Attention to the hiding iodine deficiency in pregnant and lactating women after universal salt iodization: A multi-community study in China

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ABSTRACT. ***Background:*** **Monitoring of iodine nutrition depends chiefly on the urinary iodine concentration in representative samples from the population. International groups have recommended school-age children as a convenient group for surveys, because of their accessibility and young age, but the relevance of this group to others, especially pregnant women, is not well established.** ***Objective:*** **The purpose was to compare different approaches to assessing iodine nutrition within communities, especially for pregnant and lactating women.** ***Design:*** **In an urban and a rural site from each of the 11 Chinese provinces, covering a wide geographic and socioeconomic range, we measured the iodine content of household salt and drinking water, the thyroid volume in school children, and the urinary iodine concentration in five population subsets; in some sites we also assessed iodine in breast milk and thyroid size in adult women.** ***Results:*** **The median urinary iodine concentrations for pregnant and lactating women were well below those of the schoolchildren from the same community in most study sites, the difference between medians, at overall level, being about 50 µg/l for the pregnant and 40 µg/l for the lactating, respectively. When ranked by median urinary iodine concentrations at overall level, the order of the groups was: all infants, schoolchildren, women of childbearing age, lactating women and pregnant women in both urban and rural sites. This relative distribution was constant among the study sites. From it, we derived a relationship to predict the median values for other groups, based on the data of schoolchildren. The median iodine content of salt was 30.9 ppm in urban sites and 31.3 ppm in rural sites, respectively, close to the nationally mandated 35 mg/kg. Water had low iodine content (3.7 µg/l) in both urban and rural sites except in a rural site from Tianjin. Ultrasonography showed that 6.5% of 1329 children in urban sites and 5.3% of 1431 children in rural sites had thyroid enlargement. Breast milk had a median iodine content of 135.9 µg/l in the urban and 157.5 µg/l in the rural. The goiter prevalence by palpation was low (2.0%) among all women examined (3367), but higher in pregnant women (2.7%) than in lactating women or other adult women.** ***Conclusions:*** **An effective iodized salt program has brought iodine sufficiency to most of China, but pregnant women in some areas may still risk deficiency and need further supplements. We suggest other countries and international agencies pay more attention to pregnancy, where iodine deficiency has its worst consequences.**
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Key-words: Iodine nutrition, urinary iodine, iodized salt, pregnant women, lactating women.

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INTRODUCTION

In 1992, China had the world's largest iodine deficient population (1). A historic political decision in 1993 mandated that all salt for human consumption be adequately iodized, and this policy was implemented aggressively. 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 (2, 3).

Several national and international bodies have made recommendations for daily iodine intakes (4-8). While a general agreement exists for a recommended daily intake of about 150 µg iodine in non-pregnant non-lactating adults, the optimal amounts in children, pregnancy and lactation are less well defined. For example, recommended amounts during pregnancy range from 140 to 230 µg per day; the two most recent and detailed are the US Food and Nutrition Board (FNB, 2001) and ICCIDD/UNICEF/WHO (2001), recommending, respectively, 220 and 200 µg in pregnancy and 290 and 200 µg in lactation.

The currently favored laboratory test for surveying iodine nutrition in populations is the median iodine concentration in urine (5, 9). Over 90% of ingested iodine eventually appears in urine, specimens are easy to obtain in the field, and casual samples correlate fairly well with complete 24 h collections and with iodine: creatinine ratios. The ICCIDD/UNICEF/WHO document recommended testing urinary iodine in school-age children because of their accessibility in surveys, but neither ICCIDD/UNICEF/WHO nor the FNB addressed how these translate to other segments of the population. Pregnancy is especially important because the developing human is most susceptible to the damaging effects of iodine deficiency, iodine needs are greater, the renal clearance for iodine is increased and salt intake is frequently restricted in some pregnant women.

We have approached the issue of optimal assessment of iodine nutrition by comparing data of school-age children, infants, pregnant and lactating women, and other women of childbearing age residing in the same communities.

