

## Original Article

# Assessment of iodine status and associated factors in vulnerable populations in Henan Province, China, in 2012

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**Background:** Iodine content in table salt was adjusted from 30-50 mg/kg to 21-39 mg/kg from March of 2012 in Henan Province, China. The vulnerable population may be at risk of iodine deficiency. **Objectives:** To determine whether the iodine intake was sufficient in vulnerable populations and to investigate what factors may be associated with iodine status in these vulnerable populations in Henan Province, China. **Methods:** A cross-sectional survey was conducted in 17 cities in Henan Province, China, from April 2012 to December 2012 to assess the iodine status in vulnerable populations, including women of reproductive-age (n=2648), pregnant women (n=39684), lactating women (n=6859), infants <2 years of age (n=16481), and children aged 8-10 years (n=3198). Questionnaires (n=4865) related to demographic and dietary factors were collected from the investigated women to identify factors that were related to iodine intake and iodine status. **Results:** The median urinary iodine concentrations (mUICs) were 205 µg/L, 198 µg/L, 167 µg/L, 205 µg/L and 200 µg/L, respectively, in reproductive-age, pregnant and lactating women, infants <2 years of age and children aged 8-10 years. Higher income, and consuming more poultry and fish in the diet had positive impact on UIC levels. Low salt intake, consuming more rice and vegetables in the diet were negative factors for UIC. **Conclusions:** Iodine status of the vulnerable populations was generally adequate in Henan Province, China, according to WHO criteria. But the mUICs were slightly above the adequate level in reproductive-age women and children aged 8-10 years. It's important to monitor the iodine status in vulnerable populations after the adjustment on iodine content in table salt.

**Key Words:** iodine, reproduction, pregnancy, lactation, child

## INTRODUCTION

Iodine is a trace element required for the synthesis of thyroid hormones in thyroid glands, and is crucial to children's growth and development. Iodine deficiency has many adverse effects, including hypothyroidism, goiter, cretinism, stillbirths, and so on.<sup>1</sup> Recently, severe iodine deficiencies, such as cretinism and goiter, were no longer considered as major health problems. However, iodine deficiency in vulnerable populations is still a concern.<sup>2</sup> Brain development during the intrauterine period and the first 2 years of age is very sensitive to iodine sufficiency.<sup>3</sup> Even mild maternal iodine deficiencies during this critical period may lead to abnormalities in psychomotor and intellectual development.<sup>4,5</sup> Therefore, the control and surveillance of iodine deficiency is critical in vulnerable populations, including reproductive-age, pregnant and lactating women, infants and children.

China was once a country with serious epidemic iodine deficiency disorders (IDD). A universal salt iodization (USI) program has been launched in China since 1995, which lead to a significant increase in the coverage of households using qualified iodized salt and a decline in the incidence of IDD.<sup>6</sup> This program required that the iodine content was 35 mg/kg in table salt (the concentra-

tion of elementary iodine and the permitted range is  $\pm 15$  mg/kg). From 1995 to 2011, six national IDD surveys were carried out in China.<sup>7-12</sup> In the recent surveys, the median urinary iodine concentrations (mUICs) of school children aged 8-10 years in China were 241 µg/L, 246 µg/L and 239 µg/L in 2002, 2005 and 2011, respectively,<sup>10-12</sup> which exceeded the adequate range of 100-199 µg/L recommended by WHO.<sup>3</sup> These results indicated that the iodine status of the country, as a whole, was classified as 'more than adequate' (200-300 µg/L). In view of this, the Ministry of Health issued a new standard that the iodine content should be 20, 25 or 30 mg/kg in table salt (the concentration of elementary iodine and the permitted range is  $\pm 30\%$ ) in September, 2011, according to the

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actual situation in each province.<sup>13</sup> The new standard was implemented from March of 2012 and a period of transition was allowed.

Henan is a province in the central China with a large population and is economically underdeveloped. In the 2002, 2005, 2011 national IDD Surveys, the mUICs in children aged 8-10 years in Henan province were 297, 315 and 201  $\mu\text{g/L}$ , respectively.<sup>10,11,14</sup> These data indicated that the iodine status of the general population in Henan Province exceeded the adequate range of 100-199  $\mu\text{g/L}$ . Iodine excess could induce thyroiditis, hyperthyroidism, hypothyroidism, and goiter.<sup>15</sup> So, in the latest adjustment, a new iodized salt standard of 30 mg/kg (the range is 21-39 mg/kg) was selected in Henan Province.

