Original Article

Dietary patterns and anemia morphology in young men and women in Shandong province, China

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Background and Objectives: The association between diet and macrocytic and hypochromic anemia in young Chinese men and women remains unclear. The present study aimed to investigate the relationship between dietary pattern and macrocytic and hypochromic microcytic anemia in young Chinese men and women. **Methods and Study Design:** Some 4,840 first-year students (2,385 men and 2,455 women) were recruited for this study from Qingdao University, China. Biochemical and hematological parameters, and food frequency questionnaires were obtained from the subjects. Based on dietary intake, participants were divided into three dietary patterns: seafood dietary pattern (SDP), vegan dietary pattern (VDP) and omnivorous dietary pattern (ODP). The risks for macrocytic and microcytic hypochromic anemia in three dietary patterns were assessed. **Results:** Macrocytic and hypochromic anemia were less common in participants who adhered to the omnivorous dietary pattern than to the vegan or seafood dietary patterns ($p<0.05$). Adhering to an omnivorous dietary pattern was negatively associated with macrocytic anemia in men [odds ratio (95% CI): 0.74 (0.62, 0.89), $p<0.001$] and microcytic, hypochromic anemia in both genders [men: odds ratio (95% CI): 0.64 (0.45, 0.92), $p=0.01$; women: odds ratio (95% CI): 0.71 (0.51, 0.99), $p=0.04$]. **Conclusions:** Adhering to an omnivorous dietary pattern was associated with less common macrocytic anemia in young men and microcytic, hypochromic anemia. Dietary diversity is important in preventing macrocytic anemia in men and also microcytic, hypochromic anemia in young men and women. Excessive alcohol intake is the most plausible explanation for macrocytosis in the young men.

Key Words: dietary pattern, anemia, nutrition, alcohol, menstruation

INTRODUCTION

Anemia is a global public health problem which affects one-quarter of the world's population.[1] According to a recent study on the burden of anemia, nearly two billion people (27% of the global population) were affected by anemia in 2013. While prevalence has decreased,[2] the total number of people with anemia has increased over with population size. Anemia is more prevalent in developing countries.[3] In China, anemia is common in adolescents, and one of the 'four major diseases' in children along with pneumonia, diarrhea, and rickets. Anemia may be prevalent among young adults in China.[4]

The causes of anemia are multifactorial. It is estimated that half of global anemia prevalence is attributable to iron deficiency, although not necessarily due to inadequate intake given the contribution of menstrual blood loss in women and wide prevalence of hookworm and ascariasis. Causes of anemia not related to iron intake or bioavailability include parasitic diseases and infections such as malaria,[5] hookworm,[6] schistosomiasis,[7] nutrient deficiencies including folic acid, vitamin C, and vitamin B-12,[8] trace elements,[9,10] and genetic hemoglobinopathies such as sickle cell disease and thalassemia. Anemia is categorized as microcytic anemia, macrocytic anemia and hypochromic anemia by red cell morphology. Iron deficiency is the most common cause of microcytic and hypochromic anemia, while macrocytic anemia could be the result of vitamin B-12 deficiency. As dietary factors appear to be a major cause of iron and other deficiencies that lead to the development of anemia,[11] a more integral approach to how diet and anemia are associated may be a health advantage. Public health nutrition which focusses on individual nutrient intakes may overlook relevant bioactive dietary components and their interplay which alters bioavailability. Dietary patterns matter for short-term and

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chronic health outcomes.[12] Even with anemias other than those attributable principally to nutrient deficiency, optimization of dietary pattern may ameliorate the disorder.[13]In this event, public nutrition education may contribute to reduced anemia severity while capturing a spectrum of nutrient deficiency-based anemias.

The benefits of seafood consumption in the prevention of many diseases have been shown in several studies. Seafood is an excellent source of protein, vitamins such as fat soluble vitamins A and D, selenium, and n-3 long chain polyunsaturated fatty acids (n-3 PUFA).[14,15] The dietary intake of n-3 PUFA is associated with a reduced risk of cardiovascular disease,[16] including sudden cardiovascular death.[17] The consumption of one to two servings of oily fish on a weekly basis may reduce the risk of all-cause mortality, asthma, impaired cognitive function, diabetes, inflammatory conditions, and some cancers.[18] However, whether seafood intake is associated with anemia seems unknown.

The risk of anemia in young Chinese adults may be associated with dietary pattern. In the present study, we hypothesized that dietary pattern contributes to the risk and type of anemia as judged by red cell morphology in the setting of the food cultures prevailing in the northeastern coastal province of Shandong, China. The province has the lower reaches of the Yellow River and is the birthplace of Confucius. The Shandong diet is dominated by seafood, grains, and meat. Three habitual dietary patterns are considered in the present investigation: seafood, vegan and omnivorous.