MATERIALS AND METHODS

Subjects and study design

We selected 11 provinces according to their geographic, social and economic conditions (Fig. 1). Six-Beijing, Shanghai, Tianjin, Liaoning, Guangdong and Jiangsu province are coastal, eastern, or central areas with a high economic level and good coverage with iodized salt. The remaining five – Inner Mongolia, Shaanxi, Sichuan, Guizhou, and Xinjiang – are in western China, with poorer economy and lower iodized salt coverage. Within each, we chose one urban site (a community of urban resident) and one rural site (a township of rural resident), considered typical for the province, and examined 100 subjects in each of the following five groups in each selected study site: school-age children (age 8-10 yr; the number of children for each age group should be equal); women of childbearing age (20-40 yr); pregnant women (second or third trimester); lactating women; and infants (0-2 yr). The pregnant subjects were consecutively collected in the central women health care of the selected urban and rural site; schoolchildren came from the central primary school of the selected urban and rural site; childbearing aged women came from 5 sub-communities of selected urban site and 5 villages of selected rural site (20 subjects for each from different direction in which their houses located); lactating women and

Fig. 1 - *11 provinces were selected by their location, economic level and coverage of adequately iodized salt.*

their infants usually came from at least 5 sub-communities and 5 villages of selected urban and rural site, respectively, until 100 subjects were collected. These subjects were asked to provide casual samples of urine and household salt for iodine analyses. Fifty drinking water samples were collected from the childbearing aged women households, and 50 lactating women provided samples of breast milk.

Measurement

Iodine was measured in urine by the National standard method of China's Ministry of Health (10), adapted from the general Sandell-Kolthoff technique recommended by ICCIDD (9). Iodine was measured in water and breast milk by similar adaptations after appropriate digestion (11, 12), and in salt by the National standard method of titration (13). We determined thyroid size by ultrasonography in schoolchildren, and defined goiter as above the 97th percentile of thyroid volume by age, using national reference values for iodine sufficient Chinese children, in which the cutoff values are 4.5 ml for age 8 yr, 5.0 ml for 9 yr, and 6.0 ml for 10 yr (14). Goiter was assessed in adult women by palpation, using the classification system of ICCIDD/UNICEF/WHO (5).

Statistical analysis

Results were analyzed by SPSS (version 10.0). Values for iodine concentration in urine, salt and drinking water are reported as medians. Non-parametric analyses (Kruskal-Wallis and Median tests) were used for comparisons among groups. Pearson test was used for correlation analysis between medians of urinary iodine concentrations of school children and other population groups.

RESULTS

Iodine in household salt and water

Table 1 shows that the median iodine content of salt, at overall level, was 30.9 ppm in urban sites and 31.3 ppm in rural sites, respectively, with little variation among the study sites or among the different provinces. This level is close to the nationally mandated 35 ppm at production, and shows good distribution of adequately iodized salt in most sites investigated in this survey. The median iodine content of household drinking water was low (3.7 µg/l) in both urban and rural sites, reflecting that natural iodine deficiency extensively exists (Table 2). Water from the rural Tianjin site reflected the natural high iodine content of its particular underground source (261 µg/l) and correlated with high urinary iodine concentrations in all population groups examined there (350-700 µg/l). This site was not included in calculating the overall values for the rural sites, but was in the comparisons among groups residing in the same community.

Urinary iodine concentration

The medians for the five test groups in all study sites were >100 µg/l (Tables 3 and 4) with an exception of lactating women in the urban site from Sichuan province (96.2 µg/l), which indicated fairly satisfied iodine nutrition for all group populations investigated. The medians for schoolchildren from five urban sites of Beijing, Shanghai, Tianjin, Liaoning and Sichuan and from four rural sites of Beijing, Shanghai, Guizhou and Xinjiang were in the 100-200 µg/l range defined as optimal by ICCIDD/UNICEF/WHO (5). Two urban sites from Jiangsu and Shaanxi and four rural sites from Tianjin, Liaoning, Inner Mogolia and Shaanxi (total 6 out of 22 study sites) had medians over 300 µg/l in schoolchildren, suggesting excessive iodine intake. The medians for pregnant women in four urban and two rural sites were <150 µg/l, while these values for lactating women were found in two urban and two rural sites. The 150 µg/l of median

