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A cross-sectional research of iodine status of pregnant women in Chongqing, south-west China

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Abstract

Objective: To investigate whether implementation of a universal salt iodization (USI) programme has sufficient effects on pregnant women in Chongqing, the present study evaluated the iodine nutritional status of pregnant women living in Chongqing by spot urinary iodine concentration (UIC), to provide scientific suggestions to better meet the specific iodine needs of this vulnerable group.
Design: Cross-sectional design.
Setting: A random spot urine sample and household table salt sample were provided by each participant.
Participants: A total of 2607 pregnant women from twenty-six of thirty-nine districts/counties in Chongqing participated.
Results: The overall median UIC of pregnant women was 171·80 μg/l (interquartile range (IQR) = 113·85–247·00 μg/l) and 40·97 % (*n* 1057) of participants were iodine insufficient. The median iodine in table salt samples was 25·40 mg/kg (IQR = 23·10–28·30 mg/kg); 93·26 % (*n* 2406) of samples examined were found to be adequately iodized. Iodine nutritional status was not significantly different according to table salt iodization category. Trimester was identified to be statistically associated with UIC ($P < 0·01$). Seven districts/counties had median UIC below 150 μg/l and one district had median UIC of 277·40 μg/l.
Conclusions: The USI programme in Chongqing prevents iodine deficiency generally, but does not maintain iodine status within adequate and recommended ranges throughout pregnancy. Usage of non-iodized or unqualified iodized salt and the slight change of dietary habits of iodized salt in Chongqing may present a substantial challenge to fight iodine-deficiency disorders; more efforts are needed to ensure adequate iodine intake during pregnancy besides the USI programme.

Keywords
Pregnancy
Iodine deficiency
Iodized table salt
Cross-sectional research

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Iodine deficiency occurs when iodine intake falls below recommended levels. Inadequate iodine intake may affect all stages of life, especially during pregnancy, as iodine is an essential compound for producing thyroid hormones which play a critical role in normal metabolic activities and fetal development[1]. Absorption of iodine at sufficient level is essential for the fetus and mother's thyroid glands to function healthily[2]. The harmful effects due to low level of thyroid hormones in the blood are known collectively as iodine-deficiency disorders (IDD)[3]. The most devastating consequences of iodine deficiency for pregnant women include abortion, stillbirth and congenital anomalies, and for neonates and children include neonatal hypothyroidism and retarded mental and physical development[3], with the most critical period being from the second trimester of pregnancy to the third year after birth[3]. IDD were one of the most serious public health threats in China in the 1990s, with at least 8 million endemic cretinism cases[1,4]. Pregnant women and young children are the most susceptible populations because they require higher iodine intake to maintain both maternal and neonatal normal neurodevelopment. In 1994, epidemiological studies conducted in Chongqing demonstrated that 41·48 % of schoolchildren aged 7–14 years showed visible signs of goitre, with a median urinary iodine concentration (UIC) of 53·14 μg/l, and the iodine concentration in drinking-water was 3·34 μg/l. Most of the household table

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salt samples investigated were non-iodized, and Chongqing was identified as an endemic area of IDD[5].

