

Control of Iodine Deficiency Disorders Following 10-Year Universal Salt Iodization in Hebei Province of China

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Objective To evaluate the effectiveness of universal salt iodization (USI) for the control of IDD in Hebei province since it was implemented in 1995, identify the problems currently encountered in the implementation of USI and provide practical proposals for addressing these problems. **Methods** Probability proportionate to size sampling (PPS) was employed in the surveillance of IDD, for which a total of 1200 school children aged 8-10 years were randomly selected from 30 counties around the whole province during each IDD survey. The iodine content of salt was determined quantitatively with the titration method. The iodine content of urinary samples was measured by the method of ammonium persulfate oxidation. **Results** The coverage of iodized salt increased from 65.0% in 1995 to 98.0% in 1999, then decreased to 88.1% in 2005 which was below the national standard of 90%. The median urinary iodine of children aged 8-10 years varied between 160.1 µg/L and 307.4 µg/L, which was above the national standard. The proportion of urinary samples with iodine content above 300 µg/L was over 30% in 2005, implying exorbitant iodine nutrition among the children. The goiter rate (TGR) among children aged 8-10 years dropped from 11.8% in 1995 to 2.7% in 2005, indicating that the spread of endemic goiter was under control. **Conclusion** Preliminary elimination of IDD was achieved by USI in Hebei province. Nevertheless, some problems still existed in USI such as non-iodized salt competition, over iodization and un-standardized iodization. In order to address these problems, the management and supervision of salt market needs to be strengthened to prevent non-iodized salt from reaching households; updating equipment and modifying techniques are also necessary to ensure the quality of iodized salt; to clarify the causes of excessive urinary iodine content, the various sources of iodine from the diet need to be investigated in the future.

Key words: Iodine deficiency disorders (IDD); Universal salt iodization (USI); Assessment; Effectiveness

INTRODUCTION

Iodine deficiency disorder (IDD), a major international public health problem, is the commonest preventable cause of brain damage in the world. More than 2 billion people are at risk to iodine deficiency in the world, unevenly distributed in 130 countries^[1]. Universal salt iodization (USI), which is defined as all salt for human and animal consumption iodized to the adequate levels, is the main strategy to control iodine deficiency worldwide recommended by WHO^[2]. It is now well recognized that the most effective way to achieve virtual elimination of IDD is through USI.

Due to the long lasting iodine deficiency in the environment, IDD cannot be eradicated once for all. To maintain sustainable elimination of IDD, iodine must be provided permanently to populations living

in an iodine deficient environment. Assessment and monitoring system plays a fundamental and crucial role in the sustainable control of IDD. Measurements of salt and urinary iodine provide the essential elements for monitoring whether IDD is successfully eliminated. Additional contributive measurement is estimation of thyroid size.

Hebei province is one of the provinces in China where IDD used to seriously prevail in the past. Based on the new national criteria for the classification of endemic areas, 165 counties were classified as iodine deficient areas, accounting for 95.9% of the total counties. By the end of 1995, there were over 190 000 endemic goiters and 15 000 cases of endemic cretinism^[3].

Since the implementation of USI in Hebei province in 1995, a monitoring system has been established to assess the effectiveness of IDD control

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through regular surveillance of IDD every 2 or 3 years across the whole province. The baseline survey on IDD in the province was conducted in 1995 before the implementation of USI^[4]. The latest survey on IDD was carried out in 2005, i.e. 10 years after the implementation of USI. The effectiveness of IDD control in Hebei province was assessed every 2 or 3 years through the regular surveillance. However, so far, an overall evaluation of the effectiveness of USI for IDD control has not been performed in this province.

In this study, the major indicators of the effectiveness of IDD control in 1995-2005 were compared in Hebei province. It will lay a foundation for IDD control and minor adjustment to the IDD control strategy in Hebei province or in other parts of China facing similar problems in the control of IDD.