Table 1 - *Median iodine content in household salt (mg/kg).*

Province	Urban site	Rural site	Both
Beijing	28.0 (394)	29.6 (423)	28.8 (817)
Shanghai	30.1 (404)	32.2 (402)	31.4 (806)
Tianjin	30.0 (400)	31.0 (400)	30.0 (800)
Guangdong	31.7 (1246)	32.8 (1204)	31.7 (2450)
Liaoning	25.3 (400)	29.8 (410)	27.6 (810)
Jiangsu	30.6 (406)	32.6 (495)	31.2 (901)
Inner Mongolia	30.4 (400)	27.5 (400)	29.2 (800)
Shaanxi	30.4 (436)	31.6 (600)	31.2 (1036)
Sichuan	36.7 (400)	21.4 (400)	32.8 (800)
Guizhou	35.2 (400)	33.4 (386)	34.2 (786)
Xinjiang	32.6 (385)	31.7 (396)	32.2 (781)
All	30.9 (5271)	31.3 (5116)	31.0 (10387)

Figures in parentheses are numbers of sample.

Table 2 - *Median iodine content in household drinking water (µg/l).*

Province	Urban site	Rural site	Both
Beijing	1.6 (15)	1.4 (6)	1.5 (21)
Shanghai	1.7 (49)	3.3 (51)	2.8 (100)
Tianjin	9.6 (51)	261.2 (50)*	9.6 (51)
Guangdong	15.4 (163)	3.9 (309)	7.3 (472)
Liaoning	3.3 (50)	5.0 (56)	3.4 (106)
Jiangsu	0.0 (50)	18.1 (14)	4.3 (64)
Inner Mongolia	3.7 (10)	24.6 (30)	15.4 (40)
Shaanxi	26.4 (48)	3.9 (75)	6.6 (123)
Sichuan	0.8 (50)	1.8 (49)	0.9 (99)
Guizhou	3.9 (52)	1.0 (46)	3.8 (98)
Xinjiang	3.6 (64)	3.4 (52)	3.5 (116)
All	3.7 (602)	3.7 (688)	3.7 (1290)

Figures in parentheses are numbers of sample.
*High iodine was found in drinking water from the Tianjin rural site, and this result was not included in the overall tally.

Table 3 - *Median urinary iodine concentration in 5 groups of population from urban sites of 11 provinces (μg/l).*

Province	Schoolchildren	Women of childbearing age	Pregnant women	Lactating women	Infants	All groups
Beijing	172.4 (99)	140.8 (108)	123.2 (104)	165.3 (99)	241.8 (99)	163.2 (509)
Shanghai	109.2 (94)	128.0 (100)	112.9 (100)	157.4 (110)	269.4 (100)	138.6 (504)
Tianjin	165.4 (100)	295.0 (100)	156.0 (100)	262.2 (100)	164.7 (100)	205.4 (500)
Guangdong	264.1 (321)	271.9 (338)	182.4 (294)	243.6 (262)	259.0 (269)	242.8 (1484)
Liaoning	195.8 (100)	179.8 (100)	168.6 (100)	129.4 (100)	132.5 (100)	165.5 (500)
Jiangsu	370.8 (100)	428.2 (105)	247.3 (100)	200.3 (107)	427.4 (100)	344.6 (512)
Inner Mongolia	203.4 (100)	192.9 (100)	151.0 (100)	181.8 (100)	229.8 (100)	187.6 (500)
Shaanxi	334.0 (101)	310.8 (94)	183.9 (107)	170.4 (119)	229.5 (121)	237.2 (542)
Sichuan	141.0 (100)	107.4 (100)	128.8 (100)	96.2 (100)	161.5 (100)	128.6 (500)
Guizhou	281.1(100)	247.2 (100)	234.7 (100)	289.4 (100)	231.3 (100)	247.8 (500)
Xinjiang	244.3 (103)	146.9 (87)	130.8 (91)	237.3 (98)	268.6 (90)	188.7 (469)
All	226.8 (1318)	217.8 (1332)	165.6 (1296)	188.6 (1295)	235.5 (1279)	205.5 (6520)

