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**Nutritional determinants of anemia among adults in eastern China**

Shi ZM *et al*. Nutritional determinants of anemia

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**Abstract**

Historically, Eastern China has the highest prevalence of anemia among adults in China. It is commonly believed that iron deficiency is the main cause of anemia in China. Iron fortified soysauce is used to prevent anemia. Findings from Jiangsu Nutrition Study suggest that diet is related to anemia in this region. However, iron deficiency is not the main cause. Micronutrients other than iron (*e.g.,* riboflavin) need to be considered in the prevention of anemia in the region.

**Key words**: Anemia; Diet; Iron; Riboflavin; Magnesium; China

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**Core tip:** It is commonly believed that iron deficiency is the main cause of anemia in China. Here we summarize the evidence from Eastern China showing that it is not the case.

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**INTRODUCTION**

Yangtz delta covers Jiangsu province, Zhejiang province and Shanghai city in Eastern China. Economically, it is one of the most prosperous regions in China. Historically, findings from three Chinese national nutrition surveys (1959, 1982, and 1992) showed that the prevalence of anemia among adults in this region is the highest in China[[1](#_ENREF_1)]. Over the past several decades, the prevalence of anemia decreased substantially but remains high. For example, in Jiangsu province the prevalence of anemia was 18.3% in men and 31.5% in women in 2002[[2](#_ENREF_2)]. It is commonly believed that iron deficiency (due to low intake and poor bioavailability) is the main cause of anemia in the region as the prevalence of Thalassemia and other haematological disorders is low[[3](#_ENREF_3)] and hereditary haemoglobinopathy is rare in the Chinese population[[4](#_ENREF_4)]. This concept has been challenged by recent findings from the region. Understanding the nutritional determinants of anemia in the region is the key for prevention and treatment.

The current editorial aims to summarize the findings from the Jiangsu Nutrition Study (JIN). The baseline survey of JIN was conducted in six counties and two cities in Jiangsu Province in 2002 as part of the Chinese National Nutrition Survey. In total, 2849 adults had dietary intake and haemoglobin information[[5](#_ENREF_5)]. Dietary intake was assessed using both Food Frequency Questionnaire (FFQ) and 3-day weighted food record. In 2007, a 5-year follow-up survey was conducted and 1175 participants had fasting blood measured[[6](#_ENREF_6)].

**IRON INTAKE AND ANEMIA**

The Chinese Nutrition Society set the recommended nutrient intake (RNI) for iron as 12 mg/d for adults aged above 18 years and 20 mg/d for women 18-50 years[[7](#_ENREF_7)]. The median intake of iron in the region was 23 mg/d, which is well above the RNI especially in men (Figure 1). Among adults, the prevalence of iron intake below RNI was 1.1% in men and 25.8% in women. The distribution of serum ferritin (an indicator for iron storage) also shows a low prevalence of iron deficiency (2.1% in men, 15.1% in women). In contrast, the prevalence of iron overload (ferritin > 150 μg/L) is 33.0% in men and 11.9% in women (Figure 2). In the sample, only 5.1% of women had both low intake of iron and low level of ferritin while no men had both conditions. The prevalence of iron deficiency anemia was 0.7% in men and 6.3% in women[[8](#_ENREF_8)].

The high intake of iron, low prevalence of iron deficiency and high prevalence of anemia puzzled the nutrition community in China. Currently, iron fortified soysauce is used to prevent anemia in China. The efficacy of using NaFeEDTA-fortified soy sauce to prevent anemia was tested in Guizhou, a less developed Chinese province[[9](#_ENREF_9)]. The food habits are totally different in our study region as compared with Guizhou. It is unknown whether the findings in Guizhou can be applicable in the Yangtz delta. A recent study shows that the association between dietary intake and anemia is different between migrant students and local students in the region[[10](#_ENREF_10)]. Debate on iron supplement is ongoing. Several studies in China have found that a high iron intake, especially heme iron intake or elevated serum ferritin, is associated with increased risk of diabetes[[8](#_ENREF_8),[11-14](#_ENREF_11)].

**FOOD AND NUTRIENTS OTHER THAN IRON AND ANEMIA**

Findings from JIN suggest that diet at different levels (dietary patterns, individual foods, and nutrients) is related to anemia.

***Dietary patterns and anemia***

Cross-sectional studies of dietary pattern and anemia found that a traditional dietary pattern (high intake of rice and vegetable) was positively associated with anemia[[5](#_ENREF_5)]. Compared with the first quartile of the traditional dietary pattern, the highest quartile had a higher odds ratio for anemia of 2.60 (95%CI: 1.38-4.88) in men and 3.40 (95%CI: 2.14-5.39) in women. This association was confirmed in the longitudinal study: for 1 unit change in traditional food pattern score, the OR for incident anemia was 1.35(95%CI: 1.07-1.71) after adjusting for sociodemographic and lifestyle factors.

