

## Nutritional determinants of anemia among adults in Eastern China

Zumin Shi, Anne W Taylor

Zumin Shi, Anne W Taylor, Discipline of Medicine, University of Adelaide, SAHMRI, North Terrace, Adelaide SA 5000, Australia

Zumin Shi, Department of Nutrition and Foodborne Disease Prevention, Jiangsu Provincial Center for Disease Control and Prevention, Nanjing 210009, Jiangsu Province, China

**Author contributions:** Shi Z conceived the issues which formed the content of the manuscript and wrote the manuscript; Taylor AW contributed to the manuscript revision.

**Conflict-of-interest statement:** The authors have no conflict of interests.

**Open-Access:** This article is an open-access article which selected by an in-house editor and fully peer-reviewed by external reviewers. It distributed in accordance with the Creative Commons Attribution Non Commercial (CC BY-NC 4.0) license, which permits others to distribute, remix, adapt, build upon this work non-commercially, and license their derivative works on different terms, provided the original work is properly cited and the use is non-commercial. See: <http://creativecommons.org/licenses/by-nc/4.0/>

**Correspondence to:** Dr. Zumin Shi, MD, PhD, Discipline of Medicine, University of Adelaide, Level 7, SAHMRI, North Terrace, Adelaide SA 5000, Australia. [zumin.shi@adelaide.edu.au](mailto:zumin.shi@adelaide.edu.au)  
Telephone: +61-8-83131188  
Fax: +61-8-83131228

Received: May 29, 2015

Peer-review started: June 2, 2015

First decision: June 18, 2015

Revised: July 3, 2015

Accepted: July 24, 2015

Article in press: July 27, 2015

Published online: August 12, 2015

### 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

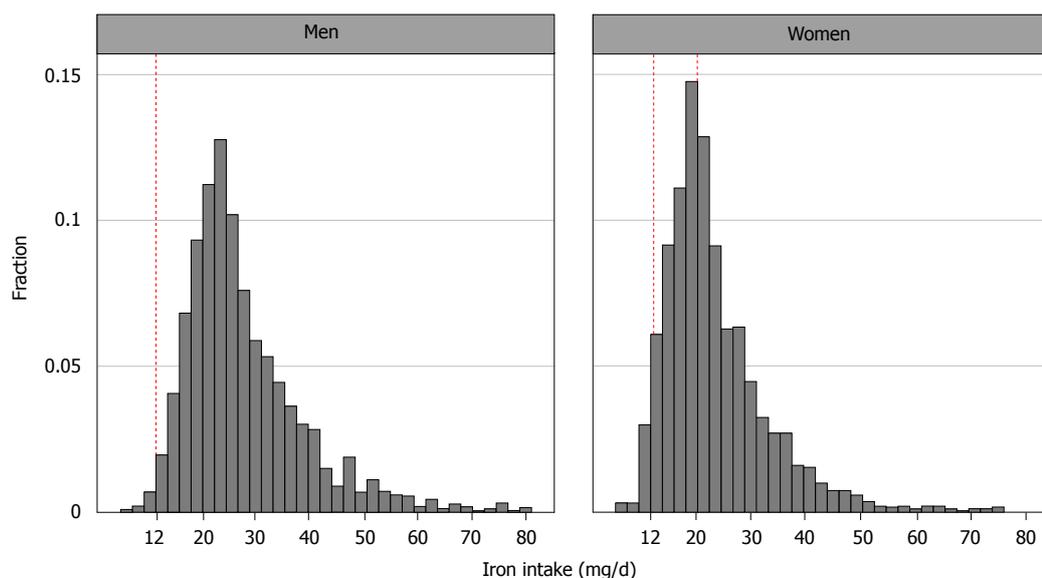
© **The Author(s) 2015.** Published by Baishideng Publishing Group Inc. All rights reserved.