Figures in parentheses are numbers of sample.

urinary iodine concentration was recommended as optimal for pregnancy and lactation by the National IDD Advisory Committee to China's Ministry of Health. When we compared the medians between schoolchildren and pregnant or lactating women, the medians of pregnant and lactating women well below those of the schoolchildren were found in 20 and 17 out of 22 study sites, respectively. The medians of pregnant women, at overall level, were respectively about 60 and 40 μg/l lower than the schoolchildren in urban and in rural sites, while these values of lactating women were about 40 μg/l lower in both urban and rural sites. When ranked by median urinary iodine concentrations, at overall level, the order of the groups was all infants, schoolchildren, women of childbearing age, lactating women and pregnant women in both urban and rural sites.

Table 4 - *Median urinary iodine concentration in 5 groups of population from rural sites of 11 provinces (μg/l).*

Province	Schoolchildren	Women of childbearing age	Pregnant women	Lactating women	Infants	All groups
Beijing	221.0 (92)	137.3 (100)	165.4 (119)	190.3 (107)	255.6 (107)	202.6 (525)
Shanghai	130.0 (106)	146.7 (102)	113.8 (100)	124.0 (96)	193.1 (101)	141.0 (505)
Tianjin*	418.8 (100)	403.9 (100)	350.4 (100)	425.3 (100)	697.0 (100)	443.0 (500)
Guangdong	203.7 (321)	222.6 (304)	178.7 (312)	193.0 (312)	266.6 (308)	215.6 (1557)
Liaoning	326.4 (104)	156.9 (105)	164.1 (101)	172.4 (100)	259.0 (100)	211.2 (510)
Jiangsu	285.0 (100)	359.6 (101)	271.8 (77)	219.9 (99)	509.8 (105)	321.5 (482)
Inner Mongolia	375.8 (100)	345.0 (100)	234.9 (100)	190.4 (100)	336.7 (100)	295.8 (500)
Shaanxi	338.8 (150)	352.8 (150)	268.0 (150)	305.8 (150)	353.3 (149)	319.2 (749)
Sichuan	231.3 (100)	169.2 (100)	171.4 (99)	228.0 (100)	173.2 (100)	189.2 (499)
Guizhou	152.3 (100)	205.2 (107)	136.8 (101)	143.2 (100)	138.8 (100)	151.2 (508)
Xinjiang	163.0 (92)	180.8 (95)	196.3 (91)	187.0 (95)	204.7 (88)	185.4 (461)
All	233.5 (1265)	221.3 (1264)	190.6 (1250)	192.1 (1259)	247.3 (1258)	216.3 (6296)

Figures in parentheses are numbers of sample.
*The urinary iodine concentrations of 5 groups in Tianjin rural site were all higher than other sites due to the high iodine in drinking water, so the result was not included in the overall tally.

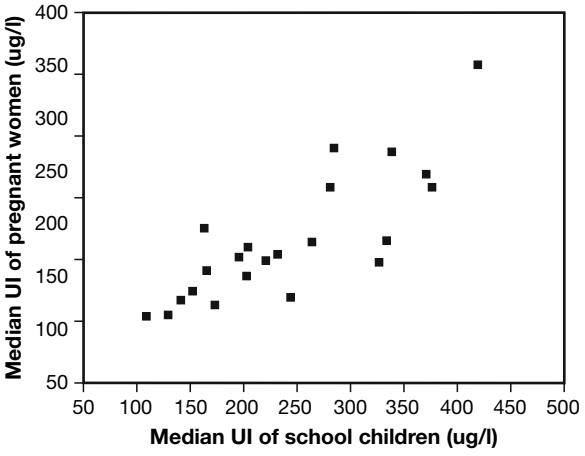

Fig. 2 - *A positive correlation between the median urinary iodine concentrations of pregnant women and schoolchildren by scatter plot (no.=22 sites).*