Salt iodization is currently the most widely used strategy to control and eliminate IDD. China adopted salt iodization as its principal control strategy in 1993[6] and established a compulsory universal salt iodization (USI) programme in 1995. As a municipality directly under the central government in the south-west of China, Chongqing introduced a USI programme in 1997. Considerable progress for the general population nationwide has been achieved after two decades' mandatory use of iodized salt. China had virtually eliminated IDD by 2000[6], and surveillance data of the national evaluation in 2010 also suggested that many of the targets of the China IDD Elimination Program had been met as twenty-eight provinces had eliminated IDD and three had 'almost eliminated' it[7]. But regional differences in the iodine nutritional status of school-aged children and pregnant women among provinces still existed. According to China's 2011 National IDD Surveillance results[6], in fourteen provinces including Chongqing (plus Xinjiang corps) the median UIC of pregnant women was in the optimal range of 150–249 μg/l and that of school-aged children was between 200 and 299 μg/l, which is considered 'above requirements' by WHO. As the incidence of thyroid disease, in particular goitre, thyroiditis, hyper- and hypothyroidism and thyroid cancer, was reported to be rising in recent years[8], the risk of excessive iodine intake was overestimated[9], and iodine concentration in household table salt started to drop from 35 mg/kg ± 30 % during 2000–2011 to 20, 25 or 30 mg/kg ± 30 % in 2012 (Chinese Standard GB 26878-2011). Each province has been mandated to choose its own iodine content standard, taking account of the actual iodine nutrition of the local population in order to prevent both iodine deficiency and iodine excess. Chongqing chose the highest level of 30 mg/kg. Previous studies showed iodine deficiency still existed among some pregnant women even with generally adequate iodine intake[10–12]. It is important to regularly monitor the iodine status in the most susceptible and vulnerable groups because even mild iodine deficiency may impair neuropsychological and motor development in children[11]. The present study aimed to assess the iodine status of pregnant women in Chongqing after the implementation of new standards for salt iodization since 2012, in order to provide scientific suggestions to better meet the specific iodine needs of this vulnerable group.

Methods

Study design and sample collection

This was a cross-sectional study embedded in the 2016 China National IDD Surveillance Program led by the National Health Commission of the People's Republic of China. From May to October in 2017, twenty-six of thirty-nine districts/counties were randomly chosen from Chongqing according to China's national surveillance guidelines of the IDD surveillance programme[1,13]. In each surveillance county, five towns were randomly selected from five different geological locations (east, west, south, north and centre). In each selected town, a convenience sampling method was used to recruit twenty pregnant women into the study from one or two clinics where they attended the prenatal examination; pregnant women in an adjacent town could be selected as a supplement if there were fewer than twenty in the target town. Only those participants residing in the selected town for at least 6 months were qualified to enrol in the study. For each participant, approximately 10 ml of a random spot midstream urine sample was collected. Each participant also provided 50–100 g of household table salt and completed a brief interview to gather information such as the date of birth, weeks of pregnancy, history of thyroid disease and intake of iodine-containing supplements. Written informed consents were obtained from all participants prior to enrolment. All procedures involving research study participants were approved by the Ethical Review Committee of Chongqing Center for Disease Control and Prevention.

Determination of iodine concentration

Iodine content in table salt was measured using a titration method with sodium thiosulfate (Chinese Standard GB/T 13025.7-2012). UIC was determined using arsenic–cerium catalytic spectrophotometry (Chinese Standard WS/T 107.1-2016). All fourteen laboratories testing the iodine content in salt and UIC were participants of an internal quality control and an external quality assurance programme run by the Chinese Center for Disease Control and Prevention. Iodine levels of 5 % of urine and salt samples were re-examined in the reference laboratory of the Chongqing Center for Disease Control and Prevention for quality control purposes.

According to the epidemiological criteria for assessing iodine nutrition based on the median UIC of pregnant women recommended by WHO, iodine nutritional status is insufficient when the median UIC is less than 150 μg/l (mild deficiency, 100–150 μg/l; moderate and severe deficiency, <100 μg/l), adequate when the median UIC is between 150 and 249 μg/l, above requirements when the median UIC is between 250 and 499 μg/l, and excessive when the median UIC is above 500 μg/l[3]. Household table salt was classified into four groups: non-iodized salt with iodine content <5 mg/kg, inadequately iodized when between 5 and 21 mg/kg, adequately iodized when between 21 and 39 mg/kg, and excessively iodized when iodine content is >39 mg/kg.