METHODS

Study participants

A total of 7,800 first-year students (3,707 men and 4,093 women) were recruited from the Qingdao University, China. We documented basic sociodemographic information, undertook anthropometry and collected blood samples from each participant. They completed a one-month recall food frequency questionnaire, disease history, and provided a list of any long-term prescription drug use. We excluded participants with an invalid questionnaire, missing covariates, or implausible energy intakes (<600 or >3,500 kcal/day for women and <800 or >4,200 kcal/day for men),[19] and women participants who were menstruating on the day of study (n=626). The remaining 4,840 participants (2,385 men and 2,455 women) had a mean age of 18.3 years (SD: 0.9) and 18.1 years (SD: 0.7), respectively. All participants gave written, informed consent before entering the study, which was approved by the Ethics Committee of Qingdao Disease Control and Prevention Center (No. 15006395).

Blood specimen collections

Subjects attended the Campus Hospital of Qingdao University in the morning following an overnight fast. Subjects sat relaxed for 10 min and blood pressure was measured, and then venous blood was taken in plain and EDTA vacuum tubes with 21-gauge needles. After blood collection, weight, height, waist and hip circumferences were measured.

Laboratory measurements

The biochemical parameters were analyzed on HITACHI 7020 chemistry analyzer using enzyme-based colorimetric test or colorimetric test supplied by Diasys Diagnostic Systems (Shanghai) Co., Ltd. Body mass index (BMI) was calculated as weight in kilograms divided by the square of height in meters (kg/m^2). Anemia was categorized as recommended by WHO: hemoglobin <120 g/L for women aged over 15 years and <130 g/L for men.[20] Microcytosis was defined as a mean corpuscular volume (MCV) <80 fL, hypochromia as mean corpuscular hemoglobin (MCH) <26 pg with mean corpuscular hemoglobin concentration <320 g/L. Macrocytosis was defined as a mean corpuscular volume (MCV) >100 fL and mean corpuscular hemoglobin (MCH) >32 pg.[21,22] Full blood examination was performed by using an automated hematologic blood counting system (Coulter Counter STKR; Coulter Electronics Inc, Hialeah, FL).

Dietary assessment and dietary patterns

For dietary intake assessment, a diet-history questionnaire was conducted on the day blood was collected to gather information regarding food intake over the previous month. The questionnaire contains 135 food and beverage items and 12 response categories ranging from “less than once/month” to “≥3 times/day”.

Using the dietary data, we classified the food into 10 food groups based on nutrient and culinary similarities within the larger categories: vegetables, fruits, meats (including poultry, livestock meat and unprocessed meat suck as liver), grains, nuts, sweets and desserts, fish and seafood, egg, milk, and legumes. Then, we classified the 10 food groups into plant food group, animal food group and seafood group (Table 1).

The average daily intake of each food was calculated, and the total amount of each food group was calculated by adding the average daily intake of all the foods in that group. Then, we created three dietary patterns: seafood dietary pattern (SDP), vegan dietary pattern (VDP), and omnivorous dietary pattern (ODP). To create the SDP, we screened participants who ate seafood groups and plant food groups with no or low meat intake (<40 g/d) into this pattern. For the VDP, participants who had plant food intake with no or low seafood and meat intake (<40 g/d) were recruited into this pattern. To create the ODP, we screened participants who ate all food groups.

Dietary diversity score (DDS) is the most commonly used tool for evaluating dietary diversity, and DDS is more effective in terms of casting nutritional adequacy. Dietary diversity score (DDS) was measured according to the Guidelines for Measuring Household and Individual Dietary Diversity provided by the Food and Agriculture Organization of the United Nations.[23] The DDS was calculated as the number of food groups that participants consumed without consideration of a minimum quantity requirement for any food group.[24] Any individual food item in each food group consumed by a participant earned one point towards their dietary diversity score, but different individual food items consumed in the same group were not recounted. Therefore, DDS ranged from 0 to 10, and a higher DDS reflected a higher dietary diversity status.

Table 1. Examples of food items constituting the 10 food groups

Food groups	Food
Plant food groups	
Fruits	Apple, banana, orange, grape, grapefruit, kiwi fruit, pear, watermelon, strawberry, cherry, mango, jackfruit, pawpaw, litchi, longan, hami melon, winter jujube
Vegetables	Green vegetables: Chinese cabbage, spinach, pak choi, oilseed rape Melon vegetables: cucumber, jiao melon, wax gourd, eggplant, tomato Root vegetables: potato, Chinese yam, taro, asparagus lettuce, onion
Nuts	Peanut, melon seeds, pine nut, pistachio nuts, cashew nut, hickory, Juglans, almond
Grains	Steamed bun, rice, noodles, steamed stuffed bun, dumplings, bread
Legumes	Tofu, thin sheets of bean curd, dried bean curd, uncongealed beancurd, soybean milk, green soybean
Sweets and desserts	Tea, coffee Carbonated beverages, non-carbonated sugar beverages, lactobacillus beverage, milk tea, fruit juice Puffed food, dried fruit, cakes, walnut cake, cookies, biscuits, sugar, chocolate French fries, potato chips
Animal food groups	
Milk	Milk
Egg	Egg
Meats	Chicken, pork, beef, lamb, duck, goose
Seafood groups	
Fish and seafood	Carp, crucian, grass carp, snakehead, Qingjiang fish, eel, weever, sea eel, hairtail, Spanish mackerel, yellow croaker, silvery pomfret, sardine, gadus, flatfish Crayfish, river prawn, maetapenaeus ensis, prawn, tiger prawn, pandalus, mantis shrimp Scallop, oyster, clam, sea snail, razor clam Sleeve-fish, octopus, sepia, cuttlefish Sea crab, river crab