Some studies found that the iodine status in children aged 8-10 years may reflect the general population, but may not represent other vulnerable populations who were more sensitive to the damage of IDD.<sup>12,16</sup> Before the latest adjustment of salt iodine standard in China, some pregnant and lactating women were found to be iodine deficient, although most school children aged 8-10 years were classified as 'more than adequate'.<sup>12</sup> In order to assess iodine status in vulnerable populations, a cross-sectional survey on reproductive-age, pregnant and lactating women, infants <2 years of age and children aged 8-10 years was conducted in Henan Province of China, in 2012. We sought to determine whether the iodine intake was adequate in vulnerable populations and to investigate the factors associated with iodine status.

## METHODS

### Data collection

Subjects were collected from 17 cities in Henan Province from April 2012 to December 2012. Initially, a subject was eligible to enter the study if she/he was resident in one of the investigating cities for more than 12 months. Those who had thyroid diseases or kidney diseases, or exposure to iodinated contrast medium, were excluded from the study. A multistage cluster sampling method was adopted to obtain samples that represent vulnerable populations. In stage of 1, a county was randomly selected in each city. In stage of 2, clinics or schools were randomly selected from the sampling county. Finally, in each sampling county, no less than 200 reproductive-age women, 200 pregnant women, 200 lactating women, 200 infants, and 200 school children, were recruited from the local hospitals and schools (Figure 1). Below are details for recruitment of subjects in different populations.

For reproductive-age women, family planning organizations were randomly selected within each sampling county. These women were equally enrolled regardless whether they were receiving premarital medical check or eugenic check (a free pre-pregnancy check provided by the government, including toxoplasma, rubella virus, cytomegalovirus and herpes virus screening), were enrolled sequentially. Most of them were newly married women of reproductive-age.

For pregnant women, hospitals or maternal and child health (MCH) hospitals with obstetric clinic within each sampling county were randomly selected. The pregnant women, who were receiving prenatal care, were enrolled sequentially.

For lactating women and infants, hospitals or immunization clinics were randomly selected within each sampling county. The lactating women, who were receiving postpartum care and consent, were enrolled sequentially. The vaccinated infants <2 years of age and their mothers, were also enrolled; 50 mother-infant pairs were selected in each city on the basis of exclusive breastfeeding and availability of urine samples from both mothers and their infants.

For the above 4 groups, the medical personals in the selected institutions undertook urine sampling, filled in the registration cards, and kept the urine samples in screw-capped plastic bottles and refrigerated; these urine samples were taken to the CDC laboratory and tested every 2-3 days.

For school children, two or three primary schools were randomly selected within each sampling county. School children aged 8-10 years (half boys and half girls), who met the inclusion criteria, were enrolled. The age of the children was obtained from the school card. The investigations and tests were completed by the CDC staff.

The survey protocol was approved by the medical ethics committee from the Centre for Disease Control and Prevention. Written informed consent was obtained from all the participants.

Subjects were excluded in the final analysis if these subjects lived in the areas where water iodine concentrations exceeded 100  $\mu\text{g/L}$ . A final sample of 68870 subjects was analyzed, including women of reproductive-age ( $n=2648$ ), pregnant women ( $n=39684$ ), lactating women ( $n=6859$ ), infant <2 years ( $n=16481$ ), children aged 8-10 years ( $n=3198$ ). Five hundred and thirty-one breast-fed pairs were included to analyze the correlation between the UIC of infants and their mothers.

### Laboratory analysis

Casual urine samples ( $\geq 10$  mL) were collected from all subjects. The samples were then sealed and stored at 4°C until measurements. UIC was measured to determine iodine in urine by  $\text{As}^{3+}$ - $\text{Ce}^{4+}$  catalytic spectrophotometry (WS/T107-2006), a national method developed by the China's Ministry of Health.<sup>17</sup> All the participate laboratories passed the external quality control by China National CDC in 2012. Based on the results, the coefficient of variation for UIC in our laboratory was 2.2% at  $71.5 \pm 9.0$   $\mu\text{g/L}$  and 1.0% at  $203 \pm 10.0$   $\mu\text{g/L}$ .

