Original Article

Iodine status and thyroid function of pregnant, lactating women and infants (0-1 yr) residing in areas with an effective Universal Salt Iodization program

Yanling Wang PhD[1,2], Zhongliang Zhang MS[3], Pengfei Ge MS[2], Yibo Wang SD[1], Shigong Wang MS[4]

[1]*College of Earth and Environment Sciences, Lanzhou University, Lanzhou Gansu, China*
[2]*Gansu center for diseases control and prevention, Lanzhou Gansu, China*
[3]*The first people hospital of Lanzhou city, Lanzhou Gansu, China*
[4]*College of Atmospheric Sciences, Lanzhou University, Lanzhou Gansu, China*

Objective: To assess the iodine nutrition and thyroid function of pregnant women, lactating women and infants residing in areas where the Universal Salt Iodization program is in place. Methods: Pregnant women, lactating women and infants were selected randomly in the regions where iodized salt coverage rate is more than 90% since 2000. Urine iodine levels of pregnant woman, lactating woman and infants, milk iodine of lactating woman, thyroid-stimulating hormone (TSH) and free T4 of women were tested respectively. Results: Median Urinary Iodine (MUI) of infants, three groups of pregnant women (first, second and third trimester) and two groups lactating women (breastfeeding less than or more than six months) were 233, 174, 180, 147, 126 and 145 μg/L, respectively. Median milk iodine of lactating women was 163 μg/L. Percentage of milk iodine < 150 μg/L of early lactating women was 40% less than that of late lactating women ($p < 0.01$).There was a positive correlation between urine iodine of infants and milk iodine of lactating women ($r = 0.526$, $p = 0.000$). T4 of two women were above or below the reference range. Total 15.4% women's TSH were abnormal. Most of these women's urinary iodine were lower than 150 μg/L. Conclusion: Iodine status of most of the target population for Universal Salt Iodization program is adequate, but iodine deficiency still existed in some. To assure every new life's brain not be damaged by iodine deficiency, iodine status of targeted populations should be monitored and supplements provided according to the monitoring outcomes.

Key Words: iodine nutrition, iodized salt, thyroid hormone, urine iodine concentration, milk iodine concentration

INTRODUCTION

Iodine deficiency (ID) has multiple adverse effects on growth and development in humans. Those are collectively termed the iodine deficiency disorders (IDD) and are one of the most important and common human diseases. [1, 2] Pregnant and lactating women and infants are most susceptible to iodine deficiency disorders. In the pregnant and lactating woman, iodine deficiency is related to disorders that affect mothers and fetuses: increased early and late miscarriage, intellectual disability, endemic cretinism, neonatal hypothyroidism, neonatal hyperthyroitropenemia, increased perinatal and infant mortality, and growth retardation. During the period of brain development, even mild iodine deficiency can cause damage. In order to protect the intelligence of those at risk, pregnant, lactating women and infants less than two years old are the targeted in iodine deficiency disorders (IDD) prevention and control.

Iodine is one of the essential trace elements for infant's growth and development. Currently the whole world is still facing a threat of iodine deficient disease. Iodine deficiency causes maternal hypothyroxinemia, which affects pregnant women even in apparently iodine-sufficient areas, and often goes unnoticed because L-thyroxine (T4) levels remain within the normal range, and thyroid-stimulating hormone (TSH) is not increased. Even a mild hypothyroxinemia during pregnancy increases the risk of neurodevelopmental abnormalities, and experimental data clearly demonstrate that it damages the cortical cytoarchitecture of the fetal brain. [3] Iodine status of breastfed infants depends on the concentration of iodine in breast milk. The activities of sodium/iodine symporter and 5'- deiodinase in mammary glands increases the concentration and activity of iodine in breast milk. Hence, the iodine status of breastfed infants is better than that of formula fed infants. However, the iodine concentration in human milk varies widely due to environmental, pharmacological and maternal physical factors,

Corresponding Author: Dr. Yanling Wang, Gansu center for diseases control and prevention, Duanjiatan 371, Lanzhou Gansu 73020, PR China
Tel: +86-931-4678766; fax; Fax: +86-931-4695985
Email: wylxiao@126.com
Manuscript received 6 October 2008. Initial review completed 5 March 2009. Revision accepted 6 March 2009.

and this change poses an important effect on infant's growth and development.