Variable assessment

BMI was categorized as per WHO definitions: underweight: BMI <18.5; normal weight: 18.5-23.9; overweight: 24.0-27.9; obese: BMI ≥28.0.[25] Based on dietary guidelines for China (2016), we identified "low intake" as no more than 40 g per day.[26] Hypertension was defined as having a history of hypertension, use of a hypertension drug, systolic pressure ≥140 mmHg, or diastolic pressure ≥90 mmHg. Dyslipidemia was defined as elevated serum concentration of cholesterol (hypercholesterolemia: TC ≥6.22 mmol/L for age ≥18, TC ≥5.18 mmol/L for age <18), LDL-C (hyperLDL-C: ≥4.14 mmol/L for age ≥18, ≥3.37 mmol/L for age <18), TG (hypertriglyceridemia: TG ≥2.26 mmol/L for age ≥18, TG ≥1.47 mmol/L for age <18), or lower HDL-C (hypoHDL-C: <1.04 mmol/L for age ≥18, <0.91 mmol/L for age <18).[27] Abdominal obesity was defined as a waist–hip ratio >0.8 for women and >0.9 for men.[28]

Statistical analysis

Statistical analysis was performed using SPSS software version 25.0. Continuous and categorical variables are presented as mean ± standard deviation (SD) and number (percentage), respectively. Pearson's Chi-square tests were used to determine statistical associations between the different risks in the three dietary patterns, and the Kruskal-Wallis test was used to compare continuous variables. A linear regression analysis was performed to examine the association between food intake with biomarkers of interest, and logistic regression was used to examine the association between dietary patterns with the risk of macrocytic anemia, hypochromic anemia and to explore the variance in macrocytic anemia, hypochromic anemia explained by dietary patterns, adjusted for potential confounders (age, gender, energy intake, blood pressure, BMI status, residence and food intake). A p-value <0.05 was considered statistically significant.

RESULTS

A total of 4,840 (2,385 men and 2,455 women) first-year students of Qingdao University were included in the final analysis, age was 18.2±0.8 and BMI was 21.5±3.4. There were 816 participants (283 men and 533 women) who had low concentrations of hemoglobin. Some 93 participants (22 male and 71 female) had microcytic hypochromic anemia and 187 had macrocytic anemia (108 male and 79 female). Additionally, 271 were obese, 512 participants exhibited abdominal obesity, 127 had hypertension, 362 had hyperlipidemia, and 6 had hyperuricemia (Table 2).

Participants adhering to an ODP were more likely to be taller, overweight, and to have higher dietary diversity scores, while participants adhering to VDP were leaner and had lower dietary diversity scores. Female participants were more likely to adhere to VDP (Table 3). The differences in anemia risk between the three dietary patterns were statistically significant. Compared with VDP and SDP, participants who adhered to ODP were more likely to have a lower risk of anemia and a higher level of erythrocytes (RBC), hemoglobin (HGB), hematocrit (HCT) and other anemic biomarkers (Table 4).

Male participants adhering to an ODP had a lower prevalence of microcytic hypochromic anemia [odds ratio (95% CI): 0.64 (0.45, 0.92), adjusted r^2=0.10, p=0.01] and macrocytic anemia [odds ratio (95% CI): 0.74 (0.62, 0.89), adjusted r^2=0.07, p<0.001]. Female participants in ODP group also had hypochromic anemia less often [odds ratio (95% CI): 0.71 (0.51, 0.99), adjusted r^2=0.11 p=0.04] (Table 5).

The association between food intake and biomarkers is shown in Table 6. Higher intake of meat was associated

Table 2. Characteristics of the study participants (n=4840)

Variable	Males (n=2385)	Females (n=2455)	*p* value†
Age, mean±SD	18.3±0.9	18.1±0.7	0.23
Height, m	1.75±5.91	1.63±5.51	<0.001
Weight, kg	67.8±12.3	55.3±8.7	<0.001
Body mass index, kg/m^2, mean±SD	22.2±3.8	20.8±3.1	<0.001
Waistline, cm, mean±SD	77.1±10.9	69.5±7.6	<0.001
Hipline, cm, mean±SD	94.9±8.2	93.4±6.3	0.15
WHR (waist–hip ratio), mean±SD	0.8±0.1	0.7±0.1	<0.001
Systolic pressure, mmHg, mean±SD	118±11.4	107±10.7	<0.001
Diastolic pressure, mmHg, mean±SD	72.3±8.0	70.6±7.5	<0.001
Residence			<0.001
Urban, %	42.6	54.1	
Village, %	57.4	46.0	
Anemia type			
Macrocytic anemia, %	4.53	3.21	0.018
Hypochromic anemia, %	0.92	2.89	<0.001
Disease			
Hypertension, %‡	4.32	0.98	<0.001
Hyperlipemia, %	10.8	4.28	<0.001
Obesity, %	8.81	2.48	<0.001
Abdominal obesity, %	5.24	15.8	<0.001

†*p* values were analyzed using Mann-Whitney U test for continuous variables and chi-square test for categorical variables, and *p* values were for differences between men and women.
‡Hypertension: having a history of hypertension, use of hypertension drug, systolic pressure ≥140 mmHg or diastolic pressure ≥90 mmHg.