Statistical analysis

Data were input in Microsoft Office Excel 2007 and data analysis was performed using the statistical software package SAS version 9.13. The Kolmogorov–Smirnov test was used to check for normality. Iodine content in table salt and UIC was summarized by median and interquartile range (IQR). The Kruskal–Wallis test was used to compare UIC between subgroups. Comparisons of iodine nutritional status between subgroups were done using the χ^2 test. $P < 0.05$ was considered to indicate a significant difference. Spearman correlation analysis was used to determine the relationship between gestational week, iodine content in table salt and UIC.

Results

A total of 2607 pregnant women participated in the study with a mean age of 28 (SD 5·26) years. Because twenty-seven of them (1·04 %) self-reported a history of thyroid disease, which mostly was hypothyroidism, the final sample size was 2580 participants. According to trimester of pregnancy, 15·35 % (*n* 396) of them were in the first trimester, 41·05 % (*n* 1059) were in the second trimester and 43·60 % (*n* 1125) were in the third trimester. UIC and salt iodine content values were non-normally distributed by the Kolmogorov–Smirnov test with *D* statistic of 0·1479 and 0·1432, respectively ($P < 0.01$).

The overall median UIC of the pregnant women was 171·80 μg/l (IQR = 113·85–247·00 μg/l); 40·97 % (*n* 1057) of the participants were iodine insufficient, of whom 47·30 % (*n* 500) were found to have mild deficiency and 52·70 % (*n* 557) to have moderate and severe deficiency. Among the others, 35·23 % (*n* 909) were iodine sufficient, 19·92 % (*n* 514) were above requirements and 3·88 % (*n* 100) were iodine excessive. The median iodine content of the table salt was 25·40 mg/kg (IQR = 23·10–28·30 mg/kg). Out of the 2580 participants who provided table salt samples, 0·27 % (*n* 7) were detected to be non-iodized salt and 99·73 % (*n* 2573) were iodized salt, but 5·23 % (*n* 135) and 1·24 % (*n* 32) of them were determined to be inadequately or excessively iodized, respectively. A large proportion of 93·26 % (*n* 2406) was found to be adequately iodized salt (Table 1). No association between iodine content in table salt and UIC was identified ($P = 0.176$).

Women in the first trimester had a significantly higher median UIC (189·70 μg/l) than those in the second and third trimester ($P < 0.01$). Multiple comparisons showed there was no statistical difference between UIC of participants in the second and third trimester ($Z = 1.69$, $P = 0.0898$). The median UIC was not statistically different among participants who provided different categories of table salt iodization using the Kruskal–Wallis test ($\chi^2 = 5.63$, $P = 0.1312$; Table 1).

A significant difference in iodine nutritional status was observed among the three trimesters of pregnancy ($\chi^2 = 17.25$, $P < 0.01$). The proportions of women in the first trimester who were iodine sufficient (39·14 %) or above requirements (26·01 %) were higher than those in the second (35·51 and 19·55 %) and third trimester (33·60 and 18·13 %). More women were found to be iodine insufficient in the third trimester (44·71 %) than in the first (31·06 %) and second trimester (40·70 %). Iodine status was not significantly different according to table salt iodization category ($\chi^2 = 4.77$, $P = 0.8537$; Table 2).

The median UIC of twenty-seven women who confirmed having a history of thyroid disease was 183·60 μg/l (IQR = 144·40–253·50 μg/l), one of them consumed non-iodized salt and the others (96·30 %) consumed adequately iodized salt. According to the WHO's criteria of UIC, 44·44 % (*n* 12) of them were iodine sufficient, 29·63 % (*n* 8) were iodine insufficient, 22·22 % (*n* 6) were above requirements and 3·70 % (*n* 1) was iodine excessive. Only 0·58 % (15/2607) of pregnant women investigated took iodine supplements; among them, eight women were previously diagnosed with hypothyroidism and reported taking Euthyrox, and the other seven did not confirm having thyroid disease. The median UIC of the fifteen women who reported having used iodine supplements was 117·20 μg/l (IQR = 77·30–213·90 μg/l), one of them consumed inadequately iodized salt and the others used adequately iodized salt. Half of them (53·33 %) were found to be iodine insufficient, about