Fortification of salt with iodine has been recognized as the most effective and cost-efficient strategy to prevent iodine deficiency disorders. Universal salt iodization was carried out in 1995 in China. The initial iodization level was set at 50 mg/kg (50 ppm), later reduced in 2000 to 35 ppm after national monitoring by urinary iodine concentration showed this intake to be excessive, the medians of urinary iodine of schoolchildren, at provincial level, were over 300 μg/L in 18 and 14 provinces in 1997 and 1999, respectively. [4,5] It is important to know if iodine status of pregnant women, lactating women and infants can be determined and to know the status of women's thyroid function at present iodine salt concentration.

MATERIALS AND METHODS

Subjects

Yongjin County was selected as study site where iodized salt coverage rate is more than 90% since 2000. Yongjin County located in Gansu province is one of the iodine deficient regions in China. More than 90% of the drinking water has a iodine content of less than 10 μg/L in Gansu. Gansu province was classified in 1995 as having a severe level of IDD according to the WHO/UNICEF/ICCIDD criteria with a total goiter rate in school children of 38.7% and median urinary iodine level of 120 μg/L. After ten years of Universal Salt Iodization (USI), the total goiter rate in school children was 13.5%, median urinary iodine level was 192μg/L and qualified iodized salt consumption rate was 88.9%. The urban sites of Yongjin County were divided into five geographic locations (east, south, west, north and center). In each location, one community was identified and ten samples of each group were selected randomly (three groups of pregnant women, first, second and third trimester, and two groups lactating women, breastfeeding less than and more than six months, and their infants). All women included in study were demanded residing in Yongjin city for more than five years. A total of 125 healthy pregnant women (first, second and third trimester), 100 healthy lactating women and their 61 healthy infants (0-1 yr) who had no previous history of thyroid disease or medications that affect thyroid status, were sequentially admitted into the study. These subjects were asked to provide casual samples of urine for iodine analyses. Pregnant and lactating women provided samples of serum for free T4 and TSH analyses, and at the same time lactating women provided samples of breast milk for iodine analyses. Because only some women provided urinary, breast milk or blood samples, the number of urinary, breast milk and blood samples differed from the total number of subjects.

The study was approved by the local institutional ethics committee. Before the study, the study was explained to the women and consents were obtained.

Measurement

Casual urine samples were collected from the above five groups of people and in bottles tightly sealed and refrigerated at 4°C until laboratory analysis. Iodine in urine was measured by the National standard method of China's Ministry of Health [6], based on the catalytic effect of iodine on the reaction between cerium IV and arsenic III, adapted from the general Sandell-Kolthoff technique recommended by ICCIDD. [7] The WHO/ UNICEF/ICCIDD established, for a given population (including lactating women), that the median urinary iodine concentrations (UICs) must be 100-199 μg/L in clinically healthy subjects and 150-249 μg/L in clinically healthy pregnant women. [8] Breast milk iodine was measured by similar adaptations after appropriate digestion [9, 10]. Non-fasting bloods were obtained from five groups of women. Serum was prepared by centrifugation within 2h of blood collection and frozen at -20°C until analysis of thyroid hormones. T4 and TSH were measured by chemiluminescent immunoassay (CLIA). The Reference range for T4 was 0.65-2.3 ng/dL and TSH was 0.4-4.0 μIU/mlL

Statistical methods

Statistical analysis was performed using SPSS for Windows (Version 10.0). Non-parametric analyses (chi-square tests and median tests) were used for comparisons among groups. Pearson test was used for correlation analysis of urinary iodine concentrations, milk iodine concentrations of lactating women, and urinary iodine concentrations of infants.