### Standard of iodine content in edible salt

The old and new standards of iodine content in table salt were 20-50 mg/kg and 21-39 mg/kg, respectively.

### Evaluation criteria for iodine status

The measurement of urinary iodine excretion was used to assess the iodine status in the collected samples. The evaluation criteria for iodine status were different among different vulnerable population according to the guidelines issued by WHO.<sup>3</sup> The following criteria were used to classify iodine nutritional status: a mUIC of 100-199  $\mu\text{g/L}$  among the general population and 150-249  $\mu\text{g/L}$  among pregnant women indicated iodine sufficiency. Additionally, among the general population, a mUIC <50  $\mu\text{g/L}$  indicated moderate to severe iodine deficiency.

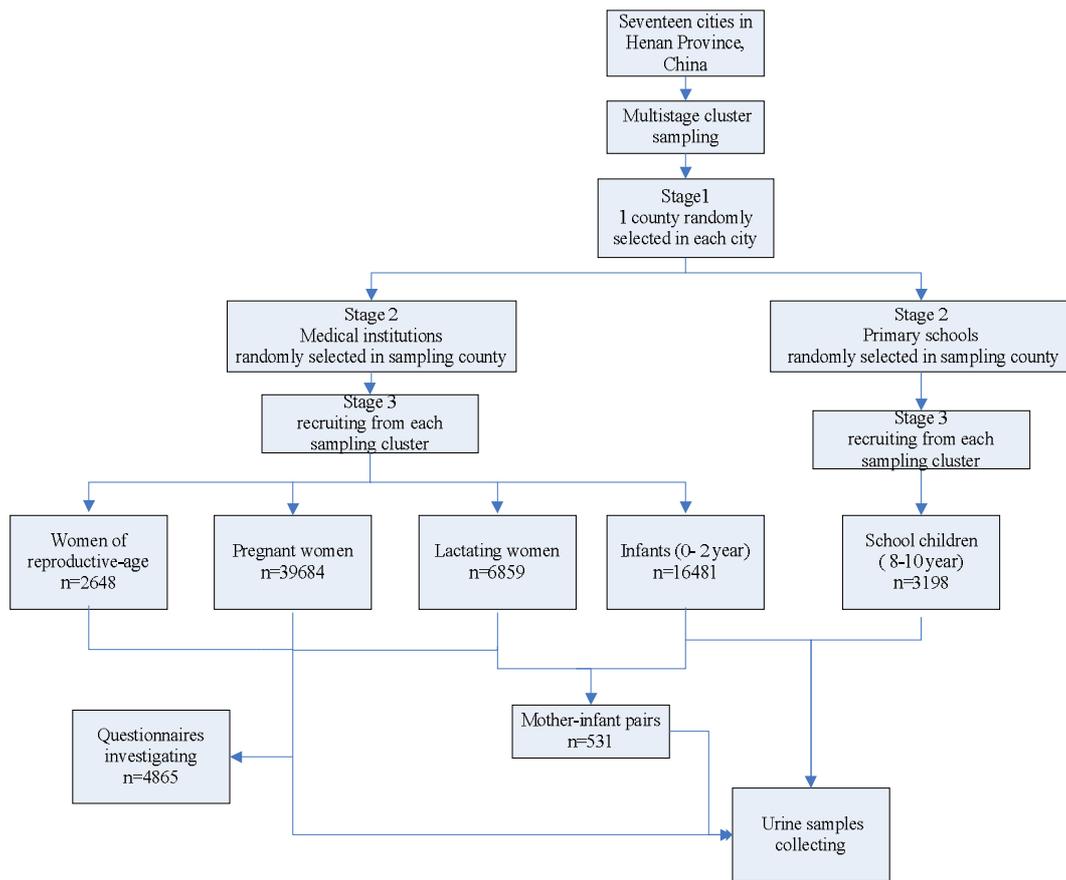


Figure 1. Flow chart of the study population

Among lactating women and infants, a  $mUIC \geq 100 \mu\text{g/L}$  was used to define iodine sufficiency; no other categorizations were used for the two groups.<sup>3</sup>