Table 3. Characteristics of participants in SDP, VDP, and ODP

Variable	Dietary patterns		
	ODP (N=4309)	SDP (N=418)	VDP (N=113)
Age, mean±SD	18.2±0.9	18.3±0.8	18.1±0.8
Height, m	1.68±8.24	1.65±7.13 ^{os*}	1.64±6.58 $^{ov*, vs*}$
Weight, kg	61.0±12.3	58.0±10.4 ^{os*}	56.0±8.7 $^{ov*, vs*}$
Body mass index, kg/m^2, mean±SD	21.7±3.3	21.0±3.0 ^{os*}	20.6±2.2 $^{ov*, vs**}$
Waistline, cm, mean±SD	72.8±9.8	71.2±9.2 ^{os*}	70.0±7.4 $^{ov*, vs*}$
Hipline, cm, mean±SD	94.2±7.4	93.9±6.5	92.0±6.1 $^{ov*, vs**}$
WHR (waist–hip ratio), mean±SD	0.77±0.06	0.76±0.06 ^{os*}	0.76±0.06 ^{ov*}
Dietary diversity scores (DDS), mean±SD	9.60±0.60	8.00±1.33 ^{os*}	5.48±1.10 $^{ov*, vs*}$
Gender			
Female, %	55.6	65.3 ^{os*}	76.1 $^{ov*, vs**}$
Male, %	44.4	34.7 ^{os*}	23.9 $^{ov*, vs**}$
Residence			
Urban, %	42.5	49.0 ^{os**}	31.9 $^{ov**, vs**}$
Village, %	57.5	51.0 ^{os**}	68.1 $^{ov**, vs**}$
Anemia type			
Macrocytic anemia, %	3.30	7.18 ^{os**}	13.27 $^{ov**, vs**}$
Microcytic hypochromic anemia, %	1.32	6.22 ^{os**}	8.85 $^{ov**, vs**}$
Disease			
Hypertension, %	2.78	1.67	0
Hyperlipemia, %	6.89	7.66	5.31
Hyperuricemia, %	0.07	0.02	0
Obesity, %	5.36	2.63 ^{os*}	0 ^{ov**}
Abdominal obesity, %	11.2	6.22 ^{os*}	3.54 $^{ov*, vs*}$

ODP: omnivorous dietary pattern; SDP: seafood dietary pattern; VDP: vegan dietary pattern.
* p<0.001; ** p<0.05.
^{os} ODP versus SDP; ^{ov} ODP versus VDP; ^{vs} VDP versus SDP.

with a higher level of anemia-related biomarkers (such as. RBC, HGB, HCT, MCH and MCHC). Furthermore, the intake of fruit and seafood was associated with an increased level of RBC (fruits: β=0.05, p<0.001; seafood: β=0.04, p=0.001), HGB (fruits: β=0.19, p<0.001; seafood: β=0.14, p<0.001), HCT (fruits: β=0.50, p<0.001; seafood: β=0.36, p<0.001) and MCHC (fruits: β=0.70, p<0.001; seafood: β=0.60, p=0.001). Intake of vegetables was associated with an increased MCH level (β=0.07, p=0.047), and intake of grains was associated with an increased level of RBC (β=0.10, p<0.001), HGB (β=0.34, p<0.001), HCT (β=0.91, p<0.001), MCH (β=0.10, p=0.003) and HCHC (β=0.11, p<0.001).

DISCUSSION

The aim of the present study was to explore the relation-

Table 4. Knowledge of coeliac disease and gluten free food preparation amongst chefs/cooks and culinary students

