selected from results on Table 2, by using the univariate regression analysis. Since most of the dietary factors were influenced

by the differences in energy intake between anemic and non-anemic subjects, percent energy from cereals was selected as the sole dietary factor.

Factors	Men							Women						
	Estimate	Standard error of estimate	95% CI of estimate	Standardized partial regression coefficient	t value	R <sup>2</sup>	p value	Estimate	Standard error of estimate	95% CI of estimate	Standardized partial regression coefficient	t value	R <sup>2</sup>	p value
Survey year (per year)	0.38	0.11	0.17, 0.59	0.052	3.54	0	<0.01	0.32	0.073	0.18, 0.47	0.056	4.36	0.003	<0.01
Age (per year)	-0.7	0.036	-0.77, -0.63	-0.276	-19.58	0	<0.01	-0.44	0.024	-0.49, -0.40	-0.235	-18.61	0.055	<0.01
BMI	0.13	0.068	1.19, 1.45	0.276	19.57	0	<0.01	0.76	0.042	0.67, 0.84	0.225	17.83	0.051	<0.01

Percent energy intake from cereals (per 10%)	-0.91	0.18	-0.13, -0.06	-0.074	-5.06	0	<0.01	-0.94	0.013	-0.12, -0.07	-0.09	-7.31	0.009	<0.01
Serum ferritin (per 10 µg/L)	0.17	0.016	0.14, 0.20	0.15	10.33	0	<0.001	0.21	0.002	0.17, 0.25	0.14	10.53	0.018	<0.001
Serum albumin (per mg/L)	18.97	0.72	17.56, 20.37	0.36	26.5	0	<0.001	15.43	0.53	14.38, 16.47	0.35	28.93	0.123	<0.001
Currently using anti-hypertensives	-0.99	0.44	-1.86, -0.12	-0.033	-2.23	0	0.026	0.31	0.31	-0.29, 0.91	0.013	1.01	0.0002	0.314
Currently using anti-arrhythmics	-3.36	0.75	-4.84, -1.88	-0.065	-4.45	0	<0.001	-1.52	0.59	-2.67, -0.37	-0.034	-2.59	0.001	0.01
Currently using anti-diabetics/insulin (yes=1, no=0)	-2.02	0.7	-3.40, -0.64	-0.042	-2.87	0	0.004	-0.17	0.59	-1.33, 1.00	-0.004	-0.28	1.00E-05	0.779
Daily drinking (yes=1, no=0)	4.39	0.45	3.50, 5.28	0.141	9.7	0	<0.001	1.03	0.85	-0.63, 2.69	0.016	1.22	0.0002	0.224
Daily smoking (yes=1, no=0)	1.09	0.44	0.22, 1.96	0.036	2.45	0	0.014	1.09	0.44	0.22, 1.96	0.036	3.31	0.001	0.014
Currently exercising (yes=1, no=0)	1.41	0.44	0.54, 2.27	0.047	3.18	0	0.001	1.6	0.32	0.98, 2.23	0.065	5.02	<0.01	<0.001

**Table 3:** Estimation of hemoglobin values in elderly men and women, by univariate regression analysis.

All of the selected factors were significantly associated to hemoglobin values in men (all  $p < 0.05$ ). In women, current use of anti-hypertensives, anti-diabetics/insulin, and daily drinking habits were not significantly associated to hemoglobin values. The multivariate model (Table 4), explained 25% and 22% of the variance in hemoglobin values in men and women, respectively. In both men and women, each unit of increase in BMI, daily smoking, serum ferritin and albumin was positively associated to hemoglobin values, and age was negatively associated. In men, daily drinking was positively associated to hemoglobin values, and current use of anti-hypertensives and anti-diabetics/insulin were negatively associated. In women, current exercising was positively associated to hemoglobin values, and percent energy intake from cereals was negatively associated. After adjusting for all factors, hemoglobin values were estimated to increase 0.66 g/L per year in men, and 0.68 g/L per year in women.

## Discussion

To our knowledge, this study is the first nationally representative cross-sectional study to evaluate the trends in nutritional status of community-dwelling elderly people [6,7,11]. In the current study, similar prevalence of anemia was observed in men (19.3%) and women (21.7%) compared to other developed countries. From the data on

NHANES III, the prevalence of anemia in American elderly population aged  $\geq 65$  years was 11.0% in men and 10.2% in women [4]. In Europe, the prevalence of anemia was 15.2% in men and 13.6% in women ( $\geq 65$  years) in Italy [21] and 23.4% in men and 19.3% in women ( $\geq 65$  years) in Austria. [22] For Korean elderly population with median age of 70 years, the prevalence of anemia was 13.6%. [23] These previous reports [4,5,21-23] have not investigated the effect of nutrient intakes, although these differences may be influenced by dietary factors such as dietary iron intake and/or intake of iron supplements. In fact, iron intakes in the current study were much lower compared with those in the US [15]. We could not examine the effect of iron supplement use to hemoglobin values, because it was not assessed in 2003-2007. But we speculate that the influence of iron supplement use is negligible, given the low proportion of users in 2008 and 2009 (Table 1). Furthermore, better iron nutrition in Europe and the US has been largely attributed to increased dietary iron via fortified foods [24,25]. Also in the US, hemoglobin values in men and women have increased after the implementation of mandatory folic acid fortification policy [26]. However, Japan does not practice a food fortification policy, so the recent improvement in hemoglobin status in elderly Japanese may be due to the improvement of better dietary habits, such as observed by the yearly increase in intakes of vegetable and meat (Supplementary Tables 1 and 2).