Table 1 Urinary iodine concentration (UIC) according to trimester of pregnancy and table salt iodization category* of pregnant women (*n* 2607) in twenty-six districts/counties of Chongqing, China, 2017

Characteristic	*n*	%	UIC (μg/l) Median	UIC (μg/l) IQR	*P*
Trimester					<0·01
First trimester	396	15·35	189·70	132·65–262·60	
Second trimester	1059	41·05	171·90	115·30–247·40	
Third trimester	1125	43·60	163·00	108·90–239·50	
Table salt					0·1312
Non-iodized	7	0·27	88·50	32·20–202·50	
Inadequately iodized	135	5·23	162·20	96·10–247·40	
Adequately iodized	2406	93·26	172·00	114·30–247·00	
Excessively iodized	32	1·24	180·715	135·05–241·185	

IQR, interquartile range.
*Non-iodized, iodine content <5 mg/kg; inadequately iodized, iodine content 5–21 mg/kg; adequately iodized, iodine content 21–39 mg/kg; excessively iodized, iodine content >39 mg/kg.

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Table 2 Iodine status according to trimester of pregnancy and table salt iodization category* of pregnant women (*n* 2607) in twenty-six districts/counties of Chongqing, China, 2017

	Iodine insufficient		Iodine sufficient		Above requirements		Iodine excessive		
Characteristic	*n*	%	*n*	%	*n*	%	*n*	%	*P*
Trimester									<0·01
First trimester	123	31·06	155	39·14	103	26·01	15	3·79	
Second trimester	431	40·70	376	35·51	207	19·55	45	4·25	
Third trimester	503	44·71	378	33·60	204	18·13	40	3·56	
Table salt									0·8537
Non-iodized	5	71·43	1	14·29	1	14·29	0	0·00	
Inadequately iodized	58	42·96	46	34·07	26	19·26	5	3·70	
Adequately iodized	982	40·81	849	35·29	480	19·95	95	3·95	
Excessively iodized	12	37·50	13	40·63	7	21·88	0	0·00	

*Non-iodized, iodine content <5 mg/kg; inadequately iodized, iodine content 5–21 mg/kg; adequately iodized, iodine content 21–39 mg/kg; excessively iodized, iodine content >39 mg/kg.

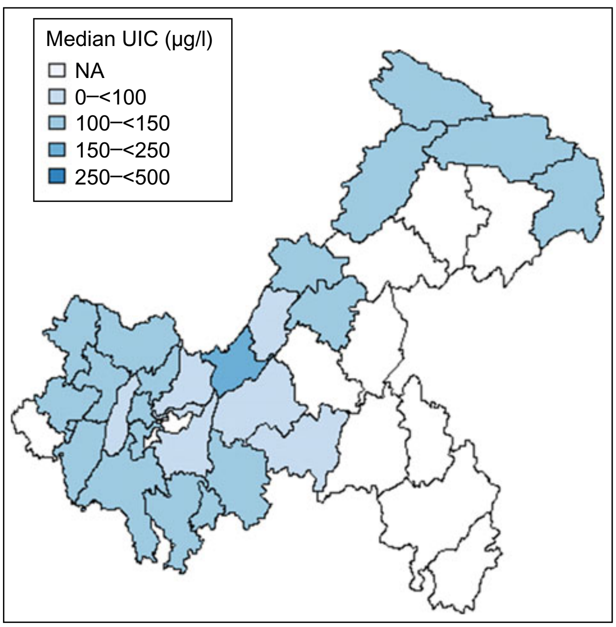

Fig. 1 (colour online) Distribution of median urinary iodine concentration (UIC) of pregnant women (*n* 2607) over twenty-six districts/counties of Chongqing, China, 2017 (NA, not investigated in this study)

one-third of them (33·33 %) were iodine sufficient and two (13·33 %) were above requirements.