	ODP (N=4309)	SDP (N=418)	VDP (N=113)	High dietary diversity (N=2135)
AST/ALT	1.35±0.47	1.41±0.47 os**	1.45±0.51 ov*, vs*	1.32±0.47 hs*, hv*
GLU (mmol/L)	3.98±0.50	3.96±0.39 os*	3.94±0.43 vs*	3.97±0.47 hv*
TG (mmol/L)	0.75±0.27	0.74±0.26 os*	0.71±0.24 ov**	0.76±0.29 hv*
CHOL (mmol/L)	3.75±0.68	3.73±0.64 os**	3.57±0.58	3.75±0.69 hv*
HDL-C (mmol/L)	1.45±0.30	1.46±0.28 os*	1.47±0.30 ov*, vs*	1.44±0.31 hs*, hv*
LDL-C (mmol/L)	1.92±0.59	1.90±0.54	1.74±0.49 vs**	1.93±0.60 hs**, hv*
CREA (μmol/L)	66.6±13.7	62.8±12.2 os*	61.2±11.1 ov*,vs*	67.8±13.8 hs*, hv*
UA (μmol/L)	346±92.0	332±89.3 os*	332±83.7 ov*, vs*	350±91.7 hs*, hv*
WBC (×10^9/L)	6.27±1.51	6.25±1.54	6.13±1.54	6.29±1.51 hv*
RBC (×10^12/L)	4.46±0.61	4.32±0.60 os*	4.22±0.68 ov*, vs*	4.52±0.61 hs*, hv*
HGB (g/dL)	13.3±1.9	12.7±1.9 os*	12.4±2.3 ov*, vs*	13.5±1.9 hs*, hv*
HCT (%)	41.9±5.5	40.5±5.5 os*	39.4±6.3 ov*, vs*	42.5±5.5 ho*. hs*, hv*
MCV (fL)	93.8±5.7	93.8±5.7	93.6±7.6	94.1±4.9
MCH (pg)	29.8±2.0	29.5±2.5 os*	29.4±3.2 vs**	29.8±2.0 hv**
MCHC (g/L)	316±10.7	314±12.6 os*	313±14.9 ov*, vs*	316±10.3 hs*, hv*

ODP: omnivorous dietary pattern; SDP: seafood dietary pattern; VDP: vegan dietary pattern; High dietary diversity: DDS=10.
AST/ALT: Aspartate aminotransferase/Alanine aminotransferase; GLU: glucose; TG: triglycerides; CHOL: total cholesterol; HDL: high-density lipoprotein; LDL: low-density lipoprotein; CREA: creatinine; UA: uric acid; WBC: leukocyte; RBC: erythrocyte; HGB: hemoglobin; HCT: red blood cell specific volume; MCV: mean red blood cell volume; MCH: mean corpuscular hemoglobin; MCHC: mean corpuscular hemoglobin concentration.
* $p<0.001$; ** $p<0.05$.
os ODP versus SDP; ov ODP versus VDP; vs VDP versus SDP; ho High dietary diversity versus ODP; hs High dietary diversity versus SDP; hv High dietary diversity versus VDP.

Table 5. Odds ratios (95% CI) and adjusted r2 for microcytic hypochromic anemia and macrocytic anemia according to dietary patterns

	Microcytic hypochromic anemia			Macrocytic anemia		
	OR (95% CI)	r^2	*p* value	OR (95% CI)	r^2	*p* value
Males						
ODP	0.64 (0.45, 0.92)	0.10	0.01	0.74 (0.62, 0.89)	0.07	<0.001
SDP	0.83 (0.58, 1.18)	0.04	0.26	0.89 (0.67, 1.20)	0.02	0.43
VDP	1.15 (0.84, 1.57)	0.07	0.25	1.07 (0.88, 1.31)	0.06	0.55
Females						
ODP	0.71 (0.51, 0.99)	0.11	0.04	0.88 (0.72, 1.05)	0.09	0.27
SDP	0.82 (0.57, 1.15)	0.04	0.70	0.84 (0.61, 1.13)	0.05	0.98
VDP	1.31 (1.06, 1.61)	0.08	0.01	1.12 (0.90, 1.38)	0.07	0.32

ODP: omnivorous dietary pattern; SDP: seafood dietary pattern; VDP: vegan dietary pattern.
Adjusted for age, gender, energy intake, blood pressure, BMI status, residence and food intake.

ship between dietary patterns and their association with red blood cell morphology in relation to anemia among young Chinese in Qingdao. Overall, 17% (men 6%; women 11%) were anemic. Hypochromic, microcytic anemia was found among 2% (men 1%; women 3%) of newly enrolled university students. It was least common for those who followed an ODP compared with those who ate a seafood vegetarian type diet. Multiple linear regression (MLR) revealed that each of ODP, SDP and VDP accounted for 10%, 4%, and 7% overall of the variance in anemia prevalence, respectively, in this population. The corollary is that around 80% of the variance was not attributable to dietary pattern as measured. Since the prevalence of anemia was greatest in young women, the population benefit of a preferred dietary pattern will be greatest for them. But, as other public health and clinical evidence shows, the most likely contributor to anemia in young women is likely to be menstrual health.[27] Findings in Tianjin indicate that hypertension and body composition are modulators of menstruation in young Chinese women.[29]

In previous studies, only a few have researched how seafood intake affects the risk of anemia, and the overall association between diet and anemia risk has also been poorly studied. Inadequate fish and meat consumption was associated with a lower prevalence of anemia in Japanese elderly males.[30] Also, high intake of fish was reported to be a factor in gout and other chronic diseases.[31] The present study showed that participants who adhered to a SDP had a lower risk of anemia compared with the VDP. And we found seafood intake was positively associated with the levels of RBC, HGB, HCT and MCHC. The reason could be related to the omega-3 fatty acids. Omega-3 fatty acids supplementation can be considered as a safe and effective treatment for sickle cell anemia and higher LC-PUFA status was associated with decreased risk of iron depletion.[32,33]