Relation of urinary iodine concentrations in schoolchildren to those in other groups

Schoolchildren are frequently used to assess community iodine nutrition, and we found a good correlation between their median urinary iodine concentrations and those of the other groups, particularly, a very good correlation with pregnant women ($r=0.814$, $p<0.01$). Figure 2 shows the good positive correlation of medians of urinary iodine between schoolchildren and pregnant women by scatter plot; this relationship was also found between schoolchildren and other groups. Table 5 shows how the median urinary iodine concentration in schoolchildren can be used to forecast that in the other groups residing in the same community. For this purpose, the categories of pregnant and lactating women were combined, because these two groups represent the period in human development most vulnerable to iodine deficiency.

Iodine in human milk

Table 6 shows values taken from 10 study sites of 6 provinces. The overall medians of 135.9 µg/l in the urban and 157.5 µg/l in the rural are all within the optimal range of 100-200 µg/l (15-17).

Thyroid size

The medians of thyroid volume by ultrasound in the schoolchildren in urban and rural sites were all 3.3 ml (Table 7). By reference to the Chinese national standard volumes for iodine sufficiency, 6.5% in the urban and 5.3% in the rural were classified as goitrous. The higher goiter rates were found mostly in those provinces located in western or middle parts of the country with a poorer economy and lower iodized salt coverage.
Estimation of thyroid size by palpation showed a higher incidence of goiter in pregnant women (2.7%) compared to the lactating women (1.8%) and other adult women (1.7%). However, the overall incidence of goiter in all women was low (2.0%).

DISCUSSION

Our results provide a useful comparison of iodine nutrition among several population groups within communities. They offer impressive evidence that in these 22 study sites from 11 provinces, the schoolchildren are now iodine sufficient. The concentrations of iodine in infant urine and in breast milk point to iodine sufficiency in the very young as well. Salt from households uniformly contained an acceptable amount of iodine. These findings could show, to a certain extent, that China's public health campaign to eliminate iodine deficiency with iodized salt has generally been quite successful.
Schoolchildren are the conventional group for assessing community iodine nutrition, because they are readily available and reflect recent rather than remote iodine availability, but we need to ask whether adequate iodine intake in them ensures that pregnant women in the same community are iodine sufficient. Pregnant women are of special concern, because iodine deficiency during

Table 5 - *Forecasted values for other groups based on the median urinary iodine of school children.*

Median urinary iodine of schoolchildren (µg/l)	Forecasted values of median urine iodine (µg/l)		
	Women of childbearing age	Pregnant and lactating women	Infants
100	112.1	106.4	124.7
150	154.7	134.0	176.8
200	197.2	161.7	228.9
250	239.8	189.4	281.0
300	282.4	217.1	333.2

Table 6 - *Median iodine content in milk of lactating women from 10 study sites of 6 provinces (μg/l).*

Province	Urban site	Rural site	Both
Tianjin	132.4 (53)	–	132.4 (53)
Guangdong	234.1 (54)	127.0 (122)	147.7 (176)
Jiangsu	126.4 (56)	204.3 (58)	167.2 (114)
Inner Mongolia	127.7 (50)	179.4 (100)	169.1 (150)
Shaanxi	130.3 (101)	125.2 (66)	127.8 (167)
Sichuan	110.0 (50)	–	110.0 (50)
All	135.9 (364)	157.5 (346)	145.7 (710)

Figures in parentheses are numbers of sample.

fetal development can produce a host of serious consequences, including fetal mortality and irreversible brain damage. The iodine requirement during pregnancy is increased to provide for the needs of the fetus and to compensate for the increased loss of iodine in urine due to increased renal clearance of iodine during pregnancy (18-20). Thus, the ICCIDD/UNICEF/WHO and FNB guidelines suggest a RDA of 200-220 μg iodine during pregnancy (5, 7). For a typical daily urine volume of 1.5 l, this means its iodine concentration should be at least 135-150 μg/l, considerably higher than the 100 μg/l cutoff for iodine sufficiency in non-pregnant adults. In view of these considerations, the National IDD Advisory Committee to China's Ministry of Health has recommended that the median urinary iodine during pregnancy and lactation should be greater than 150 μg/l (21). More recently, Dr. Delange (ICCIDD) proposed that the median level of urinary iodine indicating optimal iodine nutrition during pregnancy and lactation is in the range of 150-230 μg/l based on his extensive and critical review of relative literature (22).