***Individual food intake and anemia***

Cross-sectional analysis suggests that meat intake was positively associated with anemia[[15](#_ENREF_15)]. However, among the anemic at baseline, compared with the first quartile of pork intake, quartile 3 and 4 were 80% (95%CI: 18%-176%) more likely to be non-anemic at follow up. It is likely that a reverse causation between meat intake and anemia exists at baseline. Cross-sectionally, Tofu intake was inversely related to anemia[[16](#_ENREF_16)]. The longitudinal association between tofu intake and anemia seems complex. Although Tofu intake was inversely associated with persistent anemia during follow-up, it was positively related to incident anemia but inversely related to anemia resolving. The cause for incident anemia or anemia resolving may be different to persistent anemia. An inverse association between Tofu intake and persistent anemia may be explained by several mechanisms: (1) Tofu intake was positively associated with magnesium intake[[16](#_ENREF_16)]; (2) Tofu intake is inversely associated with blood lead levels in the Chinese population[[17](#_ENREF_17)]; and (3) soy intake is inversely associated with inflammation biomarkers[[18](#_ENREF_18)]. In the sample, there was a positive association between monosodium glutamate (MSG) and increase of haemoglobin (Hb) among men but not women[[19](#_ENREF_19)]. Among anemic participants at baseline, there was a dose response relationship between MSG intake and increase in Hb levels during follow-up. The possible mechanisms linking MSG and anemia may include the increased secretion of gastric acid and leptin [[20](#_ENREF_20),[21](#_ENREF_21)].

***Nutrients and anemia***

**Riboflavin and anemia:** Figure 3 shows the distribution of the intake of riboflavin. The majority of the population had inadequate riboflavin intake (the Chinese RNI for riboflavin is 1.4 mg/d for men and 1.2 mg/d for women aged above 18 years[[7](#_ENREF_7)]). This is in line with findings from the China Nutrition and Health Survey (CHNS), which showed that the mean intake of riboflavin was around 0.7-0.9 mg/d among adults aged 18-45 years in six surveys between 1989 and 2004 [[22](#_ENREF_22)]. The main reason for the low intake of riboflavin is the low consumption of milk and animal food.

Based on longitudinal analysis, it was found that inadequate riboflavin intake increases the risk of anemia[[23](#_ENREF_23)]. There was a significant interaction between riboflavin and iron intake in relation to anemia risk. When riboflavin intake is inadequate, a high iron intake reduces the risk of anemia. However, when riboflavin intake is adequate iron intake is not a determinant of anemia[[23](#_ENREF_23)]. The possible explanation for the link is that riboflavin can enhance iron absorption and utilization[[24](#_ENREF_24),[25](#_ENREF_25)]. If the riboflavin level is low, the ability to mobilise iron from ferritin to synthesis Hb will be limited[[26](#_ENREF_26)]. This could be one of the reasons why Hb is low but ferritin is relatively normal in the region. Thus correcting inadequate riboflavin intake may be a priority for anemia prevention in the region. A recent trial in China showed that retinol and riboflavin supplements decreased the prevalence of anemia in pregnant women who were also taking iron and folic acid supplements[[27](#_ENREF_27)]. In UK, it has been found that riboflavin supplantation improves hematologic status among women aged 19-25 years with moderate riboflavin deficiency[[28](#_ENREF_28)].

**Magnesium and anemia:** A high intake of magnesium was associated with a lower prevalence of anemia[[2](#_ENREF_2)]. Comparing extreme quartiles of magnesium intake, the odds ratio for anemia was 0.48(95%CI: 0.31-0.74). There was a joint effect between magnesium and iron intake in relation to anemia[[2](#_ENREF_2)]. Data from CHNS also shows that serum magnesium is inversely associated with anemia in both men and women[[29](#_ENREF_29)].

**Vitamin C and anemia:** In JIN, there was no association between vitamin C intake and anemia both cross-sectionaly and longitudinally.

**Other nutritional related factors and anemia:** Different from Western countries, both general and central obesity were inversely related to anemia in the region[[30](#_ENREF_30)]. Exposure to the Chinese famine in early life was positively associated with anemia in adulthood[[31](#_ENREF_31)].

**CHALLENGES AND LIMITATIONS**

Despite the known health risks of anemia, the adverse effects of anemia in this population are not well studied. There are a limited number of longitudinal studies on nutrition and anemia in the region. Surprisingly, maternal anemia is not associated with neonatal mortality in the region. The stillbirth rate was lower among those with anemia than those without anemia (6.2 *vs* 9.2 per 1000 births)[[32](#_ENREF_32)]. Based on 10-year follow-up of JIN participants, both high and low Hb are related to an increased risk of mortality in both men and women (unpublished data). While emphasizing the importance of low haemoglobin levels, we should not neglect the adverse effects of elevated levels of Hb.

**CONCLUSION**

Diet is related to anemia among adults in Eastern China. Iron intake is in general adequate in men as compared with RNI. Micronutrients other than iron (*e.g.,* riboflavin) need to be considered in the prevention of anemia. Prospective cohort studies and randomized clinical trials are needed. Iron supplement should not be the first choice of anemia prevention at the population level.

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**Figure 1 Distribution of iron intake among Chinese adults.** Data from Jiangsu Nutrition Study (2002). Dash line represents Chinese recommended nutrient intake for iron.



**Figure 2 Distribution of serum ferritin among adults in Jiangsu China.** Data from Jiangsu Nutrition Study (2002). Dash line represent low and high iron levels.



**Figure 3 Distribution of riboflavin intake among Chinese adults.** Data from Jiangsu Nutrition Study (2002). Dash line represents Chinese recommended nutrient intake for riboflavin.