MATERIALS AND METHODS

Sampling Method

A cluster sampling technique, probability proportional to size sampling (PPS)^[5], was employed in this cross-sectional survey. PPS sampling is commonly used in multistage cluster sampling, in which the probability that a particular sampling unit is selected in the sample is proportional to the population size of the sampling unit. The steps of using PPS in a multistage cluster sample are to create a list of all clusters with cumulative population size, to divide the total cumulative population size by the number of clusters to be selected to obtain the sampling interval, to choose a random number between one and the sampling interval, to select the first cluster by determining in which cluster this random number lies and subsequent clusters by adding the sampling interval to the random number, then to the result of this number until all clusters are selected.

The sampling unit was a county, and the cluster was a town where 40 children aged 8-10 years were randomly selected from local primary schools. There were 30 clusters with a sample size of 1 200. No less than 1 200 children aged 8-10 years were randomly selected during each survey conducted in 1995-2005. Edible salt samples were collected from children's households. The size of their thyroids was measured by palpation. Three hundred and sixty urinary specimens randomly selected from the 1 200 participants were collected on the spot.

Measurement of Salt Iodine

Iodine content in salt was measured by liberating iodine from salt and titrating the iodine with sodium thiosulphate using starch as an external indicator^[6] (ICCIDD/UNICEF/WHO, 2001).

Criteria for Iodizing Salt

Based on WHO's recommendation and the specific conditions in China, the current national standard for salt iodization is 35±15 mg/kg at all levels from production to households. To consolidate the sustainable elimination of IDD, availability and consumption of adequately iodized salt (35±ppm iodine) must be guaranteed. The coverage of adequately iodized salt at the household level should be more than 90%^[7].

Measurement of Urinary Iodine

The content in urinary samples was measured by ammonium persulfate oxidation. Small samples of urine (250-500 µL) were digested with ammonium persulfate at 90-110 °C. Arsenious acid and ceric ammonium sulphate were then added. The decreased yellow colour over a fixed time was detected with a spectrometer and a standard curve was plotted with a known amount of iodine^[8].

Criteria for Assessing Iodine Nutritional Status

Because over 90% of ingested iodine is excreted in the urine, urinary iodine (UI) is an excellent biomedical indicator of recent iodine intake. Urinary iodine values from populations are usually not normally distributed. Therefore, the median rather than the mean should be used as the measure of central tendency. Likewise, percentiles rather than standard deviations should be used as measures of deviation. A median urinary iodine concentration of 100 µg/L and above defines a population which is free from iodine deficiency, i.e. at least 50% of the sample should be above 100 µg/L. In addition, not more than 20% of samples should be below 50 µg/L^[9]. The criteria for assessing iodine status provided by WHO are illustrated in Table 1.

TABLE 1

Epidemiological Criteria for Assessing Iodine Nutrition Based on Median Urinary Iodine Concentrations in School-aged Children

Median UI (µg/L)	Iodine Intake	Iodine Nutrition
<20	Insufficient	Severe Iodine Deficiency
20-49	Insufficient	Moderate Iodine Deficiency
50-99	Insufficient	Mild Iodine Deficiency
100-199	Adequate	Optimal
200-299	More Than Adequate	Risk of Iodine-induced Hyperthyroidism
>300	Excessive	Risk of Adverse Health Consequences

Note. Resource: WHO/UNICEF/ICCIDD, 1994.

Thyroid Size by Palpation

Assessment of thyroid size by palpation is the time-honored method of assessing the prevalence of endemic goiter. A thyroid gland is considered goitrous when each lateral lobe has a volume greater than the terminal phalanx of the thumbs of the subject being examined^[10]. The classification of goiter grade is shown in Table 2.

TABLE 2

Simplified Classification of Goitre by Palpation

Grade	Description
Grade 0	No palpable or visible goitre.
Grade 1	A goitre that is <i>palpable but not visible</i> when the neck is in the normal position, the thyroid is not visibly enlarged. Thyroid nodules in a thyroid which is otherwise not enlarged fall into this category.
Grade 2	A swelling in the neck that is clearly visible when the neck is in a normal position and is consistent with an enlarged thyroid when the neck is palpated.

Note. Resource: WHO/UNICEF/ICCIDD, 1994.