RESULTS

Urinary iodine concentration

Infants

The median urinary iodine (MUI) of infants was 233μg/L which reached the MUI criterion recommended by WHO/UNICEF/ICCIDD (1)(Table 1).

Pregnant women

Urinary iodine medians of pregnant women in the first, second, third trimesters were 174 μg/L, 180 μg/L and 147 μg/L respectively. That of all pregnant women was 169 μg/L (Tables 2). With the exception of pregnant women in the third trimester (147 μg/L), the urinary iodine medians of pregnant women in the first and second trimesters were in the 150-249 μg/L range defined as optimal by

Table 1. Urinary iodine values of infants

N	Median urinary iodine concentration (μg/L)	Frequency distribution (%)			
		< 100	100-199.9	200-299.9	≥ 300
61	233	9.8 (6)	27.9 (17)	21.3 (13)	41.0 (25)

Figures in parentheses are the number of infants

Table 2. Urinary iodine values of pregnant women during each trimester of pregnancy

Trimester of pregnancy	Total samples	Median urinary iodine concentration (μg/L)	Samples with UIC < 50 μg/L	Samples with UIC ≥ 150 μg/L
First	30	174	3.3 (1)	56.7% (17)
Second	47	180	4.3 (2)	63.8% (30)
Third	48	147	8.2 (4)	47.9% (23)
All	125	169	5.6 (7)	56.0% (70)

Figures in parentheses are the number of pregnant women.

Table 3. Urinary iodine values of lactating women

Lactating women	Total samples	Median UIC (μg/L)	Samples with UIC < 50 μg/L	Samples with UIC ≥ 150 μg/L
Breastfeeding Less than six months	48	126	14.6 (7)	33.3% (16)
Breastfeeding more than six months	52	145	11.5 (6)	46.2% (24)
All	100	136	13.0 (13)	40.0% (40)

Figures in parentheses are the numbers of lactating women.

Table 4. Median iodine content in breast milk of lactating women (μg/L)

Lactating women	n	Median（μg/L）	iodine content in milk	
			<100 μg/L	< 150 μg/L
Breastfeeding Less than six months	49	240 (47.33-875)	10.2%(5)	24.5%**(12)
Breastfeeding more than six months	48	122(16.48-391)	25.0%(12)	64.6%**(31)
All	97	163 (16.48-875)	17.5%(17)	44.3% (43)

** $p<0.01$

WHO/UNICEF/ICCIDD.(1)

Lactating women

The median urinary iodine concentration in two groups of lactating women were 126 μg/L and 145 μg/L respectively (Table3), which reached the MUI criterion (≥ 100 μg/L) recommended by WHO/UNICEF/ICCIDD. [8] The frequency distribution of urinary iodine of lactating women is shown in Figure 1.

Iodine concentrations in human milk

Table 4 shows iodine values in breast milk of lactating women. The breast milk iodine median of 163 μg/L in all lactating women was within the optimal range of 100-200 μg/L. [11,1213] The breast milk iodine medians was 240μg/L in the women lactating for less than 6 months and was 122 μg/L in the women lactating longer than 6 month.

Table 5. Comparison of iodine concentrations in breast milk and urine of lactating women.

Lactating women	N	Breast milk Iodine median (μg/L)	Median urinary iodine concentration （μg/L）	Breast milk iodine more than urinary iodine concentration (%)	Breast milk iodine less than urinary iodine concentration (%)
Breastfeeding less than six months	47	240	126	80.90%	19.10%
Breastfeeding more than six months	47	122	145	48.90%	51.10%

The percentage of breast milk iodine < 150 μg/L of women lactating for less than 6 months was 40% less than that of women lactating for longer than 6 months ($p < 0.01$). Breast milk iodine excretion significantly decreased in women lactating of longer than 6 months. Although iodine is concentrated by the mammary gland, 17.5% of all lactating women had low iodine concentrations (< 100 μg/L) in their breast milk.