Factors	Men							Women						
	Estimate	Standard error of estimate	95% CI of estimate	Standardized partial regression coefficient	t value	R <sup>2</sup>	p value	Estimate	Standard error of estimate	95% CI of estimate	Standardized partial regression coefficient	t value	R <sup>2</sup>	p value
Intercept	65.2	4.9	55.60, 74.80	-	13.315	0.251	<0.001	65.11	3.43	58.39, 71.84	-	18.974	0.221	<0.001

Survey year (per year)	0.66	0.1	0.47, 0.85	0.09	6.926	-	<0.001	0.68	0.07	0.55, 0.81	0.119	10.19	-	<0.001
Age (per year)	-0.33	0.03	-0.40, -0.26	-0.131	-9.567	-	<0.001	-0.25	0.02	-0.29, -0.20	-0.131	-10.607	-	<0.001
BMI	1.05	0.06	0.93, 1.18	0.22	16.58	-	<0.001	0.68	0.04	0.60, 0.76	0.202	16.944	-	<0.001
Percent energy intake from cereals (per 10%)	-0.01	0.02	-0.04, 0.02	-0.011	-0.8	-	0.424	-0.07	0.01	-0.09, -0.04	-0.065	-5.614	-	<0.001
Serum ferritin (per 10 µg/L)	0.1	0.01	0.0008, 0.0013	0.093	7.187	-	<0.001	0.002	0.0002	0.0012, 0.0019	0.098	8.449	-	<0.001
Serum albumin (per mg/L)	16.1	0.71	14.71, 17.49	0.307	22.731	-	<0.001	14.31	0.53	13.27, 15.35	0.326	27.021	-	<0.001
Currently using anti-hypertensives (yes=1, no=0)	-2.15	0.4	-2.93, -1.36	-0.071	-5.357	-	<0.001	-0.52	0.29	-1.10, 0.05	-0.022	-1.802	-	0.072
Currently using antiarrhythmics (yes=1, no=0)	-0.88	0.67	-2.19, 0.43	-0.017	-1.317	-	0.188	-0.36	0.53	-1.40, 0.68	-0.008	-0.685	-	0.493
Currently using antidiabetics/insulin (yes=1, no=0)	-2.52	0.62	-3.73, -1.31	-0.052	-4.084	-	<0.001	-0.81	0.53	-1.86, 0.23	-0.018	-1.528	-	0.127
Daily drinking (yes=1, no=0)	3.54	0.41	2.73, 4.36	0.114	8.559	-	<0.001	0.4	0.76	-1.09, 1.88	0.006	0.523	-	0.601
Daily smoking (yes=1, no=0)	1.05	0.39	0.28, 1.81	0.035	2.686	-	0.007	2.26	0.58	1.13, 3.39	0.045	3.918	-	<0.001
Currently exercising (yes=1, no=0)	0.41	0.39	-0.35, 1.18	0.014	1.064	-	0.287	0.72	0.29	0.15, 1.28	0.029	2.487	-	0.013

**Table 4:** Estimation of hemoglobin values in elderly men and women, by multivariate regression analysis<sup>†</sup>, <sup>†</sup>All factors were forced into the model.

The strength of this study was our large population-based sample size. However, there were several limitations as well. First, nutrient and food intake data may not be representative of habitual dietary intake because they do not reveal day-to-day variations that would normally occur. Because the dietary survey was conducted on a single day, we could not examine the causal effects of individual food intakes to nutritional status. The only dietary factor applied was the percentage of energy from cereals (Table 4). As shown in Supplementary Tables 1 and 2, consumption of cereals (which is mainly rice in Japan), has been declining over time. But, mean percentage of energy from cereals was higher in anemic subjects compared to non-anemic subjects (Table 2). In other words, the higher the percentage of energy from cereals, the subjects are taking lower amount of foods that are rich in protein and fat, such as fish or meat. However, the negative effect of higher percentage of energy from cereals to hemoglobin value was observed only in women. Although the mean percentage of energy from cereals was higher in men (44.0 ± 12.2%) compared to women (41.8 ± 11.8%), the higher intake of fish and meat in men compared to women may have accounted to better iron status, as observed in the higher serum ferritin values in men (Supplementary Tables 1 and 2).

The results from the current study showed that current medication and life-style factors had different effects on hemoglobin values, in men and women. In men, current use of anti-hypertensives and anti-

diabetics/insulin were negatively related to hemoglobin values. This was also consistent with previous reports [27,28]. Some types of anti-hypertensives cause hemodilution, hemolytic anemia, or suppress red cell production [27]. Long term metformin treatment for diabetes suppresses absorption of vitamin B<sub>12</sub>, and may lead to anemia [28]. The reason why these relations were not observed in women is not clear, in spite of higher proportion of women taking anti-hypertensives. Detailed information on the types of medication was unavailable in the NHNS, so we could not examine whether this difference was due to gender, or due to differences in the types used in men and women. Both daily drinking and smoking were related to higher hemoglobin values in men. This was consistent with a previous study that examined the effect of smoking and drinking to hemoglobin values in adults [29]. In women, only positive relation with smoking was observed, probably due to the low proportion of daily drinkers. Current exercise habits were positively related to hemoglobin values only in women. Perhaps women who are able to keep exercising are already in good health, which is reflected in their higher hemoglobin values.

The current study demonstrated that hemoglobin values have improved over time in both men and women, after adjusting for selected factors. The background for this improvement could not be fully investigated through our present data. But we would like to note



that the national action plan for health, the "Health Japan 21" project [30] which started in 2000, may have had an impact on health of elderly Japanese. In this project, the government set goals to increase the proportion of elderly who are physically active, i.e., those with exercise habits. This health policy may have contributed to improving general health in the elderly, resulting in increase in subjects with exercise habits and decrease in anemia (Table 1), reversing previous trends [7]. Further monitoring of the health status of community dwelling elderly should be conducted, in order to investigate the effect of national health policies.

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