It is recommended that a total goitre rate or TGR (number of goitres of grades 1 and 2/total examined) of 5% or more in school children at the age of 6-12 years is used to signal the presence of a public health problem^[10].

To assure the quality of palpation in these surveys, all school children were examined by a senior professional examiner and the goiter was diagnosed by two experienced examiners.

RESULTS

Iodine Content in Edible Salt at the Household Level

The number of edible salt samples collected

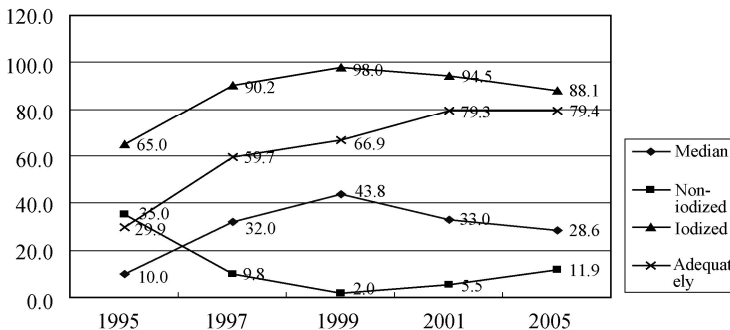


Fig. 1. Iodine content in edible salt of Hebei province from 1995 to 2005.

Salt Iodization Status at the Household Level

The median of iodine content in iodized salt samples was 19.5 mg/kg in 1995 and 44.3 mg/kg in 1999. The mean of iodine content followed the same

pattern as the median, with a lowest value in 1995 and a highest value in 1999. The maximal coefficient of variance (CV) was 76.2% in 1995, implying a high deviation of iodine content in the iodized salt. The CV value decreased to

from local households and tested in laboratories by titration in 1995, 1997, 1999, 2001, and 2005 was 1 191, 1 200, 1 200, 1 134, and 1 200, respectively. The median salt iodine concentration in these samples was 10.0, 32.0, 43.8, 33.0, and 28.6 mg/kg, in 1995-2005, respectively. Different numbers of edible salt samples was calculated as non-iodized salt with an iodine concentration below 5 mg/kg, with a non-iodized rate fluctuating from 2.0% to 35.0%. The rate of non-iodized salt in 1995 and 2005 was 35.0% and 11.9%, respectively, which was higher than the national standard (10%), while the rate of non-iodized salt in the remaining 3 years was less than 10%. The lowest coverage rate of iodized salt in 1995 was 65.0%, whereas the highest coverage of iodized salt in 1999 was 98%.

TABLE 3

Iodine Content in Edible Salt of Hebei Province from 1995 to 2005

Year	Salt Samples	Iodine Median	Non-Iodized (%)	Iodized Salt (%)	Adequately Iodized (%)
1995	1 191	10.0	417 (35.0)	774 (65.0)	356 (29.9)
1997	1 200	32.0	118 (9.8)	1 082 (90.2)	716 (59.7)
1999	1 200	43.8	24 (2.0)	1 176 (98.0)	803 (66.9)
2001	1 200	33.0	66 (5.5)	1 134 (94.5)	952 (79.3)
2005	1 200	28.6	143 (11.9)	1 057 (88.1)	953 (79.4)

46.3% in 1997, indicating that the deviation of iodine content has become smaller. The CVs ranged

between 34.4% and 37.0% in 1999-2005, indicating more standardized iodization.

TABLE 4

Salt iodization in Hebei Province from 1995 to 2005

Year	Iodized Samples	Median	Mean ±SD	CV (%)	Frequency Distribution (mg/kg, %)			
					5~	20~	35~	>50
1995	774	19.5	21.8±16.6	76.2	50.3	36.7	9.3	3.7
1997	1 082	35.0	36.7±17.0	46.3	13.6	35.8	28.2	22.4
1999	1 176	44.3	43.3±14.9	34.4	3.3	25.7	42.5	28.4
2001	1 124	34.0	36.7±13.4	36.5	2.3	49.2	37.4	11.1
2005	1 057	29.6	28.9±10.7	37.0	9.6	79.3	10.8	0.3