Comparing iodine concentrations in breast milk and urine of lactating women.

Of women breastfeeding less than six months, 80.9% had higher breast milk iodine concentrations than urinary iodine concentrations, while 48.9% of women breastfeeding more than six months had breast milk iodine concentrations higher than urinary iodine concentrations ($p < 0.01$). That showed that iodine concentrations in mammary glands during early lactation was greater than what was found when a women had been lactating for longer than 6 months (Table 5).

Relationship among urinary iodine concentrations and breast milk iodine concentrations in lactating women and urinary iodine concentrations in infants

We found a positive correlation between the urinary iodine concentrations in infants and the breast milk iodine concentrations of lactating women, ($r = 0.526$, $p < 0.01$). There were no correlation relationships among urinary iodine concentrations of lactating women, breast milk

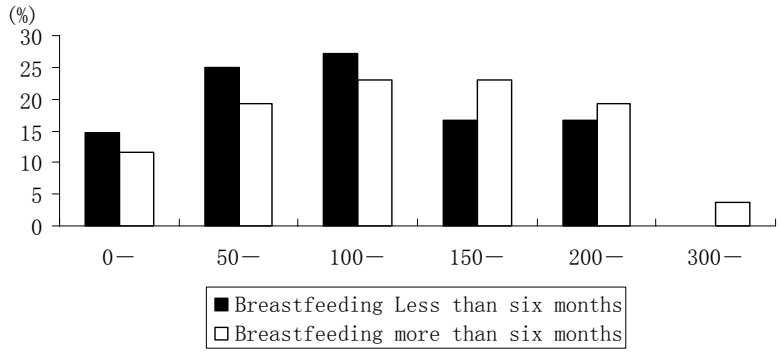

Fig 1. Frequency distribution of urinary iodine of lactating women

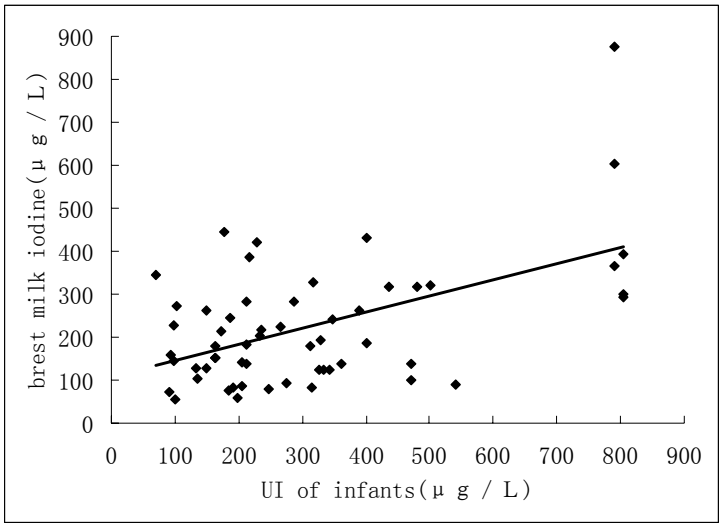

Fig 2. A positive correlation between the milk iodine concentrations of lactating women and the urinary iodine concentrations of their infants by scatter plot (no. =57 sites).