In this study, pregnant women in 6 study sites from 5 provinces and lactating women in 4 study sites from 4 provinces had median urinary iodine concentrations <150 μg/l. By comparison of medians of urinary iodine concentration between schoolchildren and pregnant women or lactating women, we found that the medians of pregnant and lactating women were below those of the schoolchildren in 20 and in 17 out of 22 study sites, respectively; the difference between medians being about 50 μg/l for the pregnant and 40 μg/l for the lactating (Tables 3 and 4). Applying the extrapolation from schoolchildren to pregnant women in Table 5, we see that the median urinary iodine in the schoolchildren would need to be nearly 200 μg/l to guarantee values of at least 150 μg/l in pregnant women. This presents a public health dilemma, because increasing the iodine content of salt to bring the intake to desirable levels during pregnancy carries the risk of iodine excess for the rest of the population. To address this concern, we propose the following approaches: 1) monitoring should include pregnant and lactating women as well as schoolchildren; 2) pregnant and lactating women should be encouraged to obtain additional iodine from other sources, such as vitamin/mineral preparations or iodine tablets; and 3) iodized oil administration in pregnancy should be considered, especially in some of the western provinces where iodized salt is not well covered.

Table 7 - *Thyroid volume and goiter rate in school children by ultrasound.*

Province	Median value of thyroid volume (ml)			Goiter rate by ultrasound (%)		
	Urban site	Rural site	Both	Urban site	Rural site	Both
Beijing	3.2 (100)	3.2 (100)	3.2 (200)	2.0	1.0	1.5
Shanghai	4.0 (94)	3.0 (106)	3.5 (200)	6.4	1.9	4.0
Tianjin	2.6 (100)	3.2 (100)	3.0 (200)	0.0	1.0	0.5
Guangdong	3.7 (321)	3.7 (325)	3.7 (646)	4.7	4.6	4.6
Liaoning	3.9 (100)	3.2 (104)	3.6 (204)	13.0	7.7	10.3
Jiangsu	1.8 (100)	2.6 (144)	2.2 (244)	0.0	1.4	0.8
Inner Mongolia	2.1 (100)	3.5 (100)	3.0 (200)	2.0	19.0	10.5
Shaanxi	3.2 (101)	3.4 (150)	3.3 (251)	6.9	8.7	8.0
Sichuan	2.5 (100)	2.8 (100)	2.6 (200)	3.0	4.0	3.5
Guizhou	4.2 (100)	3.2 (99)	3.6 (199)	28.0	5.0	16.6
Xinjiang	3.3 (113)	3.3 (103)	3.3 (216)	9.7	5.8	7.9
All	3.3 (1329)	3.3 (1431)	3.3 (2760)	6.5	5.3	5.9

Figures in parentheses are the numbers of subject.

While our data on the discrepancy in median urinary iodine concentrations between schoolchildren and pregnant women are limited to China, they likely apply elsewhere as well. For example, in NHANES III from the USA, pregnant women had a mean urinary iodine concentration of 154 µg/l, compared with means ranging from 178 to 265 µg/l in children aged 6-11 yr (23). From this discrepancy, the following questions may arise: Can the urinary iodine concentration of schoolchildren confirm adequate iodine nutrition for the other groups of population in a community? What is the optimal level of urinary iodine concentration for pregnant women? Extensive studies would be needed to answer these questions. However, our results suggest that more attention should be given to these special individuals, pregnant women, because they involve fetal development, the most vulnerable target for iodine deficiency.

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