TABLE 5

Urinary Iodine Status in Children Aged 8-10 Years in Hebei Province from 1995 to 2005

Year	Urinary Samples	Median (ug/L)	Frequency Distribution (ug/L, %)					
			<20	20-49	50-99	100-199	200-299	>300
1995	360	160.1	3.9	8.6	14.4	34.2	16.7	22.2
1997	339	276.0	1.5	4.7	11.5	14.7	21.8	45.7
1999	1 200	307.4	0.5	3.4	8.5	18.4	17.6	51.6
2001	355	258.0	0.6	3.4	7.6	23.9	23.4	41.1
2005	362	212.3	0.3	4.4	9.9	30.7	24.6	30.1

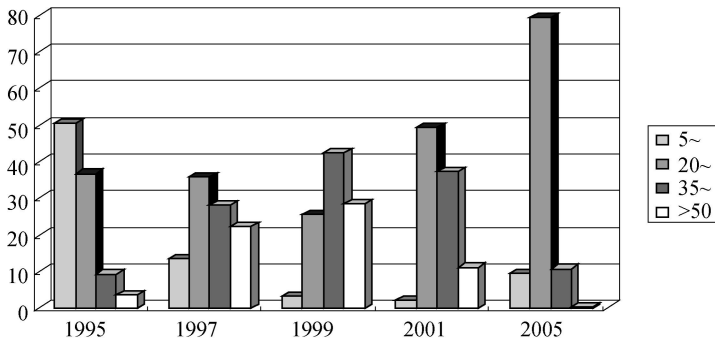


FIG. 2. Frequency distribution of iodine content in iodized salt in Hebei province from 1995 to 2005.

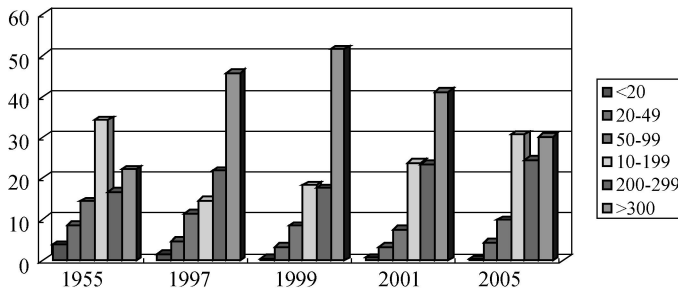


FIG. 3. Frequency distribution of urinary iodine content in children aged 8-10 years in Hebei province.

The proportion of inadequately iodized salt was 50.3% in 1995, showing remarkably inadequate

iodization. In 1997, The proportion of samples with an inadequate iodine content decreased to 13.6% in

1997, 2%-3% in 1999 and 2001, and increased to 9.6% in 2005. The frequency of salt samples with an iodine content of 20-50 mg/kg was increased to 46.0% in 1995 and 90.2% in 2005. The proportion of salt samples with an iodine content over 50 mg/kg in 1997 and 1999 was more than 20%, indicating over iodization (Table 4, Fig. 2).

Urinary Iodine Content of Children Aged 8-10 Years

The number of urinary specimens collected on the spot and measured in laboratories in 1995, 1997, 1999, 2001, and 2005 was 360, 339, 1200, 355, and 362, respectively. The median of urinary iodine in these samples from 1995 to 2005 was 160.1, 276.0, 307.4, 258.0, and 212.3 $\mu\text{g/L}$, respectively.

The distribution patterns of urinary iodine content could be classified into 2 types in general. The first pattern is characterized by the highest frequency of the interval (100-200 $\mu\text{g/L}$) in 1995 and 2005, with a respective proportion of 34.2% and 30.7%. The second distribution pattern is characterized by the highest frequency at the interval, over 300 $\mu\text{g/L}$ in 1997, 1999, and 2001, accounting for 45.7%, 51.6%, and 41.1%, respectively. The frequency at the interval less than 50 $\mu\text{g/L}$ was the highest in 1995 (12.5%). The frequency at the interval over 300 $\mu\text{g/L}$ was the highest in 1999 (51.6%), as shown in Table 5 and Fig. 3.