Table 6. Thyroid-stimulating hormone and free T4 in pregnant and lactating women

Women	Total samples	TSH median (μIU/mL)	Abnormal TSH (%)	T4 median (ng/dL)	Abnormal T4 (%)
Pregnant (first Trimester)	30	1.545 (0.41-3.57)	0 (0)	1.3 (1.00-1.60)	0 (0)
Pregnant (second Trimester)	47	1.99 (0.37-8.70)	14.9% (7)	1 (0.84-1.40)	0 (0)
Pregnant (third Trimester)	50	2.41 (0.15-6.96)	22% (11)	1.1 (0.93-1.50)	0 (0)
Lactating women (< 6 months)	49	1.775 (<0.002-5.53)	14.3% (7)	1 (0.82-1.60)	0 (0)
Lactating women (> 6 months)	52	2.605 (<0.002->75)	19.2% (10)	1.2 (0.36-3.20)	3.8% (2)
All	228	1.98 (<0.002->75)	15.4% (35)	1.1 (0.36-3.20)	0.9% (2)

Table7. Relationship between urinary iodine and thyroid function of women

Groups	N	TSH (μIU/mL)		T4 (ng/dL)	
		Median	Abnormal (%)	Median	Abnormal (%)
<150 μg/L	114	1.95	64.7% (22)	1.1	50%(1)
>150 μg/L	110	2.01	35.3% (12)	1.1	50%(1)
All	224	1.98	100% (34)	1.1	100%(2)

iodine concentrations of lactating women and urinary iodine concentrations of their infants. Figure 2 shows positive correlation between urinary iodine concentrations in infants and breast milk iodine concentrations of lactating women by scatter plot.

TSH and FT4 concentrations

The reference range of T4 was 0.65-2.3 ng/dL and that of TSH was 0.4-4.0 μIU/mL. TSH concentrations of 15.4% of all women were above or below the reference range, among that 11% of TSH were > 4.0 μIU/mL. Only one woman had T4 concentrations above the reference range and one was below the reference range (Table 6).

Relationship between urinary iodine and thyroid function

The women were divided into two groups (lower and higher urinary iodine groups) according to the urinary iodine cut-off of 150 μg/L. The percentage of TSH outside the normal range was 64.7% in women with regard to urinary iodine < 150 μg/L and 35.3% in women with urinary iodine > 150 μg/L. The percentage of TSH outside the normal range in women with lower urinary iodine was higher than that in women with higher urinary iodine, which indicated that women with lower urinary iodine concentrations may have a higher risk of developing thyroid function disorders than those with higher urinary iodine concentrations (Tables 7).

DISCUSSION

Iodine deficiency is the most important preventable cause of mental retardation worldwide. The most critical period for brain development is from the second trimester of pregnancy to the third year after birth. [14, 15] Normal levels of thyroid hormones are required for optimal development of the brain. To prevent iodine deficiency disorders, the WHO/UNICEF/ICCIDD established that the median

UICs must be 100-199 μg/L in clinically healthy subjects and 150-249 μg/L in clinically healthy pregnant women for a given population. [7, 16] According to the results of urinary iodine median in the current study population, it is indicated that pregnant women, lactating women and infants are within the range of optimal iodine status. But iodine deficiency still existed in some samples like third trimester pregnant women. These outcome are consistent with results from other studies which showed even in areas with adequate iodide intake, a significant proportion of pregnant women have UICs below the recommended level. [17, 18, 19]

Infants mainly obtain iodine from the breast milk especially within six month after birth. This study showed a positive correlation between iodine in urine of infants and breast milk, which indicated that the infants' iodine status is affected by the mother's iodine status. In addition, the activities of sodium/iodine symporter and 5'- deiodinase increases the activity and concentration of iodine in mammary glands. Hence, the iodine status of breastfed infants is better than that of formula fed infants. The advantages of beast-feeding are indisputable. However, the iodine concentration in human milk varies widely due to environmental, pharmacological and maternal physical factors, and this change has a significant effect on infant growth and development. This study found a significant decrease in milk iodine from women breastfeeding for more than six months. Even with an effective universal salt iodization program, some lactating women still had low iodine concentrations (< 100 μg/L) in their breast milk.