### Questionnaires

Within each sampling country, 100 reproductive-age women, 100 pregnant women, and 100 lactating women were randomly selected to answer a questionnaire related to demographic and dietary factors on the basis of being literate and availability of urine samples. The demographic data included age, urban/rural, education, address, and income and occupation of the subject and her spouse. The dietary data included supplement of iodized oil capsule or iodine-enriched food, daily salt intake (self-rated), and all food consumed in the past three days. It was difficult to assess the accurate amount of salt intake from each subject in daily life because most of them were recruited from the clinics. Therefore, a self-rated level was used to assess daily salt intake in our survey. Because the rate of qualified iodized salt (which met the national standard, 20-50 mg/kg) in the residents has reached 95% in investigated areas, the usage of iodized salt was not included in our survey.

The questionnaires from subjects who lived in the areas where water iodine concentration exceeded  $100 \mu\text{g/L}$  were also excluded. A total of 4865 questionnaires were included for final the analysis.

### Statistical analysis

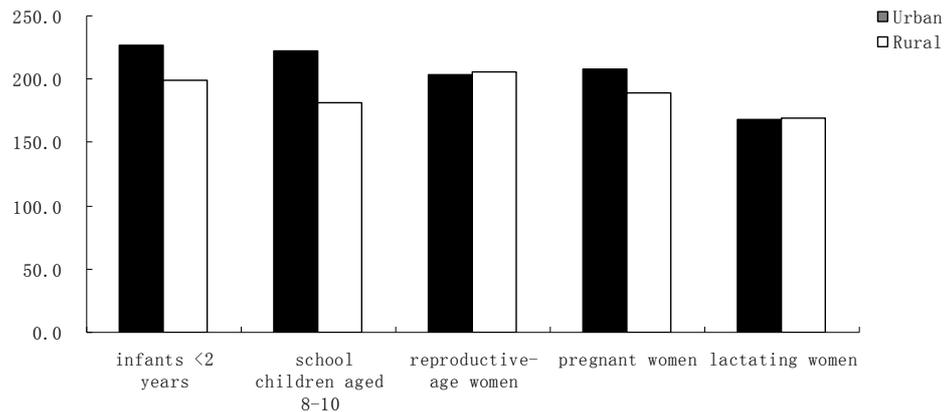
SPSS Version 17.0 was used to analyze the data. Normally distributed data was reported as the mean  $\pm$  standard deviation (SD). Non-normally distributed data was re-

ported as the median (with interquartile range, IQR). For normally distributed outcomes, t-test and ANOVA were used to test the null hypothesis that the group means were the same in two or more groups, respectively. Mann-Whitney U test or Kruskal-Wallis was used to test for differences in the distribution of non-normal continuous variables among two or more groups. Chi-squared or Fisher's exact tests, as appropriate, were used to test for association between categorical variables. To look for correlations of maternal and infant UIC, UIC from mothers and infants was natural log and Pearson correlation was performed. A multiple linear regression analysis was performed with log UIC as the dependent variable and age, education, income, occupation, supplement of iodized oil capsule or consumption of iodine-enriched food in daily life, sodium appetite, and all food types consumed in the past three days as covariates.  $p < 0.05$  was considered statistically significant.

## RESULTS

### Different mUIC levels in three subgroups of women

The average ages of reproductive-age, pregnant and lactating women were 25.8, 26.5, and 27.0, respectively. The lactating women were older than the reproductive-age women and the pregnant women ( $p < 0.001$ ). The mUIC of reproductive-age women was  $205 \mu\text{g/L}$  (Table 1), which is slightly higher than the WHO criterion for sufficiency of the general population ( $100\text{-}199 \mu\text{g/L}$ ). The mUIC of pregnant and lactating women was  $198 \mu\text{g/L}$  and  $167 \mu\text{g/L}$ , respectively, which met the WHO criterion for iodine sufficiency of pregnant women ( $150\text{-}249 \mu\text{g/L}$ ) and lactating women ( $>100 \mu\text{g/L}$ ), respectively. The mUIC of



**Figure 2.** Differences in mUIC between urban and rural areas in different population groups. mUIC: median urinary iodine concentration.

reproductive-age women was higher than both pregnant and lactating women ( $p < 0.05$  and  $p < 0.01$ ).