Thyroid Goiter Status in Children Aged 8-10 Years

A total number of 1200 children aged 8-10 years were examined by palpation during each IDD survey. The number of grade one goitrous cases identified during the survey from 1995 to 2005 was 137, 79, 60, 37, 31, respectively, while the number of grade two goitrous cases was 7, 6, 5, 1, 2, respectively. The total goiter rate (TGR) was decreased to 11.8% in 1995 and 2.7% in 2005. TGR in 1995, 1997, and 1999 was 11.8%, 7.1%, 5.4%, respectively, 5% higher than the national standard, and was 3.2% and 2.7%, respectively, in 2001 and 2005, 5% lower than the national standard (Table 6, Fig. 4).

TABLE 6

Goiter Status in Children Aged 8-10 Years in Hebei Province from 1995 to 2005					
Year	Subjects	1°GR	2°GR	TGR	95% CI (%)
1995	1 200	135	7	11.8%	9.8-14.5
1997	1 200	79	6	7.1%	5.5-9.3
1999	1 200	60	5	5.4%	4.1-7.4
2001	1 200	37	1	3.2%	2.2-4.8
2005	1 200	31	2	2.7%	1.8-4.4

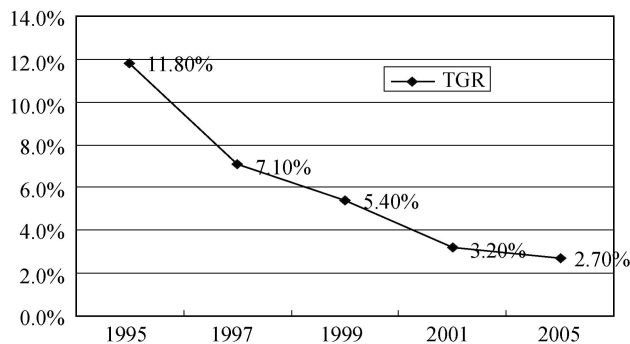


FIG. 4. TGR of children aged 8-10 years in Hebei province from 1995 to 2005.

Among the different age groups of children, TGR increased with age in 1995, 1997, 1999, and 2005, except in 2001. No significant difference was found in TGR among the children aged 8-10 years in the four years, except in 1999.

In 1999, TGR was higher in children aged 10 years than in those aged 8 and 9 years ($\chi^2=8.2$, $P<0.05$). In 1995, there was no significant difference in TGR among age groups in general. However, TGR was significantly lower in children at the age of 8 years than in those at the age of 9 ($\chi^2=4.7$, $P<0.05$) and 10 years ($\chi^2=4.8$, $P<0.05$).

TGR in male and female students was rather close in all years, with no significant difference in gender (Table 7).

DISCUSSION

Coverage of Iodized Salt at Household Level

The coverage rate of iodized salt at the household level in 1995 was much lower than in the other 4 years. This was mainly due to the fact that USI was implemented in 1995 in Hebei province, and did not cover the whole province until the end of that year^[11].

TABLE 7

TGR among Age Groups and Gender of Children Aged 8-10 Years in Hebei Province

Year Age	8 Years		9 Years		10 Years		Male		Female	
	No.	%	No.	%	No.	%	No.	%	No.	%
1995	13	6.9	58	12.8	71	12.7	68	10.8	74	13.0
1997	17	5.7	22	5.9	45	8.8	35	6.0	50	8.1
1999	10	3.1	17	4.6	38	7.5	34	5.6	31	5.2
2001	12	3.5	10	2.3	16	3.8	14	2.3	24	4.0
2005	5	1.4	12	2.9	16	3.8	14	2.3	19	3.5

There were four major factors that had led to the remarkably lower coverage rate of adequately iodized salt in the five surveys. The first factor was the competition of non-iodized salt, as a large amount of non-iodized salt was found in the 1995, 1997, and 2005 surveys. The second factor was the different criteria applied in the iodization at the production level during the implementation of USI in China, since there was no upper limit for the addition of iodine to the salt in 1995^[12], and the upper limit was set at 60 mg/kg in 1996^[13], which was decreased to 50 mg/kg in 2000 and had come into effect since then^[14]. Therefore, when judged with more strict standard currently used, the coverage of adequately iodized salt was decreased considerably. The third factor was the insufficient amount of iodine added to edible salt at the point of production. The last factor was the iodine loss during transportation and storage under inappropriate conditions^[15].