Among the twenty-six districts/counties of Chongqing, participants from seven districts/counties had median UIC below 150 μg/l and one district had a median UIC of 277·40 μg/l, which were presumed to be iodine insufficient and above requirements, respectively; the median UIC of the other eighteen areas was in the optimal range of iodine sufficient. Dianjiang County had the lowest median UIC of 121·00 μg/l and Changshou District had the highest median UIC of 277·40 μg/l. The centre, west and majority of north-east areas were identified to be iodine sufficient with median UIC between 150 and 249 μg/l (Fig. 1). The median iodine content of table salt samples from all investigated locations was between 21 and 39 mg/kg, in accordance with the provincial standard of Chongqing.

Discussion

Chongqing has achieved the goal of elimination of IDD since 2010 through implementation of the national USI programme. Because China has set an option of 20, 25 or 35 mg/kg ± 30 % for the iodine concentration of iodized salt, each province had chosen the optimal level according to local monitoring data. Compared with other research in different provinces of China, the overall median UIC of pregnant women in Chongqing (171·90 μg/l) obtained in the present study is lower than that of Henan Province (204·20 μg/l in 2013 and 202·50 μg/l in 2014), but higher than in Zhejiang (130·47 μg/l) and Fujian Provinces (136·60 μg/l of Xiamen city), which did not meet the requirement level recommended by the WHO[14]. Zhejiang and Fujian had adopted the new provincial standard for iodized salt of 25 mg/kg in 2012 and then found pregnant women overall were iodine deficient in the following years[1,12]. Inadequate iodine intake in the two coastal provinces may be related to their lower provincial standard of iodized table salt. It has been found to be efficient to choose a higher level of iodine content in salt, like in Chongqing and Henan (both are inland provinces), to meet the iodine intake needs of pregnant women.

Chongqing is an inland municipality far from the coastline, so people living in Chongqing may have been consuming less seafood like saltwater fish and seaweed which are also sources of iodine in addition to iodized salt. A study conducted in 2013 showed that iodine concentration of drinking-water in Chongqing was 1·50 μg/l[4], indicating that the environment is universally lacking iodine according to the national criteria (Chinese Standard GB 16005-2009). In other places that have both coastal and inland areas, it was found that coastal residents had lower

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median UIC and lower percentage of iodized salt than the inland residents due to low consumption of iodized salt and easy access to sea salt without added iodine[1,15]. It has been found that the main dietary source of iodine of local inhabitants in the coastal regions[16] as well as in Chongqing is iodized table salt.

Trimester was identified to be statistically associated with UIC, with the lowest median UIC recorded in the third trimester and the highest median UIC in the first, consistent with similar studies conducted in Zhejiang Province, Switzerland, Iran and Japan[1,17–19]. Frequency distributions of iodine insufficiency were more frequently represented in the second or third trimester *v.* the first trimester of pregnancy. The decreasing UIC throughout pregnancy might be explained by increased renal iodine clearance during early gestation and increased iodine shift from the maternal circulation to the growing fetal–placental unit later on[17], as well as gradual decreased consumption of iodized salt in the second or third trimester because of increased oedema by gestational age[1]. The iodine status of pregnant women is important for fetal growth and neurodevelopment[20]. The results demonstrated that the USI programme in Chongqing as well as in other iodine-adequate areas[21] prevents iodine deficiency generally, but does not maintain iodine status within adequate and recommended ranges throughout pregnancy, and more efforts are needed to ensure adequate iodine intake during pregnancy besides the USI programme.