**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.

Shi Z, Taylor AW. Nutritional determinants of anemia among adults in Eastern China. *World J Transl Med* 2015; 4(2): 55-59 Available from: URL: <http://www.wjgnet.com/2220-6132/full/v4/i2/55.htm> DOI: <http://dx.doi.org/10.5528/wjtm.v4.i2.55>

### INTRODUCTION

Yangtze 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<sup>[1]</sup>. 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<sup>[2]</sup>. It is commonly believed that iron deficiency (due to low intake and poor bioavailability) is the main



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

cause of anemia in the region as the prevalence of Thalassemia and other haematological disorders is low<sup>[3]</sup> and hereditary haemoglobinopathy is rare in the Chinese population<sup>[4]</sup>. 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 (Hb) information<sup>[5]</sup>. Dietary intake was assessed using both Food Frequency Questionnaire and 3-d weighted food record. In 2007, a 5-year follow-up survey was conducted and 1175 participants had fasting blood measured<sup>[6]</sup>.

## 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<sup>[7]</sup>. 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  $\mu$ g/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<sup>[8]</sup>.

The high intake of iron, low prevalence of iron deficiency and high prevalence of anemia puzzled the nutrition community in China. Currently, iron fortified soy sauce 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<sup>[9]</sup>. 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 Yangtze delta. A recent study shows that the association between dietary intake and anemia is different between migrant students and local students in the region<sup>[10]</sup>. 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<sup>[8,11-14]</sup>.

## 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<sup>[5]</sup>. 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.

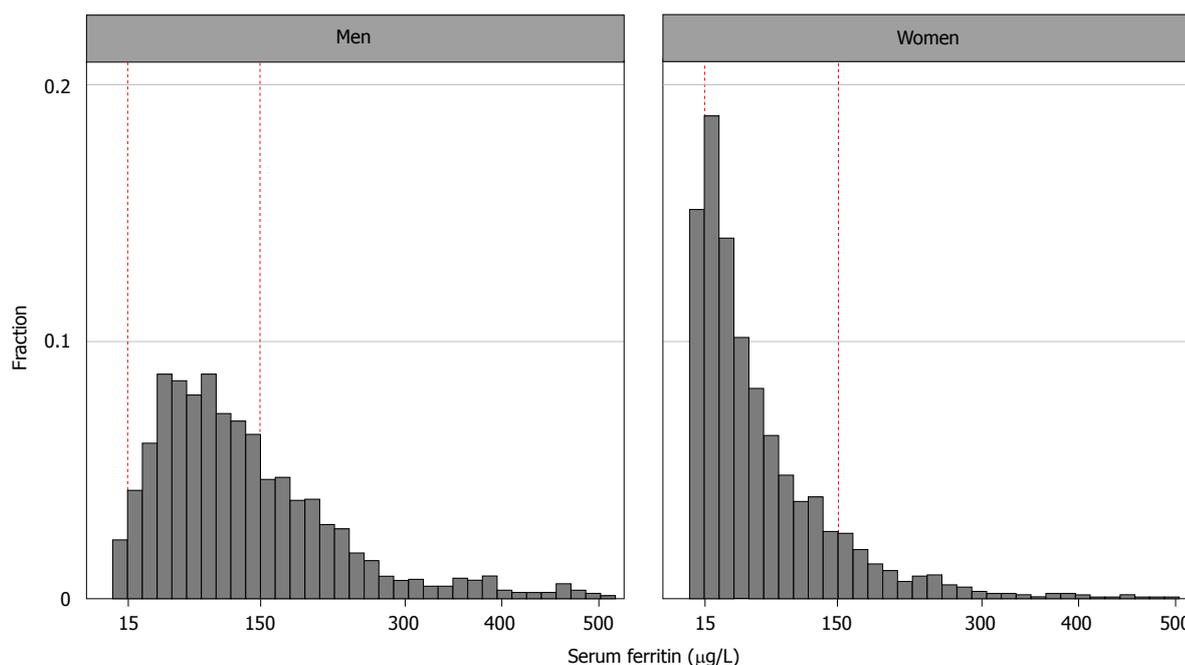


Figure 2 Distribution of serum ferritin among adults in Jiangsu China. Data from Jiangsu Nutrition Study (2002). Dash line represent low and high iron levels.