The current major problem in the supply of iodized salt is the competition of non-iodized salt and inadequate iodization, as demonstrated in 2005. The coverage of non-iodized salt and inadequately iodized salt reached 11.9% and 8.4%, respectively, resulting in the lower coverage of adequately iodized salt at the household level.

Iodization Status in Iodized Salt

The two major problems in the iodization of edible salt identified in the 1995 survey were un-standardized iodization and inadequate iodization as demonstrated by the higher coefficient of variance and large portion of iodized salt with iodine content between 5 and 20 mg/kg.

In 1997, a new problem of over iodization was demonstrated by a high proportion of iodized salt with an iodine content over 50 mg/kg, which became prominent till 1999. This problem was controlled after the upper limit of iodization was fixed at 50 mg/kg in 2000, as indicated by the dramatically decreased percentage of edible salt samples with an

iodine content above 50 mg/kg in 2001 which was further decreased to 0.3% in 2005.

The problem of un-standardized iodization was greatly improved in 1999, but remained in 2001-2005 when compared with other provinces in China where CV decreased to 20%^[13]. This problem was mainly caused by inappropriate processing techniques and out-of-date equipment which need to be improved for better performance^[4].

In general, adequate iodization, which is crucial to the control of IDD, was dramatically improved in 1995-2005, and the proportion of iodized salt samples with 20-50 mg/kg reached 90.2% in 2005.

Urinary Iodine Status in Children Aged 8-10 Years

In terms of median urinary iodine and the proportion of urinary samples with an iodine content less than 50 ug/L, the results of the 5 surveys met the national standards. This was mainly due to the fact that an appropriate urinary iodine level was achieved under incomplete USI in 1995, which could be associated with the use of other forms of iodine supplement, such as iodized oil. Before 1997, iodized oil was widely applied in the control of IDD in Hebei province, especially in remote rural areas with poor transportation.

Iodine plethora was the major problem in the iodine nutrition of children aged 8-10 years, which was consistent with the over iodization of salt from 1995 to 2000 when the upper limit of iodine content in iodized salt was too high, indicating that over iodization was an important cause for iodine plethora among children aged 8-10 years^[13]. On the contrary, after the upper limit of iodization was decreased to 50 mg/kg in 2000, the median urinary iodine and the proportion of urinary samples with an iodine content exceeding 300 ug/L was significantly decreased in 2001, which lasted till 2005. However, although over iodization was contained in 2005, the proportion of urinary samples with an iodine content exceeding 300 ug/L remained high, indicating that it might be due to other factors. One possible cause for excessive urinary iodine content was the wide distribution of underground drinking water with a high content of iodine in Hebei province^[16]. There are 173 townships located in 33 counties within the province with an iodine content in underground drinking water exceeding 150 ug/L. The median urinary iodine in children aged 8-10 years living in these regions has reached 418.8 ug/L, almost 2 times the average level of 212.3 ug/L in the whole province^[15]. Since some of these areas are included in the sampling of IDD surveys, the excessive iodine in drinking water might have aggravated the iodine plethora in these areas. Since iodine intake of human body mainly comes

from the diet, to clarify the causes for an excessive urinary iodine content, various sources of iodine from the diet need to be investigated in the future.

No significant difference was found in the urinary iodine content among different age groups and genders, which is consistent with the reported findings in China^[12].