The percentages of pregnant women ( $n = 39684$ ) in the first, second, and third trimester were 14.9%, 58.8%, and 26.3%, respectively. The mUICs in the three trimesters were 199 µg/L (IQR 125-285), 196 µg/L (IQR 132-283), and 192 µg/L (IQR 129-280), respectively. Differences in UIC among the three trimesters were not statistically significant ( $p = 0.069$ ).

The mUIC were lower in rural pregnant women compared with that in urban pregnant women (189 vs 208 µg/L;  $p < 0.001$ ). There were no significant differences in mUIC between rural and urban areas in reproductive-age and lactating women ( $p = 0.067$  and  $p = 0.577$ ) (Figure 2).

#### **Infants and school children**

The male/female ratio of infants was 1.28. The mUIC was 205 µg/L (IQR 138-294) in infants <2 years of age, which met the WHO criterion for iodine sufficiency of infants (>100 µg/L). The infants were divided into three groups according to their age: 0-0.5 years, 0.6-1 years, and 1-2 years. The mUICs of the three groups were 217 µg/L (IQR 147-298), 194 µg/L (IQR 132-289), and 188 µg/L (IQR 124-279), respectively. It showed that the mUIC of infants decreased as the age increased ( $p < 0.01$ ).

The mUIC in infant girls was significantly lower than that in infant boys (203 vs 209 µg/L;  $p < 0.01$ ) and the mUIC among rural infants compared with urban infants was less (199 vs 227 µg/L;  $p < 0.001$ ).

The male/female ratio of school children was 1.51. The mUIC of school children was 200 µg/L (IQR 127-306), which was slightly higher than the WHO criterion of iodine sufficiency for the general population (100-199 µg/L).

The mUIC of school children aged 8-10 years showed no significant difference among different gender groups ( $p = 0.980$ ), but urban school children had higher mUIC than rural ones (222 vs 181 µg/L) ( $p < 0.001$ ).

A provincial baseline survey was conducted to monitor the iodine status in vulnerable population, but only included 8 cities in 2011. To compare the two years of data (2011 and 2012), the data in the eight cities in 2012 were selected to recalculate the mUICs in vulnerable populations. The mUICs in reproductive-age women, pregnant and lactating women, infants in 2012 (only in the eight

cities) were 212 µg/L, 198 µg/L, 163 µg/L and 207 µg/L, respectively.

#### **Mother-infant pairs**

After adjustment for month age and sex of infant, the UIC of the mothers was positively correlated with the UIC of their infants ( $r^2 = 0.223$ ,  $p < 0.001$ ).

#### **Factors associated with iodine nutritional status of women**

A total of 4865 women completed the questionnaires related to sociodemographic and dietary factors. In multiple linear regression analyses, pregnant and lactating women had a lower UIC than reproductive-age women, while other confounding factors in the model were controlled (Table 2). Based on this model, those living in urban areas (compared with those living in rural areas), having income  $\geq 2000$  yuan (compared with those having income <1000 yuan) and less than high school education (compared with those having more than a high school education) had a higher UIC. Daily salt intake was positively associated with UIC. To assess dietary factors, three day food records were collected. Among them, poultry, and fish had a positive impact on UIC, while rice and vegetables were negative factors. However, there was no significant association between UIC and age, education level, iodized oil capsule, and foods like meat, milk, egg, pickled food, cereal, and beans.

#### **DISCUSSION**

Our results confirmed that iodine status of the vulnerable populations in Henan Province of China in 2012 was generally 'adequate' according to WHO criteria. However, the mUICs were 205 µg/L in reproductive-age women and 200 µg/L in children aged 8-10 years respectively, which were slightly above the adequate level (100-199 µg/L). These data indicate that the two groups of populations may be at risk of iodine excess, which can induce thyroid dysfunction, thyroiditis, hyperthyroidism, hypothyroidism, and goiter.