Thyroid hormone is important for growth and development especially for the brain during the fetal period and the first years of life. Brain development of infants has a obvious relationship with their mother's thyroid function and special attention will be paid to the role of thyroid hormone in the relationship between the mother and the fetus. Some study showed that relative hypothyroxinemia in the first trimester is a potential risk for neurodevelopment of child. [20,21]Studies by Man et al. and by Haddow et al, were carried out in pregnant women from the USA and showed respectively, the central nervous system(CNS) deficits in children born to mothers with low circulating T4 during pregnancy, and with increased TSH at midgestation. T4 in three groups of pregnant women were within the reference range. Total 15.4% women's TSH were abnormal, among that 11% was above the high value of reference range. Most of these women had urinary iodine concentrations lower than 150μg/L. This indicated that TSH is more sensitive to low iodine status than T4 and a low iodine status increases the risk of thyroid function disorders.

Optimal iodine intake is necessary to fully realize the human intellectual capabilities in a community. Previous studies have shown that not only pregnant women in iodine-deficient regions [22,23,24] but also those residing in iodine-sufficient areas [17, 18, 19] may suffer from iodine deficiency. Supplementation with iodine during pregnancy results in increased FT4, decreased T3 to T4 ratios, decreased circulating Tg, and decreased thyroid volume, both in the mother and the newborn, without adverse effects[25]. In this study, we found that an effective iodized salt program can bring iodine sufficiency to most of the targeted population. But iodine deficiency still existed in some and further supplements such as taking iodine oil or eating more food with rich iodine are required. To prevent damage to both the mother and the newborn as a result of iodine deficiency, more attention should be paid to the target population. Monitoring of both iodized salt and iodine intake should be done to ensure that an optimal state of iodine status is reached and sustained.

ACKNOWLEDGEMENT

This work was supported by National Support Projects for Science and Technology in China (2006BAI06B05, 2008BAC40B04 and 2007BAC03A10) and the Project of National Natural Science Foundation of China (40675077).

AUTHOR DISCLOSURES

All authors declare that they have no financial interest in and have received no funding for the work presented in this paper.

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Original Article

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Yanling Wang PhD[1,2], Zhongliang Zhang MS[3], Pengfei Ge MS[2], Yibo Wang SD[1], Shigong Wang MS[4]

[1]*College of Earth and Environment Sciences, Lanzhou University, Lanzhou Gansu, China*
[2]*Gansu center for diseases control and prevention, Lanzhou Gansu, China*
[3]*The first people hospital of Lanzhou city, Lanzhou Gansu, China*
[4]*College of Atmospheric Sciences, Lanzhou University, Lanzhou Gansu, China*

食盐加碘措施有效落实地区孕妇、哺乳期妇女及婴儿碘营养和甲状腺功能

本研究的目的是评价食盐加碘措施有效落实地区孕妇、哺乳期妇女及婴儿的碘营养状况及甲状腺功能。在碘盐覆盖率从 2000 年一直高於 90%的地区随机选择不同生理阶段的孕妇、哺乳期妇女及婴儿，采集其尿样进行尿碘检测，采集妇女的血样进行 T4 和 TSH 测定，同时采集哺乳期妇女的乳汁测定乳碘。早、中及晚期孕妇，哺乳不足半年及半年以上妇女及婴儿的尿碘中位数分别为 233、174、180、147、126 和 145 μg/L。乳汁碘中位数为 163 μg/L。哺乳早期妇女尿碘低於 150 μg/L 所占的比例小于哺乳晚期妇女 40% ($p < 0.01$)。婴儿尿碘与母亲乳汁碘之间存在正相关性 ($r = 0.526$, $p = 0.000$)。有两个妇女的 T4 值异常。共计 15.4%妇女的 TSH 异常，这些妇女尿碘值多数低于 150 μg/L。全民食盐加碘能满足大多数重点人群碘营养需要，但仍有部分人存在碘缺乏。为保证每个新生命免受因缺碘所造成的脑损伤，应对重点人群进行碘营养监测，并根据监测结果进行適度补充碘。

关键词：碘营养、碘盐、甲状腺激素、尿碘、乳碘