Despite the present results showing general iodine sufficiency, 40·85 % (*n* 1065) of participants were iodine insufficient. Especially among those using adequately iodized table salt, 40·81 % of them were still identified as iodine deficient, indicating that there was still a proportion of pregnant women with iodine insufficient status in some areas of Chongqing. Our study found no significant association between UIC of pregnant women and different iodine content in household table salt, which is different from other studies[11,12] and could be explained by the following two reasons. First, research has shown that iodized salt contributes 63·50 % of food iodine, but 24·60 % of this iodine is lost in cooking[16]. Second, because rates of some preventable, chronic and diet-related diseases have continued to rise over the past few decades, some authorities have provided guidelines for choosing a healthy diet in order to prevent these non-communicable diseases. The WHO recommends reducing salt intake to 5 g/person per d[22], the US Department of Health and Human Services and US Department of Agriculture have recommended consuming less than 2300 mg Na/d (equal to 5·8 g salt/d)[23], and China has set a criterion of 6 g salt/person per d by the Chinese Dietary Guidelines (version 2007 and 2016). Therefore, dietary salt consumption has declined among the whole population[24] in recent years, but a salt intake below 6 g/d in pregnancy may cause iodine deficiency in pregnant women because they may need more iodine intake during pregnancy.

Our study showed that the overall iodine status of pregnant women in Chongqing was sufficient, but regional difference still exists. A minority of districts/counties have been assessed as iodine deficient with adequately iodized table salt. Pregnant women in five districts and two suburban counties appeared to be iodine deficient and iodine sufficiency was found in the outer suburban districts and rural counties. This regional difference may be attributed to population-to-population variation in the consumption of iodized salt, which was a limitation not thoroughly investigated in the present study. High salt intake in the Chinese population in Chongqing has been found using 24 h urinary Na excretion in previous research, and people living in rural areas with lower educational levels had a higher salt intake and several unhealthy dietary habits[25]. This emphasizes that education plays an important role in public health for maintaining a healthy diet and lifestyle, which might explain the regional differences observed in our study.

According to the Chinese National Standard of IDD Elimination (GB 16006-2008), the rate of utilization of iodized salt at the household level (99·73 %) and the percentage of adequately iodized salt (93·51 %, 2406/2573) obtained in the present study satisfied the national standard (>95 % and >90 %, respectively). Only a small proportion of the table salt provided was detected to be non-iodized or inadequately/excessively iodized, indicating that non-iodized salt or unqualified iodized salt was indeed available on the market. At the beginning of introduction of USI, there was a mandatory implementation of selling only iodized salt on the market to the population in iodine-deficient areas through national legislation[26], but the salt monopoly has been relaxed after elimination of IDD had been achieved in Chongqing, as well as in other provinces in China[1,14]. From 1 January 2017, the state council initiated a reformation of the salt industry, cancelling the regional restrictions on production and marketing of household table salt. The existence of non-iodized or unqualified iodized salt on market shelves of Chongqing and the change in dietary habits of iodized salt use may present a substantial challenge to sustainably eliminate IDD.

There are some limitations in our research. First, a random spot urine sample was collected for testing, which might be affected by variability in daily water intake[27]. Some research has reported the creatinine-standardized urinary concentration instead of UIC so as to minimize the variation due to dilution and urine volume, which both vary depending on different factors of pregnancy[11,17,28]. So, median creatinine-standardized UIC might be more reliable to assess iodine nutrition in pregnancy. Second, we did not further investigate the dietary iodine sources of these pregnant women. Our study showed that only 0·58 % of pregnant women took iodine supplements, far less than in Zhejiang Province (5 %)[1] and in other countries with official suggestion of taking iodine

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supplements[29]. Similar research showed that dietary factors such as use of iodine supplements and intake of dairy products were significantly associated with UIC[27,28,30,31]. Further studies should collect the dietary data of pregnant women in order to analyse the association between iodine status and dietary factors besides iodized salt intake.

Conclusion

In conclusion, iodine deficiency was found in 40·97 % of pregnant women living in Chongqing with low iodine content in drinking-water. The daily diet including iodized table salt of pregnant women does not secure a sufficient iodine intake. There is an urgent need to provide evidence-based recommendations on ensuring adequate iodine nutrition in pregnancy.

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