### Individual food intake and anemia

Cross-sectional analysis suggests that meat intake was positively associated with anemia<sup>[15]</sup>. However, among the anemic at baseline, compared with the first quartile of pork intake, quartile 3 and 4 were 80% (95%CI: 0.18-1.76) 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<sup>[16]</sup>. 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<sup>[16]</sup>; (2) Tofu intake is inversely associated with blood lead levels in the Chinese population<sup>[17]</sup>; and (3) soy intake is inversely associated with inflammation biomarkers<sup>[18]</sup>. In the sample, there was a positive association between monosodium glutamate (MSG) and increase of Hb among men but not women<sup>[19]</sup>. 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<sup>[20,21]</sup>.

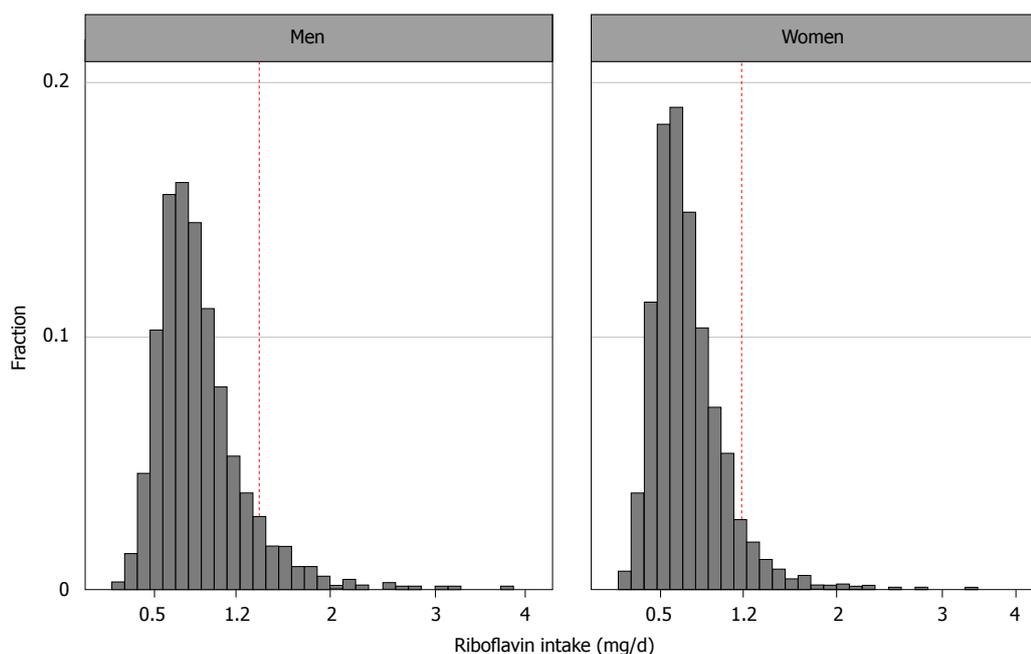
### Nutrients and anemia

**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<sup>[7]</sup>). 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<sup>[22]</sup>. 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<sup>[23]</sup>. 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<sup>[23]</sup>. The possible explanation for the link is that riboflavin can enhance iron absorption and utilization<sup>[24,25]</sup>. If the riboflavin level is low, the ability to mobilise iron from ferritin to synthesis Hb will be limited<sup>[26]</sup>. 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<sup>[27]</sup>. In United Kingdom, it has been found that riboflavin supplementation improves hematologic status among women aged 19-25 years with moderate riboflavin deficiency<sup>[28]</sup>.

**Magnesium and anemia:** A high intake of magnesium was associated with a lower prevalence of anemia<sup>[2]</sup>. Comparing extreme quartiles of magnesium intake, the odds ratio for anemia was 0.48 (95%CI: 0.31-0.74).