Meat intake was associated with an increased level of anti-anemic biomarkers in our findings, which may be due to the high level of heme iron. Heme iron is found in meat, poultry, and other animal sources. Heme iron is more easily absorbed by enterocytes than non-heme iron

Table 6. Linear association of different food intakes with BMI, WHR, blood pressure, and anemic biomarkers

	BMI		WHR		Systolic pressure		Diastolic pressure		RBC	
	β (95% CI)	*p* value	β (95% CI)	*p* value	β (95% CI)	*p* value	β (95% CI)	*p* value	β (95% CI)	*p* value
Vegetables	-0.02 (-0.34, 0.19)	0.57	0.001 (-0.004, 0.003)	0.75	-0.23 (-0.68, 0.22)	0.31	-0.07 (-0.36, 0.21)	0.61	0.01 (-0.01, 0.03)	0.31
Fruits	-0.02 (-0.19, 0.06)	0.30	-0.007 (-0.01, -0.004)	<0.001	-0.67 (-1.12,-0.22)	0.004	0.22 (-0.07, 0.58)	0.13	0.05 (0.03, 0.07)	<0.001
Grains	0.04 (0.02, 0.06)	0.004	0.011 (0.009, 0.013)	<0.001	2.03 (1.61, 2.45)	<0.001	0.31 (0.05. 0.58)	0.02	0.10 (0.08, 0.12)	<0.001
Nuts	-0.03 (-0.24, 0.00)	0.05	0.001 (-0.002, 0.003)	0.62	0.12 (-0.33, 0.56)	0.61	-0.10 (-0.38, 0.18)	0.50	-0.01 (-0.03, 0.014)	0.46
Meats	-0.01 (-0.34, 0.25)	0.77	0.001 (-0.004, 0.007)	0.61	0.85 (0.42, 1.28)	<0.001	0.08 (-0.19, 0.36)	0.54	0.075 (0.05, 0.09)	<0.001
Seafood	0.02 (-0.04, 0.21)	0.16	-0.004 (-0.006, -0.001)	0.002	-0.26 (-0.71, 0.18)	0.25	0.26 (-0.02, 0.54)	0.71	0.04 (0.01, 0.06)	0.001
Milk	-0.003 (-0.14, 0.11)	0.81	-0.002 (-0.004, 0.001)	0.20	0.008 (-0.44, 0.46)	0.97	0.09 (-0.19, 0.37)	0.53	0.008 (-0.01, 0.003)	0.46
Egg	0.08 (0.01, 0.13)	<0.001	0.002 (0.001, 0.003)	<0.001	0.03 (0.02, 0.04)	<0.001	-0.001 (-0.008, 0.01)	0.84	0.002 (0.001, 0.003)	<0.001
Dessert	0.02 (-0.03, 0.19)	0.14	0.003 (0.001, 0.005)	0.013	0.18 (-0.24, 0.60)	0.40	-0.09 (-0.35, 0.18)	0.53	0.02 (-0.005, 0.04)	0.14
	HGB		HCT		MCV		MCH		MCHC	
	β (95% CI)	*p* value	β (95% CI)	*p* value	β (95% CI)	*p* value	β (95% CI)	*p* value	β (95% CI)	*p* value
Vegetables	0.07 (-0.002, 0.13)	0.06	0.16 (-0.03, 0.36)	0.11	0.14 (-0.04, 0.32)	0.14	0.07 (0.001, 0.15)	0.047	0.34 (-0.05, 0.72)	0.08
Fruits	0.19 (0.12, 0.26)	<0.001	0.50 (0.30.0.70)	<0.001	0.02 (-0.05, 0.09)	0.85	0.07 (0.002, 0.15)	0.06	0.70 (0.31. 1.08)	<0.001
Grains	0.34 (0.27, 0.40)	<0.001	0.91 (0.73, 1.10)	<0.001	0.03 (-0.13, 0.20)	0.68	0.10 (0.04, 0.17)	0.003	0.11 (0.07, 0.15)	<0.001
Nuts	-0.001 (-0.07, 0.07)	0.98	-0.01 (-0.21, 0.18)	0.89	0.14 (-0.04, 0.32)	0.13	0.50 (-0.02, 0.12)	0.18	0.04 (-0.34, 0.42)	0.84
Meats	0.26 (.20, 0.33)	<0.001	0.74 (0.55.0.93)	<0.001	0.07 (-0.10, 0.24)	0.40	0.09 (0.02, 0.16)	0.01	0.75 (0.38, 1.11)	<0.001
Seafood	0.14 (0.07, 0.21)	<0.001	0.36 (0.17, 0.56)	<0.001	-0.07 (-0.25, 0.11)	0.45	0.07 (0.01, 0.14)	0.07	0.60 (0.23, 0.96)	0.001
Milk	0.04 (-0.03, 0.11)	0.28	0.10 (-0.10, 0.29)	0.35	0.02 (-0.17, 0.20)	0.18	0.03 (-0.05, 0.10)	0.45	-0.47 (-0.85, -0.09)	0.015
Egg	0.006 (0.005, 0.008)	<0.001	0.02 (0.01, 0.023)	<0.001	-0.002 (-0.007, 0.003)	0.39	0.001 (-0.001, 0.002)	0.53	0.25 (-0.13, 063)	0.20
Dessert	0.03 (-0.04, 0.91)	0.40	0.11 (-0.08, 0.29)	0.426	-0.10 (-0.27, 0.07)	0.25	-0.05 (-0.12, 0.02)	0.17	0.014 (0.004, 0.024)	0.004