Goiter Status by Palpation

The higher prevalence of goiter among children aged 8-10 years found in the IDD survey in 1995 might be due to the lack of adequately iodized salt supply, as the coverage of non-iodized salt and inadequately iodized salt was very high in 1995. By 1997, their proportions were decreased to 9.8% and 12.2%, respectively, while TGR was decreased to 11.8% in 1995 and to 7.1% in 1997. By 1999, with a further decrease in the coverage of non-iodized salt and inadequately iodized salt, TGR of children aged 8-10 years was dropped to 5.4%, which was higher than the national standard (5%). In 2001 and 2005, it was lower than the national standard (5%), indicating that the prevalence of IDD was under control. This correlation between iodized salt and goiter rate has been reported in other provinces of China^[13], highlighting that USI plays a crucial role in the effective control of IDD.

There was a discrepancy between urinary iodine content and goitre rate in the early years of USI implementation. When the median urinary iodine concentration reached a very high level in 1997 and 1999, TGR of children aged 8-10 years was still higher than the criteria (5%).

Urinary iodine content well reflects the recent iodine intake of the human body, and varies sensitively with the fluctuation of iodine intake in a short term. Development of goiter is a chronic process which usually takes more than half a year or even longer. Likewise, lysis of goitre also needs a long time after iodine supplement by iodized salt, which is probably the main reason for the discrepancy between urinary iodine and TGR. By 2001, this discrepancy disappeared, which might add more credit to the above explanation.

Differences in TGR among age groups in this study have also been proved by other researches. Since the thyroid gland grows with the age of children, it becomes easier to be palpated. Goitre rate is higher in girls than in boys in this province, which is consistent with the reported findings^[13]. It may be due to earlier body development of girls.

CONCLUSION

After 10 years of USI implementation in Hebei

province, a number of remarkable achievements in control of IDD have been made. By 2000, the goal of preliminary elimination of IDD was fulfilled. Nevertheless, some problems identified in USI need to be addressed in order to completely eliminate IDD.

Major Achievements

The coverage of iodized salt at the household level was increased from 65.0% in 1995 to 90.2% in 1997, and has remained above 90% since then, except in 2005. The coverage of adequately iodized salt increased steadily from 29.9% in 1995 to 79.4% in 2005, which was close to 90% of the national standard.

The quality of iodized salt has been greatly improved. The proportion of eligible iodized salt increased from 46.0% in 1995 to 90.2% in 2005. The standardized iodization has been enhanced dramatically and the CV of iodized salt was decreased from 75.9% in 1995 to 37.0% in 2005.

The iodine nutrition status in children aged 8-10 years has been maintained at a more appropriate level. The median urinary iodine in children aged 8-10 years has been within the range of 100-300 ug/L, and the proportion of urinary samples with an iodine content less than 50 ug/L has been less than 5% since 1999.

The prevalence of endemic goitre has been under control. TGR of children aged 8-10 years was declined from 11.8% in 1995 to 2.7% in 2005, which is 5% lower than the national criterion.

Problems Need to be Addressed

The coverage of non-iodized salt at the household level remains very high, which rebounded to 11.9% in 2005. The coverage of adequately iodized salt at the household level fails to reach 90% of the national standard.

There are 3 major problems in the salt iodization: namely, the inadequately iodized salt which still accounts for 9.6%, and the un-standardized iodization and over iodization persisting with the CV of iodized salt reaching 37.0%.

Iodine plethora is the prominent problem concerning the urinary iodine status which might be caused by over iodization and iodine in drinking water in some areas in Hebei province.

RECOMMENDATIONS

Based on the current problems identified in the implementation of USI in Hebei province, the following recommendations are proposed.

In order to produce eligible iodized salt, the salt industry should place greater investment in updating

equipment and techniques, and intensify internal monitoring and management of the quality of iodized salt.

To handle the issue of non-iodized salt overflow, commercial departments should enhance the management and monitoring of salt markets, so as to prevent the use of non-iodized salt in households.

In order to clarify the causes of excessive urinary iodine content, various sources of iodine from the diet need to be investigated in the future.

The health sector should strengthen regular monitoring and surveillance of iodized salt and IDD in order to provide valuable feedback of the implementation of USI to relevant sectors, so as to take necessary actions. Those areas with excessive iodine content should be excluded in sampling for IDD survey.

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