A new standard of iodine content in table salt was implemented in Henan Province, China, from March of 2012. Iodine content in table salt was reduced from 35 mg/kg to 30 mg/kg. In order to monitor the real changes of iodine status before and after the adjustment on iodine

**Table 1.** Urinary iodine concentration and demographic traits of population groups in central China

Age group	Infants (0-2 year)	School children (8-10 year)	Reproductive-age women	Pregnant women	Lactating women
n	16,481	3198	2648	39,684	6859
Men/women	9246/7235	1925/1273	All women	All women	All women
Age, (mean±SD, year)	0.7±0.6	8.9±0.8	25.8±4.5	26.5±5.7	27.0±6.4
UIC (µg/L)					
Median (IQR)	205 (138-294)	200 (127-306)	205 (134-293)	198 (131-286)	167.1 (108-258)
<50 µg/L (%)	2.0	4.5	3.6	2.3	5.4
<100 µg/L (%)	10.6	16.7	13.8	31.9	21.2
≥300 µg/L (%)	21.9	26.0	23.5	21.1	18.3

Among pregnant women, the percentage of UIC<150 µg/L instead of that of UIC<100 µg/L. IQR: Interquartile range; UIC: Urinary iodine concentration.

**Table 2.** Multiple linear regression models associating iodine deficiency with sociodemographic and dietary factors among women (n=4865)

Variables in equation	$\beta$	$S_x$	$\beta'$	$t$	$p$
Intercept	2.17	0.031		70.2	<0.001
Subgroups of women					
Newly married women of childbearing age	Reference				
Pregnant women	-0.021	0.011	-0.033	-1.88	0.047
Lactating women	-0.020	0.011	-0.031	-1.77	0.077
Urban	0.048	0.011	0.076	4.33	<0.001
Income					
<1000 yuan	Reference				
1000-1999 yuan	0.017	0.014	0.028	1.25	0.213
≥2000 yuan	0.042	0.014	0.068	3.00	0.003
Education					
< High school	Reference				
≥ High school	-0.039	0.011	-0.063	-3.62	<0.001
Daily salt intake (self-rated)					
Low	Reference				
Medium	0.055	0.019	0.057	2.87	0.004
High	0.043	0.015	0.058	2.91	0.004
The kinds of food in recent 3 days					
Poultry	0.037	0.010	0.058	3.83	<0.001
Fish	0.038	0.011	0.051	3.35	0.001
Rice	-0.026	0.010	-0.040	-2.69	0.007
Vegetable	-0.032	0.013	-0.037	-2.51	0.012

The dependent variable is log UIC.  $\beta'$  indicates the standardized coefficient.

content in table salt, we previously carried out a provincial baseline survey on vulnerable population in 2011. Due to a budget limitation, the 2011 survey only included 8 cities and had no dietary survey. The mUICs in reproductive-age women, pregnant and lactating women, infants in 2011 were 205 µg/L, 191 µg/L, 145 µg/L and 185 µg/L, respectively,<sup>18</sup> and the mUICs in 2012 (only in the eight cities) were 212 µg/L, 198 µg/L, 163 µg/L and 207 µg/L, respectively. Upon comparing the two years of data in the eight cities, there was a slight rise from 2011 to 2012 in UIC in vulnerable populations. The rise may be explained by the following reasons: the majority of salt in the market was still the old concentration salt (35 mg/kg); UIC varied highly, and different sample time and season would have an impact on UIC; iodine from iodized salt did not capture all sources of iodine in the diet; therefore it may need further adjustment of the salt iodization in the future.

Some studies have suggested that the increased need for iodine intake for fetal brain development begins even before women came to know about their pregnancy.<sup>19-21</sup>

Iodine status of newly married women at reproductive-age is more significant for fetus growth than other reproductive-age women because most newly married women plan to have babies after being married as the result of one-child policy in China. Our data indicated that the mUIC in reproductive-age women was higher than that in the pregnant and lactating women, which was similar to another finding from Ningxia Province of China.<sup>22</sup> The mUICs were 198 µg/L in pregnant women and 167 µg/L in lactating women in our study, which were higher than that in the USA,<sup>19</sup> Switzerland,<sup>23</sup> Australia,<sup>24</sup> Croatia,<sup>25</sup> and New Zealand.<sup>26</sup> This probably attributed to higher household coverage rates of iodized salt and higher levels of iodine in salt. In order to improve the iodine status in pregnant and lactating women without increasing the risk of iodine excess, we suggested that special iodized salt and individual instructions about iodine supplement should be provided to the pregnant and lactating women while reducing the iodized salt concentration.