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

There was a joint effect between magnesium and iron intake in relation to anemia<sup>[2]</sup>. Data from CHNS also shows that serum magnesium is inversely associated with anemia in both men and women<sup>[29]</sup>.

**Vitamin C and anemia:** In JIN, there was no association between vitamin C intake and anemia both cross-sectionally 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<sup>[30]</sup>. Exposure to the Chinese famine in early life was positively associated with anemia in adulthood<sup>[31]</sup>.

## 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)<sup>[32]</sup>. 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 Hb 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.

## REFERENCES

- 1 **Chang S**, Ge K, Zhai F, Jia F, Xu X. The analysis of nutritional factors on anemia in Chinese adults. *Acta Nutrimenta Sinica* 1998; **20**: 132-137
- 2 **Shi Z**, Hu X, He K, Yuan B, Garg M. Joint association of magnesium and iron intake with anemia among Chinese adults. *Nutrition* 2008; **24**: 977-984 [PMID: 18586459]
- 3 **Lin M**, Han ZJ, Wang Q, Zheng L, Wang Y, Yang H, Huang Y, Lin F, Zhan XF, Lin CP, Wu JR, Luo ZY, Liu JB, Yan ZH, Zheng SY, Zheng JK, Lu M, Zhu JJ, Xie LX, Yang LY. Molecular epidemiological survey of hemoglobinopathies in the Wuxi region of Jiangsu Province, eastern China. *Hemoglobin* 2013; **37**: 454-466 [PMID: 23806067 DOI: 10.3109/03630269.2013.807285]
- 4 **Lin A**, Yan WH, Xu HH, Zhu M, Zhou MY. Analysis of the HFE gene (C282Y, H63D and S65C) mutations in a general Chinese Han population. *Tissue Antigens* 2007; **70**: 252-255 [PMID: 17661915 DOI: 10.1111/j.1399-0039.2007.00877.x]
- 5 **Shi Z**, Hu X, Yuan B, Pan X, Dai Y, Holmboe-Ottesen G. Association between dietary patterns and anaemia in adults from Jiangsu Province in Eastern China. *Br J Nutr* 2006; **96**: 906-912 [PMID: 17092381]
- 6 **Shi Z**, Zhou M, Yuan B, Qi L, Dai Y, Luo Y, Holmboe-Ottesen G. Iron intake and body iron stores, anaemia and risk of hyperglycaemia among Chinese adults: the prospective Jiangsu Nutrition Study (JIN). *Public Health Nutr* 2010; **13**: 1319-1327 [PMID: 19860995]
- 7 **Chinese Nutrition Society**. Chinese DRIs Handbook. Beijing: Standards Press of China, 2013
- 8 **Shi Z**, Hu X, Yuan B, Pan X, Meyer HE, Holmboe-Ottesen G. Association between serum ferritin, hemoglobin, iron intake, and diabetes in adults in Jiangsu, China. *Diabetes Care* 2006; **29**:

- 1878-1883 [PMID: 16873796]
- 9 **Chen J**, Zhao X, Zhang X, Yin S, Piao J, Huo J, Yu B, Qu N, Lu Q, Wang S, Chen C. Studies on the effectiveness of NaFeEDTA-fortified soy sauce in controlling iron deficiency: a population-based intervention trial. *Food Nutr Bull* 2005; **26**: 177-186; discussion 187-189 [PMID: 16060219]
  - 10 **Hu S**, Tan H, Peng A, Jiang H, Wu J, Guo S, Qian X. Disparity of anemia prevalence and associated factors among rural to urban migrant and the local children under two years old: a population based cross-sectional study in Pinghu, China. *BMC Public Health* 2014; **14**: 601 [PMID: 24928085 DOI: 10.1186/1471-2458-14-601]
  - 11 **Luan de C**, Li H, Li SJ, Zhao Z, Li X, Liu ZM. Body iron stores and dietary iron intake in relation to diabetes in adults in North China. *Diabetes Care* 2008; **31**: 285-286 [PMID: 17909092 DOI: 10.2337/dc07-0921]
  - 12 **Sun L**, Zong G, Pan A, Ye X, Li H, Yu Z, Zhao Y, Zou S, Yu D, Jin Q, Hu FB, Lin X. Elevated plasma ferritin is associated with increased incidence of type 2 diabetes in middle-aged and elderly Chinese adults. *J Nutr* 2013; **143**: 1459-1465 [PMID: 23902953 DOI: 10.3945/jn.113.177808]
  - 13 **Guo X**, Zhou D, An P, Wu Q, Wang H, Wu A, Mu M, Zhang D, Zhang Z, Wang H, He L, Liu Y, Wang F. Associations between serum hepcidin, ferritin and Hb concentrations and type 2 diabetes risks in a Han Chinese population. *Br J Nutr* 2013; **110**: 2180-2185 [PMID: 23742704 DOI: 10.1017/S0007114513001827]
  - 14 **Han LL**, Wang YX, Li J, Zhang XL, Bian C, Wang H, Du S, Suo LN. Gender differences in associations of serum ferritin and diabetes, metabolic syndrome, and obesity in the China Health and Nutrition Survey. *Mol Nutr Food Res* 2014; **58**: 2189-2195 [PMID: 25163435 DOI: 10.1002/mnfr.201400088]
  - 15 **Shi Z**, Pan X, Holmboe-Ottesen G. Meat consumption and anemia in Chinese adults in Jiangsu Province. In: Amesel L, Hirsch L, editors. *Food Science and Security*: Nova Science Publisher, 2009: 267-280
  - 16 **Shi Z**, Hu X, Yuan B, Pan X, Dai Y, Holmboe-Ottesen G, Byles JE. Strong negative association between intake of tofu and anemia among Chinese adults in Jiangsu, China. *J Am Diet Assoc* 2008; **108**: 1146-1153 [PMID: 18589021]
  - 17 **Chen C**, Wang X, Chen D, Li G, Ronnenberg A, Watanabe H, Wang X, Ryan L, Christiani DC, Xu X. Tofu consumption and blood lead levels in young Chinese adults. *Am J Epidemiol* 2001; **153**: 1206-1212 [PMID: 11415956 DOI: 10.1093/aje/153.12.1206]
  - 18 **Azadbakht L**, Kimiagar M, Mehrabi Y, Esmailzadeh A, Hu FB, Willett WC. Soy consumption, markers of inflammation, and endothelial function: a cross-over study in postmenopausal women with the metabolic syndrome. *Diabetes Care* 2007; **30**: 967-973 [PMID: 17392557 DOI: 10.2337/dc06-2126]
  - 19 **Shi Z**, Yuan B, Taylor AW, Dal Grande E, Wittert GA. Monosodium glutamate intake increases hemoglobin level over 5 years among Chinese adults. *Amino Acids* 2012; **43**: 1389-1397 [PMID: 2222358 DOI: 10.1007/s00726-011-1213-7]
  - 20 **Boutry C**, Matsumoto H, Airinei G, Benamouzig R, Tomé D, Blachier F, Bos C. Monosodium glutamate raises antral distension and plasma amino acid after a standard meal in humans. *Am J Physiol Gastrointest Liver Physiol* 2011; **300**: G137-G145 [PMID: 21030612]