WHR: waist-to-hip ratio, RBC: erythrocyte, HGB: hemoglobin, HCT: red blood cell specific volume, MCV: mean red blood cell volume, MCH: mean corpuscular hemoglobin, MCHC: mean corpuscular hemoglobin concentration, adjusted by age, gender, energy intake, residence, and other food intake.

and serves as the predominant source for erythropoiesis.[34] The absorption of heme iron from a composite meal not containing meat is less than half than if meat is present in the meal. This finding may have implications for the interpretation of the meat effect and in considering heme iron as a source of iron supplementation or fortification.[35] Fruit and grains intake was also associated with an increased level of RBC, HGB, HCT, and MCHC. This might be related to the non-heme iron. Non-heme iron is the main part of dietary iron and most of it comes from grains, vegetables, fruits, eggs and iron used for fortification of foods. Non-heme iron absorption has been shown to be affected by several factors in the diet. Ascorbic acid increases the absorption markedly. This increase is obtained both by adding ascorbic acid as such or by adding foods with a high content of ascorbic acid.[11]

VDP was positively associated with macrocytic anemia in men participants while an ODP was negatively associated with microcytic hypochromic anemia in both genders. We supposed the reason of these results could be diet diversity. Dietary quality and quantity were confirmed to be associated with anemia in the previous study,[36] and diet diversity resulted in an adequacy of macro- and micronutrient intake and can be used as a standard for assessing micronutrient adequacy. We used dietary diversity score (DDS) as a tool to evaluate dietary diversity status and three dietary patterns, dietary diversity score (DDS) in VDP was significantly lower than ODP and VDP. Higher diversity of food is associated with higher nutrient intake.[37] While adhering to VDP resulted in dietary imbalance which could decrease the intake of nutrients and the level of hemoglobin and erythrocyte (Figure 1).

Chronic disease, unlikely in the present population, can itself result in anemia of various types, particularly that which is normochromic and normocytic.[38] Participants with this RBC morphology in our study were 11% of the population. Major infectious diseases which are associated with anemia include malaria, helminthiases like hookworm and ascariasis leading to blood loss, and schistosomiasis. So could nutrient deficiencies other than iron (for hypochromic microcytic anemia), folic acid and vitamin B-12 (for macrocytic anemia), trace elements like copper, zinc, and selenium could also be a factor.[39] Genetic factors most obviously contribute to anemia with haemoglobinopathies like thalassemia and in metabolic disorders like G-6-PD deficiency and sickle cell anemia, each of which can be found in people of Chinese ancestry, but not documented in this study.[40,41]

China has a long history of drinking alcohol, especially in Qingdao. Older adolescents (>18 years old) are even encouraged by their parents to drink alcohol as drinking behavior has been deemed a useful and necessary social skill in society.[42] However, alcohol abuse, liver disease, and vitamin B-12 and folate deficiency are the most common etiologies of macrocytosis.[43] Acute alcohol ingestion causes reduced erythropoiesis with decreased marrow cellularity and vacuolization of the red cell precursors, and alcohol or acetaldehyde preferentially suppress erythropoiesis, and chronic alcohol abuse leads to typical megaloblastic hematopoiesis, which is associated with malnutrition and folate deficiencies. After abstinence from alcohol, the MCV and RDW were reduced significantly and were associated with an increasing serum folic acid level.[44] We did not collect the information on alcohol intake since 95% of subjects had just turned 18 years old, and the Chinese government has a rule that drinking is not allowed under the age of 18. Alcohol drinking status as a risk factor of macrocytic anemia should be considered in follow up.

The reason for the different findings between urban and village populations for the three dietary patterns is not clear. This may reflect differences in income or other cultural factors. The lower intake of plant foods may be due the shift in dietary habits such as increased intake of convenience foods, which has raised concerns regarding the nutritional status of the population in both developing and developed countries.[45,46] Although the present study did not provide insight on dietary preferences among participants, the dietary transition and low plant consumption might offer some explanation for the higher prevalence of anemia.

The novelty of the present study is the idea to use RBC morphology to define different types of anemia and consider to what extent it could be accounted for by dietary patterns or diversity. The strengths of the study are studying anemia morphology and dietary patterns in young men and women partly fills a publication gap for anemia and dietary patterns among young Chinese adults; it offers insight into and possible recommendations to improve their dietary intake, particularly that of young women.