In pregnant women, the mUIC was highest in the first trimester and then decreased in the following trimesters.

But statistically the trend was not significant. Similar results were reported in a cross-sectional study conducted in Japan.<sup>27</sup>

The first two years of life are crucial for infants' physical and intellectual development hence iodine deficiency in this period would cause irreversible brain damage. Infants do not have enough iodine storage capacity so that they are dependent on regular supply of iodine for adequacy.<sup>28</sup> The mUIC levels decreased by 30 µg/L in infants, from 0-0.5 years to 1-2 years, in our study, which may be due to the failure in the use of iodine-containing adjunctive food after weaning. These facts suggest that iodine supplementation is necessary for infants who deprive of iodine rich sources.

WHO recommends that school children aged between 8-10 years are suitable for monitoring iodine nutrition in a population because of their easy availability as subjects and vulnerability to the adverse effects for iodine deficiency.<sup>29,30</sup> In our study, we found that rural students were more affected by threat of iodine deficiency than urban students, although iodine status of school children aged 8-10 years was sufficient in general.

UIC varied highly and reflected iodine intake over the past few days rather than usual intake.<sup>23</sup> Therefore, we surveyed the food types in past three days instead of food frequency questionnaire which generally overestimates the level of iodine intake.<sup>27</sup> Our results also confirmed that higher income, fish, poultry, high salt intake, were possible important contributors to iodine status in women. Dairy may be an important source of iodine in industrialized countries, such as Australia,<sup>31</sup> the USA,<sup>19</sup> Italy,<sup>32</sup> and Norway.<sup>33</sup> There was no significant correlation between dairy product intake and iodine status in our study. One possible reason was that the use of iodophor cleansers in the dairy industry and iodine supplementation of cattle feed resulted in milk and other dairy products containing iodine in these countries.<sup>34</sup>

Our results confirmed that iodine status of the vulnerable populations, as a whole, was sufficient in Henan Province, China. But these data were not enough to reflect the real change of population iodine status after adjustment on iodine salt content in table salt. So, a continuous surveillance and evaluation on iodine status in the next two years is necessary. It is also necessary for ongoing monitoring of iodized salt and other dietary iodine sources in order to prevent iodine deficiency as well as iodine excess in vulnerable populations or the general population.

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#### AUTHOR DISCLOSURES

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The authors declare that they have no conflicts of interest.

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## Original Article

## Assessment of iodine status and associated factors in vulnerable populations in Henan Province, China, in 2012

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### 2012年中国河南省重点人群的碘营养状况及影响因素

**背景：**从2012年3月起，中国河南省食盐中碘浓度从30-50 mg/kg调整到21-39 mg/kg。由于食盐中碘浓度的下调，重点人群可能有碘缺乏的风险。**目的：**了解河南省重点人群的碘营养状况是否适宜，并探索与碘营养相关的影响因素。**方法：**从2012年4月至2012年12月，在中国河南省的17个城市对重点人群的碘营养状况开展横断面调查，包括育龄妇女2648名、孕妇39684名、哺乳期妇女6859名、0-2岁婴幼儿16481名和8-10岁儿童3198名。通过问卷形式收集调查对象的人口学因素和膳食情况，共收集问卷4865份。**结果：**2012年河南省育龄妇女、孕妇、哺乳期妇女、0-2岁婴幼儿和8-10岁儿童的尿碘中位数分别为205  $\mu\text{g/L}$ 、198  $\mu\text{g/L}$ 、167  $\mu\text{g/L}$ 、205  $\mu\text{g/L}$ 和200  $\mu\text{g/L}$ 。高收入、膳食中摄入更多的禽类和鱼类因素与尿碘浓度呈正相关，而低盐膳食、膳食中摄入更多的大米和蔬菜与尿碘浓度呈负相关。**结论：**按照WHO的标准，河南省重点人群的碘营养状况总体适宜，但育龄妇女和8-10岁儿童的尿碘浓度略高于适宜水平。食盐中碘浓度调整后，对重点人群的碘营养状况进行监测是十分必要的。

**关键词：**碘、生育、妊娠、哺乳、儿童