  - 21 **Diniz YS**, Faine LA, Galhardi CM, Rodrigues HG, Ebaid GX, Burneiko RC, Cicogna AC, Novelli EL. Monosodium glutamate in standard and high-fiber diets: metabolic syndrome and oxidative stress in rats. *Nutrition* 2005; **21**: 749-755 [PMID: 15925301 DOI: 10.1016/j.nut.2004.10.013]
  - 22 **Zhai F**, Wang H, Du S, He Y, Wang Z, Ge K, Popkin BM. Lifespan nutrition and changing socio-economic conditions in China. *Asia Pac J Clin Nutr* 2007; **16** Suppl 1: 374-382 [PMID: 17392135]
  - 23 **Shi Z**, Zhen S, Wittert GA, Yuan B, Zuo H, Taylor AW. Inadequate riboflavin intake and anemia risk in a Chinese population: five-year follow up of the Jiangsu Nutrition Study. *PLoS One* 2014; **9**: e88862 [PMID: 24533156 DOI: 10.1371/journal.pone.0088862]
  - 24 **Powers HJ**, Wright AJ, Fairweather-Tait SJ. The effect of riboflavin deficiency in rats on the absorption and distribution of iron. *Br J Nutr* 1988; **59**: 381-387 [PMID: 3395601 DOI: 10.1079/BJN19880047]
  - 25 **Powers HJ**, Weaver LT, Austin S, Wright AJ, Fairweather-Tait SJ. Riboflavin deficiency in the rat: effects on iron utilization and loss. *Br J Nutr* 1991; **65**: 487-496 [PMID: 1878361 DOI: 10.1079/BJN19910107]
  - 26 **Sirivech S**, Frieden E, Osaki S. The release of iron from horse spleen ferritin by reduced flavins. *Biochem J* 1974; **143**: 311-315 [PMID: 4462557]
  - 27 **Ma AG**, Schouten EG, Zhang FZ, Kok FJ, Yang F, Jiang DC, Sun YY, Han XX. Retinol and riboflavin supplementation decreases the prevalence of anemia in Chinese pregnant women taking iron and folic acid supplements. *J Nutr* 2008; **138**: 1946-1950 [PMID: 18806105]
  - 28 **Powers HJ**, Hill MH, Mushtaq S, Dainty JR, Majsak-Newman G, Williams EA. Correcting a marginal riboflavin deficiency improves hematologic status in young women in the United Kingdom (RIBOFEM). *Am J Clin Nutr* 2011; **93**: 1274-1284 [PMID: 21525198 DOI: 10.3945/ajcn.110.008409]
  - 29 **Zhan Y**, Chen R, Zheng W, Guo C, Lu L, Ji X, Chi Z, Yu J. Association between serum magnesium and anemia: china health and nutrition survey. *Biol Trace Elem Res* 2014; **159**: 39-45 [PMID: 24789475 DOI: 10.1007/s12011-014-9967-x]
  - 30 **Qin Y**, Melse-Boonstra A, Pan X, Yuan B, Dai Y, Zhao J, Zimmermann MB, Kok FJ, Zhou M, Shi Z. Anemia in relation to body mass index and waist circumference among Chinese women. *Nutr J* 2013; **12**: 10 [PMID: 23311667 DOI: 10.1186/1475-2891-12-10]
  - 31 **Shi Z**, Zhang C, Zhou M, Zhen S, Taylor AW. Exposure to the Chinese famine in early life and the risk of anaemia in adulthood. *BMC Public Health* 2013; **13**: 904 [PMID: 24079608 DOI: 10.1186/1471-2458-13-904]
  - 32 **Zhang Q**, Ananth CV, Rhoads GG, Li Z. The impact of maternal anemia on perinatal mortality: a population-based, prospective cohort study in China. *Ann Epidemiol* 2009; **19**: 793-799 [PMID: 19648029 DOI: 10.1016/j.annepidem.2009.06.002]

**P- Reviewer:** Han Q, Kyriazis M, Ong HT

**S- Editor:** Tian YL **L- Editor:** A **E- Editor:** Jiao XK





Published by **Baishideng Publishing Group Inc**

8226 Regency Drive, Pleasanton, CA 94588, USA

Telephone: +1-925-223-8242

Fax: +1-925-223-8243

E-mail: [bpgoffice@wjgnet.com](mailto:bpgoffice@wjgnet.com)

Help Desk: <http://www.wjgnet.com/esps/helpdesk.aspx>

<http://www.wjgnet.com>