The present study has several limitations. Firstly, the cross-sectional study design could not identify causal associations. Secondly, there were low numbers of participants in the SDP and VDP groups. Thirdly, the self-reported questionnaire may have had reporting bias, although participants were supervised by professionals. Fourthly, other factors such as hemoglobinopathies, G-6PD deficiency and intestinal helminthiasis associated with dietary patterns and/or anemia were not documented. Fifthly, the present study did not collect information about the alcohol intake.

Conclusion

The present study suggested that adhering to an omnivorous dietary pattern was associated with a lower hypochromic anemia risk for both genders and with a lower macrocytic anemia risk in men. Dietary diversity was in general associated with less prevalence of anemia in this study population in Shandong Province, China. Excessive alcohol intake is the most plausible explanation for macrocytosis in the young men.

AUTHOR DISCLOSURES

The authors declare no conflicts of interest in relation to the content of this study.

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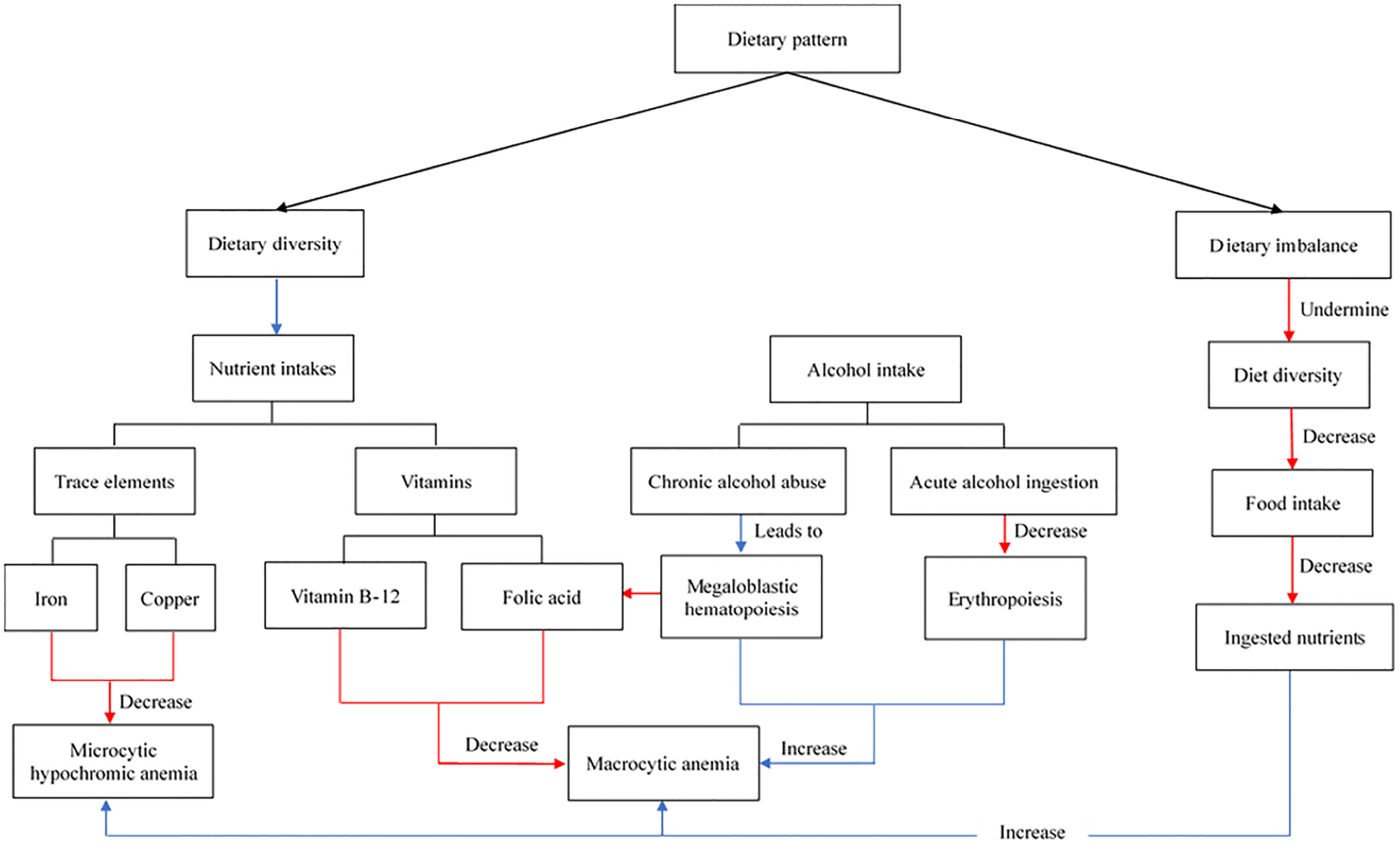

Figure 1. A conceptual diagram for the linkages between dietary pattern and anemia.

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